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Laparoscopic Surgery for Rectal Cancer: Outcomes in 513 Patients

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Abstract

Background Few reports have demonstrated the feasibility and efficacy of laparoscopic resection in patients with rectal cancer (RC). The objective of the present study was to assess the effectiveness of laparoscopic resection for RC, with an emphasis on perioperative variables and long-term oncological outcomes.

Methods This prospective study was carried out between January 2005 and September 2010 and included 513 patients diagnosed with RC who underwent laparoscopic surgery. Patients with locally advanced RC (cT3/cT4 or N+) received neoadjuvant treatment. Adjuvant treatment was applied to patients with stage II/III disease or according to the neoadjuvant protocol. All patients were followed-up prospectively for the evaluation of complications and oncological outcome. Survival rate analysis was performed using the Kaplan–Meier method.

Results Sphincter-preserving surgery was performed on 389 patients, and the remaining 124 patients underwent abdominoperineal resection. Perioperative mortality occurred in only one patient (0.2 %), and 27 (5.3 %) intraoperative complications were recorded. The most common postoperative complication was anastomotic leakage (5.5 %). The conversion rate was 6.4 %. The mean number of harvested lymph nodes was 23.6 ± 13. The mean distance to the distal margin was 2.6 ± 1.9 (0–7) cm. Distal margin positivity was detected in 9 (1.7 %) patients. The circumferential margin was positive in 39 (7.6 %) cases. After a median follow-up period of 30 (1–78) months, recurrence occurred in a total of 59 patients (11.5 %). Local recurrence was detected in 16 patients (3.1 %), and both local and distant recurrence was found in 7 patients (1.4 %). Distant recurrence only was detected in 43 patients (8.4 %). The overall 5-year survival rate was 84 %, and the 5-year disease-free survival rate was 77.4 %. The local recurrence-free survival rate was 98.4 % at 2 years, 95.7 % at 3 years, and 94.3 % at 5 years.

Conclusions Our results, together with the review of the literature, clearly demonstrate that laparoscopic resection for RC is a feasible method at specialized high-volume centers. The long-term outcomes are at least as good as those from open surgery as long as the principles of oncologic surgery are respected and faithfully performed.

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Introduction

For rectal cancer (RC), laparoscopic surgery has been reported to achieve better short-term outcomes than open surgery, including earlier postoperative recovery, less postoperative morbidity, and a better quality of life [1–3]. According to the numerous studies in the current literature, laparoscopic colon cancer (CC) surgery is accepted to have similar results when compared with open CC surgery, in terms of oncological outcomes, recurrence, and survival rates. However, this judgment has not yet been clearly demonstrated for laparoscopic RC surgery. Even though laparoscopy is now widely employed for RC surgery in daily practice, the efficacy of laparoscopy for RC remains controversial because of the lack of data concerning long-term oncological outcomes. Laparoscopic resection of the rectum is a technically demanding procedure because the surgical space is surrounded by the narrow bony pelvic cavity, because the laparoscopic instruments have technical limitations, and because learning to perform such resections safely is a long process that requires continuous training [4]. The purpose of this prospectively conducted study was to record the perioperative and follow-up results of 513 patients who underwent laparoscopic RC resections in our department, with an emphasis on complications and long-term oncological outcomes. Our goal was to compare our results with other recent studies to investigate the feasibility and oncological quality of laparoscopic resections for RC in a high-volume single center.

Methods

In total, 1,300 laparoscopic colorectal surgeries were performed at Istanbul University, Istanbul Faculty of Medicine, Department of General Surgery between January 2002 and September 2010. In our institution, laparoscopic colorectal surgery was started in 2002 for the treatment of benign colorectal diseases, such as diverticulitis, endoscopically unremovable polyps, rectal prolapse, and inflammatory bowel disease. We then moved our practice to laparoscopic CC surgery, and after gaining adequate experience, in 2005 we started to perform laparoscopic RC surgery. The operations were performed by seven senior surgeons who were experienced with both colorectal and laparoscopic surgery; each surgeon annually performs a minimum of 15 RC cases. Laparoscopic RC surgery has been offered to all patients requiring resection since 2005. Between 2005 and 2010, 116 patients underwent open surgery because of patient preference or previous major abdominal surgery (gastric surgery, colon resection, etc.). A subgroup of 513 RC patients were treated laparoscopically, and it is these patients who constitute the subjects of the present study. An additional 18 patients were treated by laparoscopic total mesorectal excision (TME) with the diagnosis of endoscopically unremovable large sessile rectal polyps. Five of them had carcinoma in situ (Tis) and those five were included in the study group of 513 RC cases according to TNM 2010 classification. Approval for this study was obtained from the local Ethics Committee of Istanbul University, Istanbul Faculty of Medicine.

The data had been collected prospectively and were analyzed retrospectively with a computer-based program. Following the declaration of the definitive diagnosis, a laparoscopic approach was offered to all patients. The decision for laparoscopic surgery was reached mutually by the surgeon and the patient. The exclusion criteria were emergency surgical cases (patients with ileus) and inoperable cases as determined via preoperative imaging studies and other diagnostic methods. Inoperable cases were determined to be patients in stage cT4b, presence of sacrum invasion, prostate invasion, the need of a pelvic composite resection, and pelvic exenteration. For stage cT4b tumors, long course neoadjuvant therapy was carried out for circumferential margin (CRM) positivity. Signed informed consents were obtained from the patients prior to operation.

