adjuvant radiotherapy or chemoradiotherapy was not performed in this series, because preoperative therapy for resectable rectal cancer was not standard in Japan.

Synchronous resections included 20 extended resections for direct invasion of adjacent organs, 13 hepatectomies for liver metastasis, and five resections of double primary cancers.

Morbidity and mortality

The overall rate of anastomotic leakage was 10.0% (33 of 329). We experienced only one mortality in this series (0.3%; 1/329). This patient died from a septic complication caused by anastomotic leakage in the case of LAR with DS 6 days after initial surgery.

Diverting stoma

A DS was constructed in 120 patients (36.5%; 120 of 329) in initial LAR, respectively. Among the colorectal surgeons participating in this study, ileostomy was major and chosen for 92 (76.7%) patients, while transverse colostomy was done for 28 (23.3%) patients.

The DS construction rate had a significant association with tumor location. DS was constructed in only 12.7% of middle rectal cancer patients, but in 48.3% of low rectal cancer patients who experienced temporary stoma at initial LAR, respectively.

Other factors found to be significantly associated with DS construction included tumor location, operation time, intraoperative bleeding, lateral lymph node dissection,

Table 2 Univariate analysis of factors related with DS construction

	Diverting stoma		Rate	*p*-value
	DS(−)	DS(+)		
Gender				
Male	130	85	39.5	0.11
Female	79	35	30.7	
Age (years)	58.8±10.7 (23–87)	59.4±10.2 (29–75)		0.42
Tumor location (cm)	6.4±1.6 (4.0–12.0)	5.9±1.7 (4.0–12.0)		0.001
Bowel obstruction				
No	195	110	36.1	0.76
Yes	11	7	38.9	
Tumor invasion				
T1,T2	71	37	34.6	0.50
T3,T4	133	82	38.1	
Neoadjuvant chemo Tx				
No	204	120	37.0	0.10
Yes	5	0	0.0	
Anastomosis				
SST	8	7	46.7	0.40
DST	201	113	36.0	
High ligation				
No	125	58	31.7	0.12
Yes	82	60	42.3	
LLND				
No	146	51	25.9	<0.0001
Yes	63	69	52.3	
Level of anastomosis (cm)	4.2±1.4 (1.0–9.0)	3.8±1.4 (1.0–9.5)		0.002
Intraoperative bleeding (ml)	505±524 (10–2985)	760±662 (17–3723)		<0.0001
Operating time (min)	231±90.6 (90–559)	318±102.7 (130–620)		<0.0001
BMI (k/m^2)	22.9±3.0 (14.1–31.2)	22.3±3.2 (15.8–30.8)		0.07
Tumor size (cm)	4.4±2. (0–12.0)	4.4±2.3 (1.0–10.0)		0.97
Simultaneous resection				
No	192	100	34.2	0.02
Yes	17	20	54.1	

Values are number or mean± standard deviation (ranges)

BMI body mass index, *SST* single stapling technique, *DST* double stapling technique, *LLND* lateral lymph node dissection simultaneous resection of other organs, and level of anastomosis (Table 2).

Risk factors of anastomotic leakage

Clinical variables were analyzed to investigate the risk factors for anastomotic leakage (Table 3). On univariate analysis, LAR with high ligation of IMA had a significantly high leakage rate ($p<0.05$). There were increased but statistically insignificant impacts on leakage in males, bowel obstruction, massive intraoperative bleeding, and simultaneous resection of other organs.

Nine (7.5%) of 120 patients with DS had leakage, compared with 24 (11.5%) of 209 patients without DS ($p=0.25$). DS construction also had no relevance to the overall anastomotic leakage.

Risk factors of leakage limited to the LAR without DS were also investigated. As shown in Table 4, no obvious statistical significance was found with any clinical factor.

A multivariate analysis of risk factors for anastomotic leakage showed every factor including high ligation of IMA construction as not statistically significant (Table 5).

Table 3 Univariate analysis of leakage risk factors

	Leakage		Rate	*p*-value
	No leakage	Leakage		
Gender				
Male	190	25	11.6	0.19
Female	106	8	0.7	
Age(years)	58.8±10.6 (23–87)	61.1±10.0 (40–76)		0.20
Tumor location (cm)	6.2±1.7 (4.0–12.0)	6.5±1.7 (4.0–10.0)		0.31
Bowel obstruction				
No	276	29	9.5	0.16
Yes	14	4	22.2	
Tumor invasion				
T1,T2	101	7	6.5	0.12
T3,T4	189	26	12.1	
Neoadjuvant chemo Tx				
No	291	33	10.2	0.59
Yes	5	0	0.0	
Anastomosis				
SST	13	2	13.3	0.66
DST	283	31	9.9	
High ligation				
No	135	7	4.9	0.02
Yes	157	26	14.2	
LLND				
No	177	20	10.1	0.93
Yes	119	13	9.8	
Level of anastomosis (cm)	4.1±1.4 (1.0–9.5)	4.4±1.3 (1.9–7.0)		0.13
Intraoperative bleeding (ml)	573±559 (10–3365)	817±791 (40–3723)		0.06
Operating time (min)	261±102 (90–616)	273±118 (113–620)		0.70
BMI (k/m^2)	22.7±3.1 (14.1–31.2)	22.5±3.2 (16.1–27.0)		0.87
Tumor size (cm)	4.4±2.3 (0–12.0)	5.0±2.3 (2.0–11.0)		0.18
Simultaneous resection				
No	266	26	8.9	0.06
Yes	30	7	18.9	
DS construction				
No	185	24	11.5	0.25
Yes	111	9	7.5	

Values are number or mean± standard deviation (ranges)

BMI body mass index, *SST* single stapling technique, *DST* double stapling technique, *LLND* lateral lymph node dissection

Table 4 Univariate analysis of leakage risk factors (without DS patients)

	Leakage		Rate	p-value
	No leakage	Leakage		
Gender				
Male	114	16	12.3	0.63
Female	71	8	10.1	
Age(years)	58.7±10.8 (23–87)	59.7±10.1 (40–76)		0.65
Tumor location (cm)	6.4±1.6(4.0–12.0)	6.3±1.6 (4.0–10.0)		0.61
Bowel obstruction				
No	173	22	11.3	0.64
Yes	9	2	18.2	
Tumor invasion				
T1,T2	65	6	8.5	0.28
T3,T4	115	18	13.5	
Neoadjuvant chemo Tx				
No	180	24	11.8	0.54
Yes	5	0	0.0	
Anastomosis				
SST	7	1	12.5	0.63
DST	178	23	11.4	
High ligation				
No	108	17	13.6	0.47
Yes	75	7	8.5	
LLND				
No	130	16	11.0	0.72
Yes	55	8	12.7	
Level of anastomosis (cm)	4.2±1.4 (1.0–9.0)	4.2±1.1(2.2–7.0)		0.89
Intraoperative bleeding (cm)	480±502 (10–2985)	703±650 (40–2720)		0.07
Operating time (cm)	228±88 (90–552)	248±108(113–559)		0.60
BMI (k/m^2)	22.9±3.0 (14.1–31.2)	22.7±3.1 (16.1–27.0)		0.82
Tumor size (cm)	4.3±2.3 (0–12.0)	5.0±2.4 (2.0–11.0)		0.26
Simultaneous resection				
No	171	21	10.9	0.31
Yes	14	3	17.6	

Values are number or mean± standard deviation (ranges)

BMI body mass index, *SST* single stapling technique, *DST* double stapling technique, *LLND* lateral lymph node dissection

Clinical course affected by DS construction

The clinical course affected by DS was also investigated, focusing on the necessity of urgent abdominal reoperation for anastomotic leakage. Nine of 120 (7.5%) patients who underwent LAR with DS experienced leakage. Of these nine, only one patient (11.1%) needed urgent reoperation for peritonitis, and eight patients were treated conservatively. Twenty-four of 209 (11.5%) patients who underwent LAR without DS experienced leakage, and 13 (54.2%) of them needed urgent reoperation, while 11 patients were treated conservatively (Table 6). The need for reoperation was significantly increased in patients without DS compared to those with DS, 54.2% and 11.1%, respectively (p=0.04).

Table 5 Multivariate analysis of leakage risk factors

	p-value	Odds ratio (95% CI)
High ligation	0.17	1.9 (0.77–4.54)
Intraoperative bleeding	0.78	1.0 (0.99–1.00)
Simultaneous resection	0.12	2.2 (0.82–6.09)

Discussion

LAR was the safe and preferred option for middle or low rectal cancer patients with very low mortality and an acceptable leakage rate among the institutes participating in this study. DS did not have a statistically significant

Table 6 Clinical course affected by diverting stoma

DS in initial LAR		Leakage		Conservative therapy	Urgent operation	Rate of urgent operation	
			%			%	
DS(+)	120	9	7.5	8	1	11.1	$p=0.04$
DS(−)	209	24	11.5	11	13	54.2	

relationship with the overall leakage rate. Although we cannot conclude the value of DS in terms of leakage prevention from this retrospective study, DS did seem to mitigate the consequences of leakage and reduce the need for urgent abdominal reoperation for leakage. There have been few reports about this issue in multicenter studies with a large number of patients from Japan.

With the advances in surgical procedures and devices in recent decades, sphincter-preserving surgery has become the treatment of choice for rectal cancer patients. In addition, simple and easy reconstruction has become possible thanks to circular stapling devices, even in low-level anastomosis within a narrow pelvis.

However, anastomotic leakage is still a major problem in rectal cancer surgery, sometimes resulting in severe morbidity or mortality. Since stapled anastomosis developed in the 1970s, the mortality of sphincter-preserving operations has decreased. In 1975, Fain et al. [11] reported their experience of mechanical suturing in 165 rectal cancer patients with a mortality of 2.4%. Now, symptomatic anastomotic leakage has been reported to occur in 5% to 20% of cases [12–20], and when present, the associated risk of postoperative mortality is increased to between 6% and 22% [15]. The present study encountered very low mortality (1/329; 0.3%), which is not inferior to the 0.8% recently described [2]. Our result shows the obviously improved safety of LAR using mechanical anastomosis in the Japanese cancer centers participating in this study.

Several risk factors for anastomotic leakage have been reported [12–20], and the relationship between DS and leakage was discussed in many retrospective or non-randomized prospective studies. Wong et al. [21] reported no statistical difference between patients who were defunctioned (3.8%; 28/742) and those who were not (4%; 13/324). So, they concluded that DS did not reduce the postoperative leak rate. They also concluded that a stoma carried a certain morbidity and also added to the cost of the entire operation, so it should not be performed routinely. On the other hand, Peeters et al. [18] reported that the absence of DS was significantly associated with a higher leakage rate: 43 (8.2%) of 523 patients with DS had leakage, compared with 64 (16.0%) of 401 patients without DS ($p<0.001$). In the present study, DS construction had no association with the overall anastomotic leakage rate. This reflects our low leakage rate in cases without DS (11.5%; 24 of 209). This rate is comparable to the leakage rate in cases with DS in a randomized controlled trial by Matthiessen et al. (10.3%; 12 of 116) [1].

Although absence of DS was not a risk factor of leakage in this study, because of a general selection bias of nonrandomized study including ours, we cannot conclude whether or not DS can prevent the leakage. This bias results from the selective creation of DS for the patients anticipated to undergo "risky" anastomosis by each surgeon as shown in this investigation. We can also point out another bias, namely that clinically unapparent leakages might have been missed in either group because no systematic assessment of the anastomosis for clinically stable patients was performed in the present study.