Preoperative evaluation

All patients were carefully assessed preoperatively. The preoperative evaluation and staging included a physical examination, a complete blood count and assessment of biochemical parameters, a chest X-ray, an assessment of carcinoembryonic antigen (CEA) levels, abdominal computed tomography (CT), pelvic-phased array magnetic resonance imaging (MRI), and/or endorectal ultrasound. All patients were evaluated with a rigid rectoscope for exact tumor localization. A total colonic examination was performed in each case to detect the presence of synchronous lesions by use of either the flexible or virtual colonoscopic technique. The tumors were classified into one of three groups according to their localization from the anal verge as follows: distal (0–5 cm), middle (6–10 cm), or proximal (11–15 cm). Patients who were clinically diagnosed as T3 or T4, as well as any lymph node positive middle and distal RC patients, were treated with either neoadjuvant long-course chemoradiotherapy [45–50.4 Gy pelvic irradiation with concomitant 5-fluorouracil (5-FU) and leucoverin (FUFA)], or short-course radiotherapy (25 Gy pelvic irradiation). Short-course radiotherapy was preferred in a selected group of patients without any risk of lateral margin positivity. The waiting period was 4–8 weeks for long course radiotherapy, and 1–3 weeks for short course radiotherapy. After operation, all patients who were treated by a neoadjuvant protocol diagnosed with pT3, and/or any N positivity were treated with four courses of FUFA. Stage IV patients were treated with metastatic chemotherapy regimens with or without short course radiotherapy for middle and distal RC. Bowel preparation was carried out by the administration of both oral and rectal sodium phosphate preparations the day before surgery. All patients received preoperative antibiotic prophylaxis as a combination of single doses of 1.5 g cefuroxime axetil and 500 mg metronidazole administered intravenously. Prophylaxis for deep vein thrombosis was carried out via the administration of low molecular weight heparin and the application of anti-embolic stockings. According to the protocol of our department, this prophylaxis was continued until the end of the 30th day after discharge.

Surgical technique

At our institution, we used the straight laparoscopic technique with four trocars ranging in size from 5 to 15 mm. When necessary, one or two additional trocars were inserted according to the surgeon's preference and the patient's anatomy. During surgery, the basic dissection and divisions were performed with monopolar scissors, an ultrasonic dissection device (Ultracision Harmonic Scalpel Ethicon, Cincinnati, OH), or a bipolar vessel-sealing device (LigaSure, ValleyLab, Inc., Boulder, CO).

Partial or total mesorectal excision was performed depending on the tumor's location. The dissection was always performed from right to left. For proximal cancers, the mesorectum and the rectum were divided perpendicularly 5 cm below the tumor, and a partial mesorectal excision was performed. For middle and distal tumors, TME was performed. Sphincter-preserving surgery was performed mostly with a double-stapling technique. The rectum was divided by the use of a 45 or 60 mm endostapling device inserted through the right lower quadrant trocar or, occasionally, through the suprapubic trocar. The specimen was removed through a small suprapubic (Pfannenstiel) incision after placement of a wound protector. The length of this incision depended on the tumor size. Colorectal anastomosis was performed under laparoscopic control through the use of a circular stapling device with a diameter of 28, 29, 31, or 33 mm. A protective loop ileostomy was created according to the surgeon's preference. In patients with very low localized RC, after the completion of the pelvic dissection, the specimen was removed transanally; hand-sewn colo-anal anastomosis was then performed to accomplish a partial intersphincteric resection. In patients undergoing an abdominoperineal resection (APR), the specimen was extracted through the perineal incision, and a suction drain was generally placed through the right lower quadrant port site into the pelvis.

The operative time was measured from the first skin incision and ended at the application of wound dressings as the final phase of the operation. The conversion criterion was defined as enlargement of the wounds for mobilization and or securing the vascular pedicle. All intraoperative complications were recorded during the procedure, such as bleeding, injury to any visceral organ, trocar complications, and staple complications.

Postoperative period

Postoperative complications were assessed daily in the hospital and during regular office visits during the follow-up. Respiratory/cardiovascular/urinary complications, wound infection, anastomotic leakage, trocar site hernias, postoperative ileus, stomal problems, intra-abdominal abscess formation, and secondary admission were evaluated in two groups as either early or late-term complications. An anastomotic leak was defined according to the criteria of the Cleveland Clinic [5]. The patients were monitored for clinical evidence of anastomotic leakage with the presence of any of the following: fecal fistula to the wound, drain, tract, or vagina; and/or pelvic sepsis documented by radiological imaging. Postoperative complications were graded according to the Clavien–Dindo classification [6].

Operative mortality was defined as any death occurring during the hospital stay or within 30 days of the primary operation. Operative morbidities were defined as complications that contributed to a prolonged hospital stay or led to additional procedures. All morbidities were documented prospectively.

A local recurrence was defined as the presence of a radiologically confirmed or histologically proven tumor in the pelvis within the field of surgery. Isolated local recurrences, as well as the presence of both locoregional diseases and distant metastases, were included. The time to local recurrence was the duration between the time of surgical resection and the time the recurrence was documented.