Only four randomized control studies sought to investigate the association between DS and leakage [1, 2, 22, 23]. Matthiessen et al. [1] reported the result of intraoperative randomization of a patient undergoing LAR for rectal cancer within 15 cm from the anal verge, and anastomosed within 7 cm. 10.3% (12 of 116) of patients with defunctioning stoma ($n=116$) had symptomatic leakage, against 28.8% (33 of 118) of those without stoma ($n=118$). They concluded that defunctioning stoma significantly decreased the rate of symptomatic leakage and was therefore recommended in LAR for rectal cancer. Pakkastie et al. [22] and Graffner et al. [23], on the other hand, could not find any statistical difference between the two groups in their randomized studies comprising 50 and 38 patients, respectively. But due to the small sample, no firm conclusion could be made. So, it is still controversial whether DS can prevent anastomotic leakage. The problem is the limited evidence about this issue. The value of DS in preventing leakage should be evaluated by more prospective studies in the future. And prospective, randomized studies are also warranted to address this issue.

Other reported risk factors include male gender [13–16], level of anastomosis [12–15], previous radiation therapy [13, 14], absence of pelvic drainage [18], poor bowel preparation [12], blood transfusion [12], immunosuppression, and underlying vascular insufficiency. Among these risk factors, male gender and level of anastomosis were widely accepted as significant for leakage. In the present study, there were increased impacts on leakage in male gender, bowel obstruction, massive intraoperative bleeding, and simultaneous resection of other organs. Although statistical significance was not reached, these factors were comparable to those in previous reports. In the present investigation, due to the retrospective nature of the study design, the level of anastomosis was calculated from the tumor location and distal resection margin when data were not available. And in some patients, tumor location was measured only by digital examination and not by rectoscopy, these might introduce bias. Although the anastomotic level was not associated with leakage, this data should be evaluated with caution.

High ligation of IMA was the only leakage risk factor on univariate analysis in the present study. Lange et al. [24] systematically reviewed the literature concerning the level of ligation and concluded that preserving IMA and left colic artery was anatomically less invasive with respect to circulation and autonomous innervations of the proximal limb of anastomosis. Seike et al. [25] measured the colonic blood flow at the proximal site of the anastomosis by laser Doppler flowmetry to evaluate the influence of high ligation. They proved a significant reduction of colonic blood flow at the proximal site after clamping IMA. Our result also suggested the possibility that blood flow reduction on anastomotic sites leads to more leakage.

In the present study, we reported our low leakage rate in cases without DS (11.5%; 24 of 209). This rate is comparable to the leakage rate in cases with DS in a randomized controlled trial by Matthiessen et al. (10.3%; 12 of 116) [1]. This may have some association with our patient population that neoadjuvant radiotherapy or chemoradiotherapy was not performed in this series. Neoadjuvant radiation therapy is considered to be a risk factor by some authors [13, 14]. Although randomized multicenter trials have shown that neoadjuvant radiation does not increase postoperative morbidity [26–28], Peeters et al. [18] retrospectively analyzed risk factors from the database of the Dutch Colorectal Cancer Group, and reported that a defunctioning stoma was constructed more often in patients who had received radiation, and that the absence of a DS was significantly associated with a higher leakage rate.

We also reported our low mortality. This reflects our low leakage rate in cases without DS and our appropriate decision of reoperation for peritonitis in cases without DS. We considered that our appropriate decision lead to low mortality rate and high reoperation rate (54.2%). In the present study, a DS constructed at the time of initial surgery obviously reduced the necessity of an urgent reoperation after overt leakage, proving the clinical benefits of DS in this regard. The important objective of DS was not to eliminate leakage but to decrease the risk of reoperation. However, DS construction did not guarantee the complete safety of LAR. In fact, we experienced one mortality in a patient with DS in this series, so complete elimination of leakage and severe septic complications was not feasible.

In conclusion, we clearly demonstrated the outstanding safety of LAR with very low mortality and acceptable leakage rate in our group. Although this retrospective study could not prove whether DS can prevent leakage itself, we found that it could mitigate the need for urgent abdominal reoperation for leakage. To define clear criteria for DS construction, a well-designed randomized control study is genuinely needed in the future.

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ORIGINAL ARTICLE

Comparison of short, long-term surgical outcomes and mid-term health-related quality of life after laparoscopic and open resection for colorectal cancer: a case-matched control study

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Abstract
Background A multicenter randomized study is high quality, but it is also true that there are differences between institutions. The quality of treatment is consistent in a single center so comparisons in a retrospective study can be matched for many variables.
Methods This single-center study examined short-term and long-term outcomes for colorectal cancer in 258 patients who underwent laparoscopic resection (LC) and 258 matched open resection (OC) cases. The health-related qualities of life (HRQOL) at 1–2 years after the operations in 62 patients (35 LC and 27 OC) were compared by SF-36.
Results The conversion rate was 5.0%. Mean follow-up periods in LC and OC were 62.3 and 62.1 months, respectively. Operation time was longer in LC than in OC, although the difference was not significant in the later period. Bleeding and postoperative stay were reduced in LC. The morbidity rate was 18.6% in LC and 26.4% in OC. The 5-year overall survival in LC and OC were 94.6% vs. 92.0% for stage I, 95.2% vs. 91.8% for stage II, and 80.9%

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vs. 79.1% for stage III, respectively. The corresponding 5-year disease-free survival were 94.0% vs. 88.4%, 92.1% vs. 84.0%, and 64.3% vs. 65.4%, respectively. Recurrence rates did not differ between groups. In the analysis of HRQOL scores, role physical, bodily pain, social functioning, role emotional, and physical component summary scores in LC were better than in OC.

Conclusions In LC for colorectal cancer, short-term outcomes except operation time and mid-term HRQOL were better than in OC, and there were no adverse effects relating to long-term outcomes.

Keywords Case-matched study · Colorectal cancer · Laparoscopic resection · Health-related quality of life

Introduction

The use of laparoscopic resection (LC) for colon cancer has been prevalent worldwide since the early 1990s [1] but has become increasingly important in recent years, as studies have shown that its outcomes are better than or equal to those of open abdominal surgery (OC) for colon cancer [2–5]. Some randomized multicenter studies have compared short-term or long-term outcomes of LC and OC for colon cancer. However, the conversion and mortality rates in these studies have been relatively high because of differences in the techniques used at each institution. Although the results appear to be consistent in a large-scale multicenter study, differences have been reported in short-term outcomes depending on the number of cases at registration [6]. There is the potential for meta-analyses to give inconsistent results if the methodological quality is poor, even for randomized controlled trials (RCTs) [7]. Case-control studies are thought to provide weaker evidence than randomized studies, but enable sample characteristics to be better controlled. Several such studies have compared LC and OC for colorectal cancer [8–12]. Most have shown no adverse oncologic outcomes in either the short term or the long term. However, the sample sizes in these studies have been small or limited, and the case-selection criteria have tended to be poorly defined.

Moreover, there are few large-sized randomized studies of mid-term health-related quality of life (HRQOL) in colorectal cancer patients, and the results are controversial [5, 13, 14].

The current study analyzed our experience with LC for colorectal cancer over the past 15 years. Patients undergoing LC were matched to cases undergoing conventional OC in terms of several characteristics, including physical status. We compared the short-term and long-term outcomes for cases undergoing LC and OC for colorectal cancer in a single-center study. The mid-term HRQOL at 1–2 years after the operations was compared and assessed using the SF-36 Health Survey Questionnaire Second Japanese Version [15].

Patients and methods

Data for cases treated in our department were registered prospectively from 1992 and included patient characteristics, surgical outcomes, and long-term outcomes. Between June 1993 and March 2008, a total of 2,521 patients underwent resection for colorectal cancer at Yokohama City University Hospital, Japan. Among these, 570 patients underwent LC, the use of which for early colon cancer was initiated at our institution in June 1993.

Until March 2000, surgical indications for this technique were limited to a preoperative diagnosis of colon cancer with invasion through the muscularis mucosa into the submucosa (T1), no lymph node involvement (N0), and a non-bulky tumor. However, as our experience increased, the indications were gradually extended in April 2000 to include cancer with invasion through the submucosa into the muscularis propria (T2) and no lymph node invasion (N0). In April 2002, indications included cancer with invasion of the surrounding structures or with tumor cells on the free external surface of the bowel (T4) with the involvement of one to three nodes (N1) but excluding adjacent organ infiltration. In April 2005, cancer with the involvement of four or more nodes (N2) was included. Surgical indications for rectal cancer were extended to T2 N0 in 2001 and were expanded to include invasion through the muscularis propria into the subserosa but not to any neighboring organs or tissues (T3) and N1 for upper rectal cancer in 2007. In total, 246 patients underwent LC in the 12-year period up until 2004; the number increased rapidly after 2005, with 324 patients undergoing LC over a period of 3 years and 3 months. In most cases, the decision to use the LC or OC technique was made with the patient's informed consent, after the attending physician had presented the latest evidence concerning LC.

In order to compare outcomes, the LC and OC groups were matched in terms of the following variables: gender, age (within 10 years), American Society of Anesthesiologists (ASA) score (within one point), operative year, tumor location (right side of the colon, transverse colon, left side of the colon, upper rectum, and lower rectum), operative procedure (right-sided colectomy, transverse colectomy, left-sided colectomy, anterior resection of the rectum, abdominoperineal resection, and intersphincteric resection of the rectum), and International Union Against Cancer Tumor–Node–Metastasis (TNM) stage (0, I, IIA, IIB, IIIA, IIIB, IIIC, or IV). The exclusion criteria were as follows: emergency surgery, adjacent organ infiltration, histological types other than adenocarcinoma, simultaneous multiple cancers, and follow-up of the surviving patient for <1 year. The operation was carried out according to the standard radical cure procedure described in the seventh edition of the *Japanese General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus* [16]. Specifically, all operations were colectomies with dissection of the intestinal lymph nodes and the middle lymph node along the feeding blood vessels. In cancers classified as T2 or above, lymph node dissection around the root of the main feeding vessel was also performed. The same procedures were used for the lymph node dissections in the LC and OC cases. For rectal cancer, pelvic sidewall lymph node dissection was excluded for cases classified as T2 or below. All the operations in both groups were performed by a team from the same colorectal cancer treatment specialty. Operations enforced by the general surgeon and emergency operations were excluded. Three surgeons up to 1999 and four surgeons from 2000 onwards worked as colorectal cancer treatment specialists. There were replacements in personnel, and the surgeon's experience ranged from 3 to 13 years. The operations were performed by eight surgeons in total. All colorectal surgeons performed both the open and the laparoscopic surgery.

The oncologic outcomes of the surgery were compared between the LC and OC groups using the following variables: the proximal margin (millimeters), the distal margin (millimeters), and the number of harvested lymph nodes. The latter variable was compared in each respective cancer location. The distal margin in rectal cancer was also compared. The histopathological workup was described in detail. After excision of the specimen, the surgeon removed the lymph nodes from the mesocolon, and it was submitted to the pathology department. The pathologic diagnosis was made using hematoxylin–eosin staining.

Short-term results were defined as the operative results and the complications that occurred within 30 days after the operation. The following short-term results were recorded for all patients: the operation time (minutes), the operative blood loss (milliliters), the blood transfusion rate (percent), the details and rates of mortality and morbidity within 30 days, and the duration of the postoperative stay (days). Mortality was defined as death that occurred prior to leaving the hospital after the operation. Morbidity was defined by adverse events classified as grade 1 or above according to version 3.0 of the *Common Terminology Criteria for Adverse Events* [17]. These data were compared between the LC and OC groups. The years before 2004 were categorized as the earlier period, and those after 2005 were categorized as the later period. There were many limitations of the indication for LC in 1993–2004. It was expanded to include T4a and N2 in colon cancer after 2005, and the number of cases also increased. The learning curve rose with an increase in the number of cases. The LC and OC groups were compared in each of these periods. The short-term outcomes were also analyzed according to tumor location.

Long-term was defined as the period of more than 5 years after the operation. The long-term outcomes were evaluated according to the 5-year overall survival and the 5-year disease-free survival in the respective TNM stages, and the initial cancer recurrence rate in patients with curative resection (R0) except for stage IV. Curative resection (R0) was defined as having no vestigial remnant of cancer in histology [16]. The initial recurrence pattern was defined as local recurrence, peritoneal recurrence, or distant organ metastases (such as liver, lungs, and bones). Port-site recurrence was also included. The survival rates were calculated from the time of resection of the primary lesion to the date when either death or recurrence occurred. Survival was also compared according to the tumor location.