The end points of the study were survival and the presence of recurrence during the most recent follow-up. Survival and the time to recurrence were calculated from the time of the initial operation. According to our follow-up protocol, CEA and CA 19-9 levels were measured every 3 months. Abdominal CT scan, chest X-ray, and colonoscopy were also ordered annually. In case of progressive tumor marker elevation, a positron emission spectroscopy (PET)-CT scan was required as well.

Statistics

For differences in continuous variables, the statistics were summarized as means. Differences among the variables were tested with either Student's t test or the Wilcoxon rank sum test. The comparisons across multiple means were carried out with one-way analysis of variance (ANOVA). For categorical data, the summary statistics consisted of proportions, and the comparisons were carried out with either the chi-square test or Fisher's exact test. The survival rate analysis was performed with the Kaplan–Meier method. Statistical significance was attributed at the 5 % level ($p < 0.05$). The data were analyzed with the SPSS Program for Windows (version 12.0; SPSS, Inc., Chicago, IL).

Results

Patient characteristics

The patients' demographic and operative characteristics are summarized in Table 1.

Surgical technique

The most common procedure was sphincter-saving surgery (SSS), which was performed on 389 (75.8 %) patients; 39 underwent intersphincteric resections and hand-sewn coloanal anastomoses (Table 2). APRs were performed in a total of 124 patients. The mean operative time was 160 ± 51 (40–330) min. The conversion rate was 6.4 % ($n = 33$). The reasons for conversion were as follows: seven huge tumors, six insufficient vascular supply to the descending colon (insufficiency of the marginal artery in three patients and insufficient flow in the left colic artery in three patients), six major bleeding (early intraoperative bleeding during either the mobilization, or sealing of the inferior mesenteric artery that could not be controlled laparoscopically), five intra-abdominal dense adhesions, two technical difficulties associated with the laparoscopic tools, two obscure anatomy (long and deep S-shaped sigmoid colon with impossible vascular identification and dissection), one tumor perforation (occurred during traction and dissection), one sacral invasion, one colonic perforation, one major vascular injury (injury to the iliac artery during dissection with scissors), and one adjacent organ invasion. The mean time to the return of bowel function was 2.6 ± 1.8 days (range: 0–21 days) and that to the resumption of oral feeding was 2.9 ± 2.3 days (range: 1–25 days).

Table 1 Patient demographics and operative characteristics

	Patients *n* (%)
Age, years (mean ± SD)	57.84 ± 13.9 (19–91)[a]
Gender	
Male	294 (57.3)
Female	219 (42.7)
Patients older than 70 years of age	118 (23.0)
Body mass index (BMI)	25.6 ± 3.2 kg/m^2
American Society of Anesthesiologists (ASA) Classification	
1	82 (16.0)
2	220 (42.9)
3	131 (25.5)
4	51 (9.9)
Missing data	29 (5.7)
Localization	
Upper	145 (28.3)
Middle	106 (20.7)
Lower	262 (51.1)
Neoadjuvant therapy	
None	191 (37.2)
Chemoradiotherapy	286 (55.8)
Short-term radiotherapy	36 (7.0)

[a] Range

Table 2 Data related to surgery ($n = 513$)

	n	%
Surgical technique		
Double-stapled anastomosis	350	68.2
Pull-through hand-sewn anastomosis	39	7.6
Abdominoperineal resection	124	24.2
Conversion to open surgery	33	6.4
Operative time, min (mean ± SD)	160 ± 51 (40–330)	

Intraoperative complications were encountered in 27 (5.3 %) patients, and one perioperative death was recorded in an 84-year-old man who lost consciousness as a result of metabolic acidosis that developed at the fourth postoperative hour. We surgically explored him immediately at bedside, and could not find any intra-abdominal abnormalities except for a low-flow-state of the small bowel segments (mesenteric ischemia). He died at the postoperative twelfth hour at the intensive care unit. Postoperative complications were observed in 127 (24.8 %) patients, and were graded according to the Clavien–Dindo classification [6]. The most common complication was anastomotic leakage.

Histopathological results

The distribution of the patients' pathological diagnoses according to their TNM classification was as follows: stage 0, 57 patients (11.1 %); stage I, 84 (16.4 %); stage II, 170 (33.1 %); stage III, 178 (34.7 %); and stage IV, 24 patients (4.7 %) (Table 3). The mean tumor size was 3.5 ± 1.9 cm. The mean distal margin was 2.6 ± 1.9 cm (range: 0–7 cm). Distal margin positivity was detected in 9 (1.7 %) patients. Transanal excision and hand-sewn coloanal anastomosis were performed in four of these patients, and APR was performed in the remaining five patients. No surgical margin positivity was detected following the definitive surgeries of these patients.

Circumferential margin involvement was present in 39 (7.6 %) cases. The mean number of harvested lymph nodes was 23.6 ± 13 (range: 0–98). The mean number of metastatic lymph nodes was 1.8 ± 3.8.

Mesorectum integrity evaluations performed by the Department of Pathology revealed that the mesorectum was totally resected or nearly so in 404 cases. Hohenberger's description [7] was modified for the grading system of the quality of TME and is summarized below:

Complete TME Good bulk of mesorectum, smooth surface, good clearance anteriorly, no defects in mesorectum.

Nearly complete TME Moderate bulk of mesorectum, but some irregularity; moderate coning distally may be present.