The postoperative follow-up methods were as follows: patients at stages 0 and I were followed-up with outpatient examinations and tumor-marker measurements once a year for 5 years; if an abnormality was detected, computed tomography (CT) and/or colonofiberscopy were performed. Patients at stage II were examined by CT and tumor-marker measurements every 6 months for 2 years, then once a year for the next 5 years. Patients at stage III were examined by CT and tumor-marker measurements every 4 months for 3 years, and then once a year for the next 5 years.

Postoperative adjuvant chemotherapy was administered to patients at stage III and high-risk stage II who were 75 years old or less, except in cases where this approach was rejected by the patient. The cases who received adjuvant chemotherapy before 1999 were excluded from the analysis because the adjuvant chemotherapies were not uniform. Beginning in 2000, intravenous 5-fluorouracil/leucovorin therapy was performed for stage III colonic cancer. Each course of treatment was 500 mg/m^2 5-Flourourcil and 75 mg/kg body weight 5-fluorouracil/leucovorin weekly for 6 weeks, followed by 2 weeks rest. Three courses of treatment were performed. In stage II colonic cancer, oral uracil-tegafur (UFT) was administered for 5 days per week at 500–600 mg/day. UFT therapy was performed for 52 weeks. No radiation therapy was administered. Neoadjuvant chemoradiotherapy was not performed on all rectal cancers, as neoadjuvant chemoradiotherapy for rectal cancer is not a standard treatment in Japan.

Mid-term was defined as the period between 12 and 24 months after the operation. HRQOL at 12–24 months after the operation was assessed using the SF-36 Health Survey Questionnaire Second Japanese Version. A question regarding the period until recovering to daily life besides the SF-36 was added to the questionnaire. Self-administered questionnaires were mailed to the patient's home with the agreement, and questionnaires that were returned were analyzed. SF-36 scores were based on the Japanese National Reference value [15]. They were compared for eight different health-related quality items that consisted of physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). The Physical and Mental Component Summaries (PCS, MCS) that were calculated from these eight items were compared. Additionally, the periods until recovering to daily life were compared.

Statistical analysis The statistical analysis was performed with the SPSS software package (version 11.0J for Windows; SPSS Inc., Chicago, IL, USA). The continuous variables were compared between groups using the Student's *t* test. Pearson's Chi-squared test or Fisher's exact test was used to compare discrete variables. Survival curves were produced using the Kaplan–Meier method. Statistically significant differences between the groups were determined by the log-rank test. A p value <0.05 was considered statistically significant (two-tailed test).

Results

During the 15-year study period, 258 of the 570 patients who underwent LC for colorectal cancer were matched to patients who underwent conventional OC. Among these, 252 underwent operations during the earlier period, and 264 patients underwent operations during the later period. The number of registrations and the number of patients with advanced cancer increased annually based on the extension of the surgical indications for LC (Table 1). However, this ceased after 2006, because we participated in the multicenter Japan Clinical Oncology Group Randomized Controlled Trial to Evaluate Laparoscopic Surgery for Colorectal Cancer (JCOG 0404) [18]. The demographic characteristics of both groups are shown in Table 2. The numbers of patients in each category of gender, operative year, operative procedure, tumor location, and TNM stage were the same in both groups, due to the matched control study design. Most of the other demographic data showed similar patterns between the two groups. Approximate values were used for age, ASA score, body surface area, and body mass index. The mean follow-up period of surviving patients was 62.1±31.3 months (range, 14–161 months) for the LC group and 62.3±30.5 months (range, 14–164 months) for the OC group (p=0.961).

Table 1 Number of registered patients and tumor–node–metastasis staging in every year

	TNM stage								Total
	0	I	IIA	IIB	IIIA	IIIB	IIIC	IV	
1993		4							4
1994	4	2	2						8
1995		2					2		4
1996	2	4			4				10
1997		12			2				14
1998	2	4							6
1999	1	7							8
2000	1	15	2		4	4	2		28
2001	2	18	4			8	2		34
2002		10	12		4	8			34
2003	4	20	10			6	4		44
2004	2	30	10		2	8	4	2	58
2005	2	20	24	2	4	14	10	4	80
2006		18	24	4	6	18	6	2	78
2007		40	28	2	6	14	10	2	102
2008			2		2				4
Total	20	206	118	8	34	80	40	10	516

Postoperative adjuvant chemotherapy was administered to 69 patients (26.7%) in the LC group and 60 patients (23.3%) in the OC group (p=0.416). The use of adjuvant chemotherapy did not differ significantly based on stage between the LC and OC groups (stage II, 7.9% vs. 4.8%, respectively, p=0.717; stage III, 77.9% vs. 70.1%, respectively, p=0.358; and stage IV, 80.0% vs. 60.0%, respectively, p=1.000). There were two patients in stage II and eight patients in stage III before 1999 who did not receive adjuvant chemotherapy.

There were ten stage IV patients. The sites of metastasis were three liver cases and two lung cases in LC, and four liver cases and one lung case in OC. In the LC group, two patients had liver metastases, and one patient had lung metastasis excised from 1 to 2 months after the colectomies. They received adjuvant systemic chemotherapy (5-fluorouracil/leucovorin) and have been living for 28–54 months. One patient with multiple liver metastases received systemic chemotherapy (Irinotecan/5-fluorouracil/leucovorin) and died of cancer 47 months later. One patient with lung metastases wanted only supportive care and died of cancer 22 months later. In the OC group, two patients had liver metastases excised 1 month after the colectomies. One patient has been living for 31 months without chemotherapy. The other had cancer relapses to the bone throughout the body and died of cancer 25 months later, although he received systemic chemotherapy (5-fluorouracil/leucovorin). Two patients with multiple liver metastases received systemic chemotherapy

Table 2 Patient demographics

Variable	Laparoscopic	Open	*P*
Mean age (years, mean ± SD)	64.8±9.8	65.8±10.5	0.266
Gender			
Female	100	100	1.000
Male	158	158	
American Society of Anesthesiologists score (mean ± SD)	1.50±0.60	1.53±0.63	0.475
Body surface area (m^2, mean ± SD)	1.59±0.19	1.58±0.18	0.627
Body mass index (kg/m^2, mean ± SD)	22.6±3.5	23.1±3.6	0.451
Tumor location			1.000
Right-sided colon	53	53	
Transverse colon	16	16	
Left-sided colon	110	110	
Upper rectum	63	63	
Lower rectum	16	16	
Operative procedure			1.000
Right colectomy	53	53	
Transverse colectomy	16	16	
Left-sided colectomy	110	110	
Anterior resection of rectum	77	77	
Intersphincteric resection of rectum	1	1	
Abdominoperineal resection of rectum	1	1	
TNM stage			1.000
0	10	10	
I	103	103	
IIA	59	59	
IIB	4	4	
IIIA	17	17	
IIIB	40	40	
IIIC	20	20	
IV	5	5	
Follow-up period of survival (months, mean ± SD)	62.1±31.3	62.3±30.5	0.961
Postoperative adjuvant chemotherapy	69 (26.7%)	60 (23.3%)	0.416
Stage II	5 (7.9%)	3 (4.8%)	0.717
Stage III	60 (77.9%)	54 (70.1%)	0.358
Stage IV	4 (80.0%)	3 (60.0%)	1.000

SD standard deviation

(Irinotecan/5-fluorouracil/leucovorin) and died of cancer 7 and 48 months later, respectively. One patient with lung metastases wanted only supportive care and died of cancer 7 months later.

In total, 13 patients underwent conversion from LC to OC, and the conversion rate was 5.0%. These included 11 cases of technical problems, eight cases in which the operative view could not be obtained (because of obesity in five patients and a narrow pelvis in three patients), two cases in whom bleeding could not be controlled, one case due to problems with the separation device, two cases based on progression of the cancer, and one case due to T3 in the operative finding, because the indication for LC was limited to T1 in 1995. The other case was diagnosed as peritoneal metastasis, so the peritoneal nodule was excised. However, it was not metastasis.

Oncologic outcome of surgery The mean number of lymph nodes harvested was 24.1±13.4 (range, 1–92) in the LC group and 25.2±15.3 (range, 1–107) in the OC group (p+ 0.408; Table 3). Because the indication for LC was expanded to include advanced colon cancer in the latter term, the number of harvested lymph nodes was more in the latter than in the first term. There were no differences between LC and OC in harvested LN number at first and latter term, so there was no difference of the background (Table 3). There was no significant difference between the groups with respect to cancer location. The mean proximal margin and mean distal margin was 111±54 and 84±63 mm, respectively, in the LC group and 118±66 and 83±58 mm, respectively, in the OC group (p=0.239, p=0.864, respectively). The mean distal margin for rectal cancer was

Table 3 Oncologic outcome of surgery

Variable	Laparoscopic	Open	*P*
Number of lymph nodes harvested (mean ± SD)	24.1±13.4	25.2±15.3	0.408
Term			
First (mean ± SD)	20.4±11.4	23.5±15.1	0.063
Latter (mean ± SD)	27.7±14.3	26.7±15.4	0.606
Location			
Right-sided colon (mean ± SD)	28.0±13.9	28.5±13.9	0.851
Transverse colon (mean ± SD)	18.6±13.4	20.0±14.9	0.776
Left-sided colon (mean ± SD)	23.0±14.4	22.2±15.5	0.672
Upper rectum (mean ± SD)	25.5±10.7	28.1±15.1	0.273
Lower rectum (mean ± SD)	18.6±11.6	26.6±15.0	0.102
Proximal margin (millimeter, mean ± SD)	111±54	118±66	0.238
Distal margin (millimeter, mean ± SD)	84±63	83±58	0.864
Distal margin in rectal cancer (millimeter, mean ± SD)	43±24	37±24	0.164

43±24 mm in the LC group and 37±24 mm in the OC group (p=0.164). In both groups, the circumferential margins were negative in all patients.

Short-term outcomes There was no mortality in either group (Table 4). There was a significant difference in the operation time between the LC and OC groups (255±77 vs. 210±85 min, respectively, p<0.001). The analysis according to time period showed that a difference of 78 min during the earlier period (p<0.001) was shortened to 16 min during the later period and was no longer significant (p=0.100). The analysis according to tumor location revealed significant differences at all sites except for the transverse colon (p=0.074). The overall amount of bleeding differed significantly (125±214 vs. 254±266 g in the LC and OC groups, respectively, p<0.001) and differed significantly for all periods and locations (Table 4), except for the right side of the colon (p=0.486). The analysis of total patient morbidity within 30 days revealed that the rate was significantly lower in the LC group than in the OC group (18.6% vs. 26.4%, respectively, p=0.045). However, there were no significant differences between the two periods at each location. The analysis of morbidity showed that the digestive disorder rate was lower in the LC group than in the OC group (p=0.030). There was no significant difference in the rate of bowel obstruction (2.3% vs. 5.8%, respectively, p=0.072) or respiratory disorder (0.4% vs. 2.3%, respectively, p=0.122), although both tended to be lower in the LC group. The estimated rate of anastomotic leakage in cases with reconstruction after rectal cancer was similar between the LC and OC groups (9.0% vs. 12.8%, respectively, p=0.609). The overall duration of postoperative stay differed significantly among all periods and locations, except for the transverse colon (p=0.660). The duration of postoperative stay in the LC group was shorter than that in the OC group (11.7±8.4 vs. 16.4±10.3 days, respectively, p<0.001) and differed significantly for all periods and locations (Table 4), except for the transverse colon (p=0.660). In both groups, most of the short-term outcomes were improved in the later period compared with the earlier period, with the exception of the morbidity rate in the LC group.