Table 3 Histopathological data

	Patients *n*	%
TNM stage		
0	57(5* Tis)	11.1
I	84	16.4
II	170	33.1
III	178	34.7
IV	24	4.7
T stage (depth of tumor invasion)		
Is	5	11.5
0	54	10.7
1	19	3.7
2	102	19.9
3	317	61.8
4	16	3.1
N stage		
N0	319	62.2
N1	106	20.7
N2	88	17.2
Tumor size, cm (mean ± SD)	3.5 ± 1.9 (0–15)[a]	–
Distal margin		
Positive	9	1.8
Negative	504	98.2
Distal resection margin distance (cm) (mean ± SD)	2.6 ± 1.9 (0–14)[a]	–
Positive circumferential margin	39	7.6
Number of harvested lymph nodes (mean ± SD)	23.6 ± 13 (0–98)[a]	–
Number of metastatic lymph nodes (mean ± SD)	1.8 ± 3.8 (0–29)[a]	–
Total mesorectal excision		
Complete	251	48.9
Nearly complete	153	29.8
Incomplete	109	21.2

[a] Range

Incomplete TME Irregular mesorectum with defects greater than 1 cm^2 or incision down to muscularis propria; irregular circumferential resection margin with little bulk and little clearance anteriorly.

The incomplete TME rate was found to be 21 %, and these cases were considered mainly to have resulted from traction, dissection, and surgical manipulation during operation (Table 3). No relation between incomplete TME and either tumor localization or tumor size was detected in our study.

In our series 16 patients had pT4 tumors. Eight of these pT4 tumors were localized in the distal rectum, one in the middle, and seven at the proximal rectum. Additional laparoscopic surgical procedures were performed in these patients: three had resections of the posterior vagina, two had salpingo-oophorectomy, one had a total abdominal hysterectomy plus bilateral salpingo-oophorectomy, and one had a partial urinary bladder resection. Conversion to open surgery was needed in one of the 16 patients with a stage pT4 tumor. In addition, six of these pT4 patients who had not received any neoadjuvant therapy had CRM positivity, and two of them had an incomplete mesorectum. In the group of patients who had received neoadjuvant therapy, there was only one incomplete mesorectum.

Oncologic treatment and pathologic outcomes

Three hundred twenty-two patients in this series had received neoadjuvant treatment. Their clinical and pathologic staging distribution is shown in Table 4. Pathologic complete response was noted in 54 patients (17 %), 52 of whom were in stage 0 (T0N0) and the remaining two were in stage III (T0N+). 471 of the 513 cases received adjuvant chemotherapy, and 322 of them received adjuvant chemotherapy adjunct to the neoadjuvant treatment protocol. The rest of the patients did not receive any neoadjuvant treatment but had adjuvant therapy because of their pathologic stage (pT3N0, pT any N+, pT any pN, any M+).

There were 24 patients with stage IV disease. Eight of them with proximal RC were treated with rectal surgery, and one of those patients underwent synchronous liver metastasectomy (and is still alive in the twenty-third month). Two of them underwent staged liver metastasectomies (one is alive in the thirteenth month, one died in the ninth month), and the rest (5 patients) received adjuvant chemotherapy (all are alive at a median of 31 months [range: 7–64 months]). 16 patients with stage IV disease had been treated with metastatic chemotheraphy regimens preoperatively. Five of these 16 patients were also treated with short course radiotherapy for local control. One of them had synchronous adrenalectomy (and is still alive in the twenty-first month), two had staged liver metastasectomies (still alive in the thirty-fourth and thirty-seveth months), and two were treated with adjuvant chemotherapy (one died in the seventh month, one remains alive in the fifteenth month). The rest of the patients were treated with adjuvant chemotherapy after rectal surgery [five died in a median period of 9 months (range: 3–24 months), six are alive in a median period of 18 months (range: 8–49 months)].

Oncological results and survival rates

After a median follow-up of 30 (1–78) months, tumor recurrence occurred in 59 (11.5 %) of the 513 patients. The crude rates for recurrence are summarized in Table 5. Local recurrence occurred in 16 (3.1 %) patients. Seven of them had both local recurrence and systemic metastasis. Pure systemic metastasis was found in 43 patients (8.4 %).

The tumors of the 6 of 16 locally recurrent patients were in the proximal rectum; therefore, they had not received any neoadjuvant therapies. All of these recurrent proximal tumors were pT3, and in every case, the mesorectum was completely excised. In two of these six patients CRM positivity was detected. Ten of the 16 patients with local recurrence had received neoadjuvant treatment because of locally advanced tumors. The mesorectum was incomplete in four of these ten patients, and CRM was positive in only one case. There was a total of three CRM positivities, one in the proximal RC group and the other two in the mid-distal RC group. Incomplete mesorectum was detected in four patients all in the mid-distal RC group. The summary of the subgroup analysis of these 16 patients revealed that the median radial margin was 5.21 (0–20) mm, and the median number of harvested lymph nodes was 22 (6–39). There was no technical failure during surgery, and the proximal and distal margins of all specimens were noted to be clear of tumoral tissue.