Long-term outcomes The 5-year overall survival rates for the LC and OC groups were 94.6% vs. 92.0%, respectively, for stage I (log-rank test, p=0.249, Fig. 1a), 95.2% vs. 91.8%, respectively, for stage II (p=0.521, Fig. 1b), and 80.9% vs. 79.1%, respectively, for stage III (p=0.822, Fig. 1c). The corresponding 5-year disease-free survival rates were 94.0% vs. 88.4%, respectively, for stage I (p=0.139, Fig. 2a), 92.1% vs. 84.0%, respectively, for stage II (p=0.328, Fig. 2b), and 64.3% vs. 65.4%, respectively, for stage III (p=0.629, Fig. 2c). Based on the analysis of tumor location, there was no significant difference in overall and disease-free survival at all stages (Table 5).

R0 with the exception of stage IV was performed in 253 patients in both groups. In total, 27 patients (10.7%) in the LC group and 28 patients (11.1%) in the OC group showed recurrence (p=0.100). One patient in the LC group had a port-site recurrence accompanied by peritoneal metastases 25 months after surgery. This patient had stage IIIC rectosigmoid cancer that involved massive lymph node metastases; there was a metastasis in 30 of 36 dissected lymph nodes. The patient underwent chemotherapy after the first recurrence but died of peritoneal and lung metastases 47 months postoperatively. There was no difference in the recurrence pattern including repetition between the two groups (Table 6). There was no difference in the causes of death between the two groups (Table 6).

Table 4 Short-term outcomes

Variable	Laparoscopic	Open	*P*
Operative time (minutes, mean ± SD)	255±77	210±85	<0.001
Term			
First (1993–2004; minutes, mean ± SD)	298±68	220±74	<0.001
Latter (2004–2008; minutes, mean ± SD)	217±63	201±93	0.100
Location			
Right-sided colon (minutes, mean ± SD)	226±76	179±57	0.001
Transverse colon (minutes, mean ± SD)	261±100	204±63	0.067
Left-sided colon (minutes, mean ± SD)	251±73	203±94	<0.001
Upper rectum (minutes, mean ± SD)	265±63	222±68	<0.001
Lower rectum (minutes, mean ± SD)	326±82	298±105	0.410
Blood loss (gram, mean ± SD)	125±214	254±266	<0.001
Term			
First (gram, mean ± SD)	167±207	279±250	<0.001
Latter (gram, mean ± SD)	88±214	232±279	<0.001
Location			
Right-sided colon (gram, mean ± SD)	125±296	157±122	0.486
Transverse colon (gram, mean ± SD)	95±70	179±122	0.030
Left-sided colon (gram, mean ± SD)	104±142	212±208	<0.001
Upper rectum (gram, mean ± SD)	118±167	346±359	<0.001
Lower rectum (gram, mean ± SD)	325±390	521±338	0.141
Blood transfusion (%)	0 (0%)	8 (3.1%)	0.007
Mortality rate (%)	0	0	1.000
Morbidity within 30 days	48 (18.6%)	68 (26.4%)	0.045
Term			
First	22 (17.5%)	34 (27.0%)	0.095
Latter	26 (19.7%)	34 (25.8%)	0.304
Location			
Right-sided colon	10 (18.9%)	17 (32.1%)	0.180
Transverse colon	2 (12.5%)	6 (37.5%)	0.220
Left-sided colon	20 (18.2%)	19 (17.3%)	1.000
Upper rectum	11 (17.5%)	19 (30.2%)	0.142
Lower rectum	5 (31.3%)	7 (43.8%)	0.716
Surgical site infection	25 (9.7%)	22 (8.5%)	0.650
Bowel obstruction	6 (2.3%)	15 (5.8%)	0.072
Respiratory disorder	1 (0.4%)	6 (2.3%)	0.122
Circulatory disorder	1 (0.4%)	2 (0.8%)	1.000
Digestive disorder	0 (0%)	6 (2.3%)	0.030
Anastomotic leakage	10 (3.9%)	13 (5.0%)	0.671
Anastomotic leak in rectal cancer	7 (9.0%)	10 (12.8%)	0.609
Duration of postoperative stay (days, mean ± SD)	11.7±8.4	16.4±10.3	<0.001
Term			
First (days, mean ± SD)	12.7±9.2	17.8±10.7	<0.001
Latter (days, mean ± SD)	10.9±7.6	15.2±9.7	<0.001
Location			
Right-sided colon (days, mean ± SD)	9.8±3.7	16.6±11.6	<0.001
Transverse colon (days, mean ± SD)	14.3±16.2	16.4±9.0	0.660
Left-sided colon (days, mean ± SD)	10.8±5.3	14.7±9.3	<0.001
Upper rectum (days, mean ± SD)	12.8±11.1	17.6±10.3	0.013
Lower rectum (days, mean ± SD)	18.5±10.6	22.6±11.4	0.305