The Kaplan–Meier estimate of the 5-year overall survival (OS) rate for laparoscopic rectum resection was 84 % (Fig. 1). The 5-year disease-free survival (DFS) was 77.4 % (Fig. 2). The local recurrence-free survival rate was 98.4 % at the end of 2 years, 95.7 % at the end of 3 years, and 94.3 % at the end of 5 years (Fig. 3). The stage-specific survival rates for laparoscopic rectum resection at the end of 5 years as estimated by Kaplan–Meier were 96 % for stage 0, 87 % for stage I, 87 % for stage II, 79.5 % for stage III, and 65 % for stage IV (Fig. 4).

Discussion

The most important variable in assessing the feasibility and efficacy of laparoscopic versus open resection for RC is the pelvic dissection. This variable can primarily be measured by the adequacy of the CRM and distal margin, the completeness of the mesorectum, the recurrence rate, and overall survival rates.

Circumferential margin positivity is a well-known marker for the increased risk of local recurrence (Tables 6, 7) [24]. It is essential to put the principles of TME into practice to save the mesorectal envelope, to obtain an adequate CRM and distal margin, and thereby to reduce local recurrence rates [24, 25]. The reported rates of CRM positivity in laparoscopic resection for RC range between 0 and 16 %. The first randomized study for laparoscopic rectal resection showed that a positive CRM was identified in 14 % of patients who underwent open resection and 16 % of those who had laparoscopic resection (p: 80) [26]. Among patients undergoing anterior resection (AR), the rate of CRM positivity was 12 % in the laparoscopy group versus 6 % in the open surgery group (p: 0.19). Among patients undergoing APR, no difference in CRM positivity was reported between the laparoscopy and open surgery groups (20 vs 26 %, respectively). The authors concluded that the routine use of laparoscopic resection for RC was not yet justified. Although this statement was initially alarming, several surgeons involved in the study were still within their learning curve at that time, and preoperative chemoradiotherapy was not yet standardized. In the largest retrospective evaluation to date, Ng et al. [21] reported 579 laparoscopic resections for RC with a CRM positivity rate of 2.14 %. Milsom et al. [22], Laurent et al. [12], and Cheung et al. [23] reported CRM positivity rates of 0, 7, and 1.2 %, respectively. In our series, the CRM positivity rate was 7.6 % in 513 RC patients. The CRM positivity rate depends on patient selection, the surgeons' proficiency and case volume, the choice of preoperative treatment, and the quality of the pathological evaluation. For surgeons who have achieved proficiency and who are working in high-volume centers, the CRM positivity rate should not be different from that of open RC resections.

The distal resection margin is another important factor contributing to local recurrence. In the CLASICC trial, within the actual treatment group, 87 patients (51 ARs and 36 APRs) underwent open TME, and 189 patients (129 ARs, and 60 APRs) underwent laparoscopic TME [26]. Despite the fact that the median distance of rectal tumors from the anal verge was similar in the two groups, the

Table 4 The clinical and pathologic staging of patients with and without neoadjuvant treatment

	Direct surgery group	Neoadjuvant treatment and surgery group		
	p Staging ($n = 191$)	c Staging ($n = 322$)	yP Staging ($n = 322$)	Total
Stage 0	5	–	52	57
Stage I	37	5	47	84
Stage II	65	42	105	170
Stage III	65	270	113	178
Stage IV	19	5	5	24
Total	191	322	322	513

Table 5 Tumor recurrence and/or metastasis types and rates [median follow-up: 30 months (range: 1–78 months)]

Recurrence/metastasis	Patients *n*	%
Local recurrence	16	3.1
Systemic metastasis	43	8.4
Liver metastasis	22	4.3
Peritoneal metastasis	9	1.8
Lung metastasis	5	1.0
Liver and lung metastasis	5	1.0
Bone metastasis	1	0.2
Liver, lung, and bone metastasis	1	0.2
Local recurrence and systemic metastasis	7	1.4
Local recurrence and peritoneal metastasis	3	0.6
Local recurrence and liver metastasis	2	0.4
Local recurrence and lung metastasis	1	0.2
Local recurrence and bone metastasis	1	0.2
Total	59	11.5

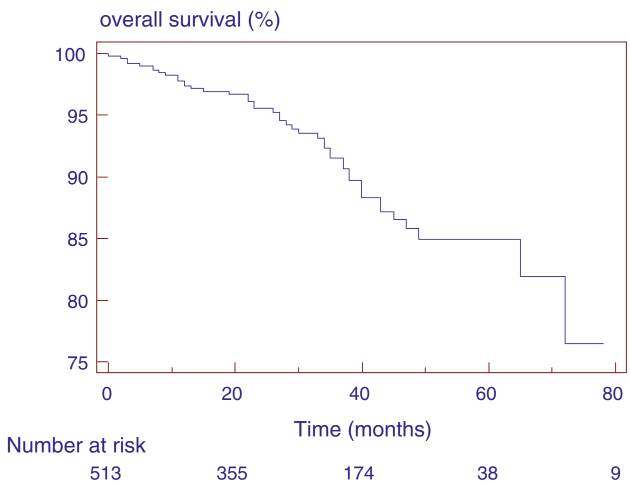


Fig. 1 Kaplan–Meier estimates of overall survival for laparoscopic rectum resection ($n = 513$)

greater proportion of patients undergoing TME in the laparoscopic AR group may be related to the inability of the surgeon to palpate the tumor during laparoscopic surgery. Dividing the rectum laparoscopically is not always feasible. The limited angulation of the stapler and the physical limitations of working in the bony confines of the pelvis are common obstacles. In our series, distal margin positivity was present in nine cases; of these, transanal re-excision and hand-sewn coloanal re-anastomosis was performed in four patients, and APR was performed in the remaining five patients to obtain R0 resection; this is essential for a better oncological outcome because margin positivity cannot be compensated for with adjuvant therapy [27].

The local recurrence rate was <7 % in the reported series that had adequate long-term follow-up periods, except for Feliciotti's series (20.8 %) [8–23]. The 5-year results of the MRC CLASICC trial reported similar local recurrence rates for laparoscopic versus open resection of RC [13, 28]. The 10-year results from a prospective randomized trial of laparoscopic resection of upper RC demonstrated a regional recurrence rate of 7 % [10]. Laurent et al. [12] aimed to evaluate long-term oncological outcomes after laparoscopic versus open surgery for RC in a retrospective comparative study. A total of 471 patients had rectal resections for invasive RC during the trial period; 238 were treated laparoscopically, and 233 were treated with open surgery. At the end of 5 years, there was no difference in terms of the local recurrence rate (3.9 vs 5.5 %; $p = 0.371$) between the laparoscopy and open surgery groups. Preoperative radiotherapy for RC was proven to reduce local recurrence rates in Swedish, Dutch, and German studies of open surgery [20–31]. Selective neoadjuvant chemoradiotherapy is commonly adopted for

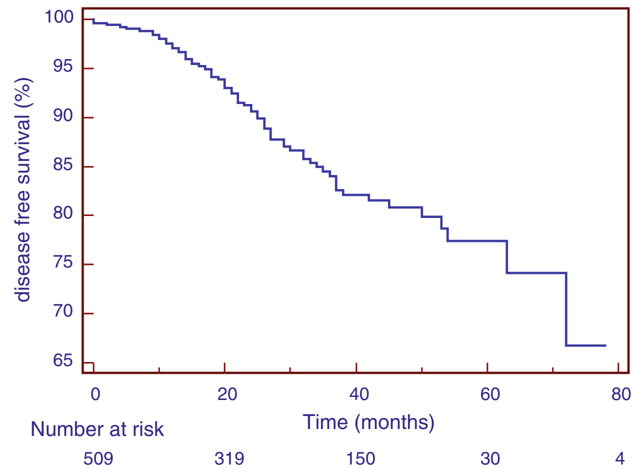


Fig. 2 Kaplan–Meier estimates of disease-free survival for laparoscopic rectum resection ($n = 513$)

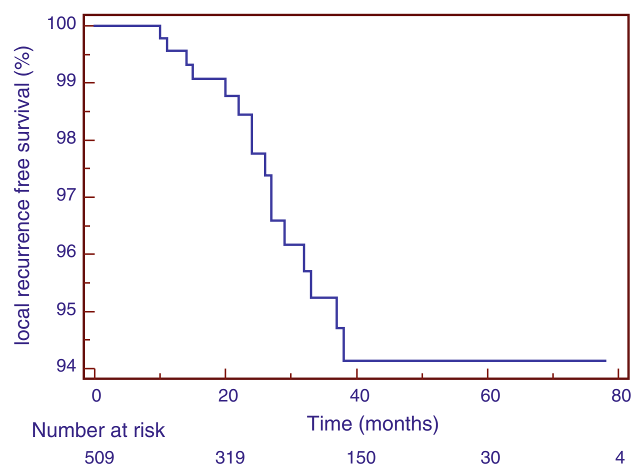
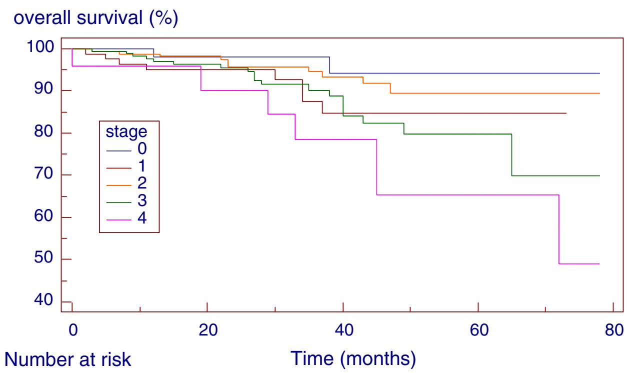


Fig. 3 Kaplan–Meier estimates of local recurrence-free survival for laparoscopic rectum resection ($n = 513$)



Number at risk

	0	20	40	60	80
Group: 0	57	43	21	5	3
Group: 1	84	53	28	5	0
Group: 2	170	125	65	11	2
Group: 3	178	118	52	13	2
Group: 4	24	16	8	4	2

Fig. 4 Kaplan–Meier estimates of stage-specific survival for laparoscopic rectum resection ($n = 513$)

laparoscopic RC surgery. No studies have reported whether the effects of radiotherapy differ between laparoscopic RC resection and open surgery in terms of characteristics and outcomes. In our experience, neoadjuvant chemoradiotherapy has the benefit of tumor downstaging and allows some locally advanced tumors to be excised via laparoscopy.

In 2010, the UK MRC CLASICC trial reported long-term outcomes for RC. The 5-year OS rate was 52.9 % for open surgery and 60.3 % for laparoscopic surgery ($p = 0.132$) [13]. No difference in OS was detected between the two techniques for patients with RC undergoing either AR or APR. For AR, the 5-year OS rate was 56.7 % for open surgery and 62.8 % for laparoscopic surgery ($p = 0.247$). For APR, the 5-year OS rate was 41.8 % for open surgery and 53.2 % for laparoscopic surgery ($p = 0.310$). The results of a prospective randomized trial of laparoscopic versus open APR for low RC were reported by Ng et al. [9] with a median follow-up period of 90 months. The survival rate at the end of 5 years after curative resection was 75.2 % for the laparoscopy group and 76.5 % for the open surgery group. A single-institution, large retrospective review of 579 patients who underwent laparoscopic resection for rectosigmoid cancer or RC was also reported by Ng et al. [21], and long-term survival was also evaluated. Over a 15-year period, 316 patients underwent laparoscopic AR; 152 patients, SSS; and 92 patients, APR. The median follow-up period was 56 months. The 5- and 10-year OS rates were 70, and 45.5 %, respectively. Other reported series with median follow-up periods that were longer than 30 months are shown in Tables 6 and 7. The survival rates are comparable with those of open surgery.

Table 6 Comparative series

Reference	Year	Patients (n)	Harvested lymph nodes (n) (median)	Specimen margin positivity (%) (CRM/DM)	Tumor recurrence (%)	Follow-up (months)	Overall survival
Feliciotti et al. [8]	2003	L:81	10.3	NR	20.8	43.8	62.5
		O:43	9.8		18.2		60.6
Ng et al. [9]	2008	L:51	12.4	5.8/0	5	87.2	75.2
		O:48	13	4.1/0	11.1	90	76.5
Ng et al. [10]	2009	L:76	11.5	2.6/	7.1	112.5	63.9
		O:77	12	1.2/	4.9	108.8	55.1
Law et al. [11]	2009	L:111	NR	NR	8.2	34	71.1
		O:310			8.7		59.3
Laurent et al. [12]	2009	L:238	NR	7/2.9	3.9	52	82
		O:233		6/0.9	5.5		79
Jayne et al. [13]	2010	L:160		16/	7.6	56.3	60.3
		O:123		14/	9.4		52.9
Li et al. [14]	2011	L:113			9.1	74.8	77.9
		O:123			6.4		78.9
Liang et al. [15]	2011	L:169	19.1	NR		44	76
		O:174	18.97				82.8
Baik et al. [16]	2011	L:54	11.2	1.9/NR	2	60	90.8
		O:108	10.7	6.9/NR	4.2		88.5

Table 7 Case series

Reference	Year	Patients (*n*)	Harvested lymph nodes (*n*) (median)	Specimen margin positivity (%) (CRM/DM)	Tumor recurrence (%)	Follow-up (months)	Overall survival
Leroy et al. [17]	2004	L:99	8	NR	6	36	65
Dulucq et al. [18]	2005	218	24.5	NR/0	6.8	57	67
Agha et al. [19]	2008	225	14	2/NR	5.8	36.4	75.7
Pugliese et al. [20]	2009	252	12	NR/0	3.9	48	73.7
Ng et al. [21]	2009	579	12	2.1/4	4.6	56	70
Milsom et al. [22]	2009	185	15	0/0	5	42.1	91
Cheung et al. [23]	2011	247		1.2/2.02	5.1	49	74
Present series actual results	2011	513	23.6	7.6/1.7	3.1	30	84

The prospective observational characteristic of our trial constitutes the limitation of our study. The study design was lacking a control group, which should have been an open surgery group. The results of the laparoscopic RC surgery cases were not compared with an open RC surgery group statistically, and this issue brings about the fact that the study was not randomized. We are also conducting a randomized study in our current clinical practice, and the data for it are still being collected.

The advantages of laparoscopic RC surgery are high-definition visual access, increased anatomic view, better sexual and urinary functional results, fast early postoperative recovery, shorter hospital stay, and better cosmetic results. For surgeons who have achieved proficiency who are working in high-volume centers, the CRM positivity rate should not be different from that of open RC resections. Current evidence suggests that the long-term outcomes of laparoscopy are at least as good as those of open surgery as long as surgical oncological principles are respected and faithfully executed. Our results match well with the literature. However, the comparison depends primarily on case series, comparative series, and a few randomized controlled trials. Results from large, multicenter, prospective, randomized studies, such as the American College of Surgeons Oncology Group Z6051, are needed before a final decision can be made on the efficacy of laparoscopic treatment of RC. The main determinant of good oncologic outcome is specialized multidisciplinary teamwork in the treatment of RC.

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References

1. Aziz O, Constantinides V, Tekkis PP et al (2006) Laparoscopic versus open surgery for rectal cancer: a meta-analysis. Ann Surg Oncol 13:413–424
2. Gao F, Cao YF, Chen LS (2006) Meta-analysis of short-term outcomes after laparoscopic resection for rectal cancer. Int J Colorectal Dis 21:652–656
3. Asoglu O, Matlim T, Karanlik H et al (2009) Impact of laparoscopic surgery on bladder and sexual function after total mesorectal excision for rectal cancer. Surg Endosc 23:296–303
4. Balik E, Asoglu O, Saglam S et al (2010) Effects of surgical laparoscopic experience on the short-term postoperative outcome of rectal cancer: results of a high volume single center institution. Surg Laparosc Endosc Percutan Tech 20:93–99
5. Vignali A, Fazio VW, Lavery IC et al (1997) Factors associated with the occurrence of leaks in stapled rectal anastomoses: a review of 1,014 patients. J Am Coll Surg 185:105–113
6. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213
7. Hermanek P, Hermanek P, Hohenberger W et al (2003) The pathological assessment of mesorectal excision: implications for further treatment and quality management. Int J Colorectal Dis 18:335–341
8. Feliciotti F, Guerrieri M, Paganini AM et al (2003) Long-term results of laparoscopic versus open resections for rectal cancer for 124 unselected patients. Surg Endosc 17:1530–1535
9. Ng SS, Leung KL, Lee JF et al (2008) Laparoscopic-assisted versus open abdominoperineal resection for low rectal cancer: a prospective randomized trial. Ann Surg Oncol 15:2418–2425; Erratum. Ann Surg Oncol 2009 16:229
10. Ng SS, Leung KL, Lee JF et al (2009) Long-term morbidity and oncologic outcomes of laparoscopic-assisted anterior resection for upper rectal cancer: 10-year results of a prospective, randomized trial. Dis Colon Rectum 52:558–566
11. Law WL, Poon JT, Fan JK et al (2009) Comparison of outcome of open and laparoscopic resection for stage II and stage III rectal cancer. Ann Surg Oncol 16:1488–1493
12. Laurent C, Leblanc F, Wütrich P et al (2009) Laparoscopic versus open surgery for rectal cancer: long-term oncologic results. Ann Surg 250:54–61
13. Jayne DG, Thorpe HC, Copeland J et al (2010) Five-year follow-up of the Medical Research Council CLASICC trial of laparoscopically assisted versus open surgery for colorectal cancer. Br J Surg 97:1638–1645
14. Li S, Chi P, Lin H et al (2011) Long-term outcomes of laparoscopic surgery versus open resection for middle and lower rectal cancer: an NTCLES study. Surg Endosc 25:3175–3182
15. Liang X, Hou S, Liu H et al (2011) Effectiveness and safety of laparoscopic resection versus open surgery in patients with rectal cancer: a randomized, controlled trial from China. J Laparoendosc Adv Surg Tech A 21:381–385

16. Baik SH, Gincherman M, Mutch MG et al (2011) Laparoscopic vs open resection for patients with rectal cancer: comparison of perioperative outcomes and long-term survival. Dis Colon Rectum 54:6–14
17. Leroy J, Jamali F, Forbes L et al (2004) Laparoscopic total mesorectal excision (TME) for rectal cancer surgery: long-term outcomes. Surg Endosc 18:281–289
18. Dulucq JL, Wintringer P, Stabilini C et al (2005) Laparoscopic rectal resection with anal sphincter preservation for rectal cancer: long-term outcome. Surg Endosc 19:1468–1474
19. Agha A, Fürst A, Hierl J et al (2008) Laparoscopic surgery for rectal cancer: oncological results and clinical outcome of 225 patients. Surg Endosc 22:2229–2237
20. Pugliese R, Di Lernia S, Sansonna F et al (2008) Results of laparoscopic anterior resection for rectal adenocarcinoma: retrospective analysis of 157 cases. Am J Surg 195:233–238
21. Ng KH, Ng DC, Cheung HY et al (2009) Laparoscopic resection for rectal cancers: lessons learned from 579 cases. Ann Surg 249:82–86
22. Milsom JW, de Oliveira O, Trencheva KI Jr et al (2009) Long-term outcomes of patients undergoing curative laparoscopic surgery for mid and low rectal cancer. Dis Colon Rectum 52:1215–1222
23. Cheung HY, Ng KH, Leung AL et al (2011) Laparoscopic sphincter-preserving total mesorectal excision: 10-year report. Colorectal Dis 13:627–631
24. Nagtegaal ID, Quirke P (2008) What is the role for the circumferential margin in the modern treatment of rectal cancer? J Clin Oncol 26:303–312
25. Wiggers T, van de Velde CJ (2002) The circumferential margin in rectal cancer. Recommendations based on the Dutch Total Mesorectal Excision Study. Eur J Cancer 38:973–976
26. Franks PJ, Bosanquet N, Thorpe H et al (2006) Short-term costs of conventional vs. laparoscopic assisted surgery in patients with colorectal cancer (MRC CLASICC trial). Br J Cancer 95:6–12
27. Marijnen CA, Nagtegaal ID, Kapiteijn E et al (2003) Radiotherapy does not compensate for positive resection margins in rectal cancer patients: report of a multicenter randomized trial. Int J Radiat Oncol Biol Phys 55:1311–1320
28. Guillou PJ, Quirke P, Thorpe H et al (2005) Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet 365(9472):1718–1726
29. Folkesson J, Birgisson H, Pahlman L et al (2005) Swedish Rectal Cancer Trial: long lasting benefits from radiotherapy on survival and local recurrence rate. J Clin Oncol 23:5644–5650
30. van Gijn W, Marijnen CA, Nagtegaal ID et al (2011) Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. Lancet Oncol 12:575–582
31. Sauer R, Becker H, Hohenberger W et al (2004) Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med 351:1731–1740