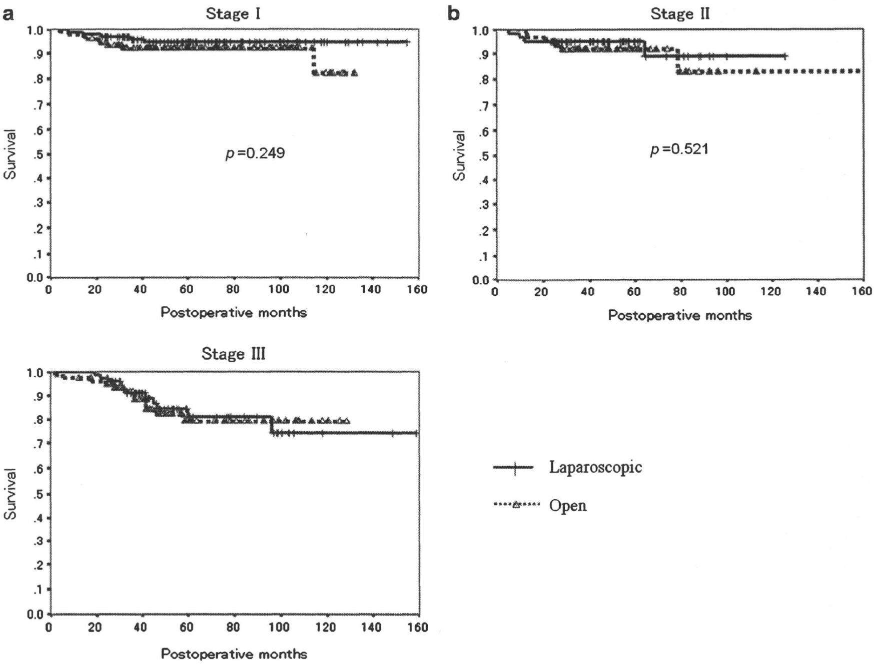

Fig. 1 There were no significant differences in overall survival at all stages

Mid-term HRQOL Seventy-eight patients 1–2 years after operation in 2007–2008 were research subjects. Of 78 patients, 62 replied to the questionnaire (79.5%). A total of 35 of 43 LC patients (81.4%) and 27 of 35 OC patients (77.1%) were analyzed. No significant differences were found between LC and OC groups in characteristics (Table 7). There were significant differences in RP (53.0±8.3 vs. 44.2±13.5, respectively, p=0.002), BP (57.3±7.4 vs. 52.7±10.3, respectively, p=0.046), SF (53.2±10.5 vs. 47.6±11.1, respectively, p=0.049), RE (53.6±6.2 vs. 45.4±12.5, respectively, p=0.002), and PCS scores (46.2±7.4 vs. 41.4±10.4, respectively, p=0.039) between the two groups (Fig. 3). There were no other statistically significant differences; however, all HRQOL scores of the LC group were better than those of the OC group. The periods until recovering to daily life did not differ significantly between the two groups; however, they tended to be shorter in the LC group (73.5±89.4 vs. 111.4±98.4 days, respectively, p=0.145). Postoperative adjuvant chemotherapy affected the period until recovering to daily life in both groups (chemotherapy, 143.1±111.5 days versus surgery alone, 68.1±77.7 days, p=0.007).

Discussion

Several reports on short-term and long-term studies and large-scale RCTs have demonstrated that LC is equal to OC in terms of morbidity and survival rates [2–5]. A retrospective large-scale multicenter study of LC in 1,495 cases of colon cancer and 541 cases of rectal cancer in Japan showed, in the short term, that the conversion rate was 4.8% for colon cancer and 4.4% for rectal cancer, 1.4% of patients experienced complications during surgery, and the morbidity rate was 11.2% [19]. Another large-scale retrospective study compared 1,092 patients who underwent sigmoid colectomy with LC and 9,511 patients who underwent sigmoid colectomy with OC and demonstrated advantages of the former in terms of a shorter postoperative hospital stay and a lower wound infection rate [20].

Significant advantages with respect to short-term results have also been shown in larger-scale studies, such as nationwide trials or those exceeding 100 centers, even when the differences have been relatively small [21, 22]. However, these large-scale examinations tend to have been limited by

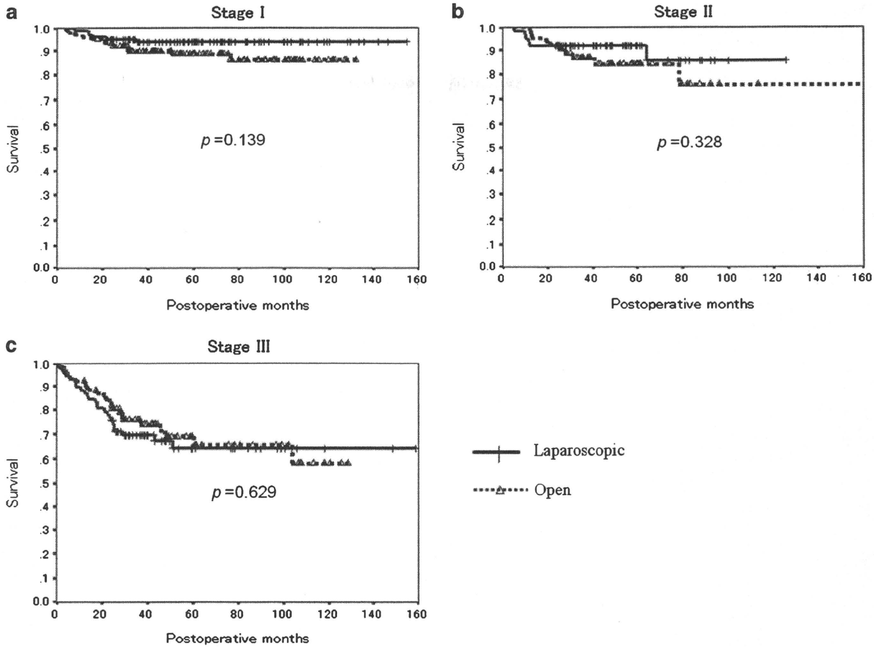

Fig. 2 There were no significant differences in disease-free survival at all stages

poorly defined registration conditions. In addition, the maintenance of quality appears to be difficult in research relating to surgical techniques. The conversion rate was comparatively high (11–23%) in some well-known RCTs [2–5]. One trial reported a mortality rate of 5%, although it was possible that the quality of the analysis was limited. By contrast, several case-matched control studies have reported comparisons between LC and OC [8–12]. In these reports, the comparisons between open and laparoscopic surgery were done with two to five matched variables, including gender, age, year of surgery, site of cancer, staging of cancer, operating procedure, and surgeon. We matched seven variables (gender, age, ASA score, operative year, tumor location, operative procedure, and TNM stage) in the present study to more carefully compare short-term and long-term results. The case-matched control study design allows the quality of the data and various conditions to be maintained. The quality of surgical techniques can also be controlled in single-facility studies. However, one limitation of this approach is the reduced number of patients, which might bias the results. In the present study, to maximize the quality of the comparison, many of the registration conditions were matched. Moreover, to include a large number of registrations, the registration period was set at 15 years. A previous case-matched control study compared 172 examples [9]. By contrast, the current study compared 258 examples, with a conversion rate of 5.0%, a morbidity rate of 18.6%, and no mortality. We therefore believe that the results of the current analysis are comparable to those of a large-scale multicenter study with advanced facilities. The use of propensity score is appropriate for matching of a case-matched control study. There is a limitation in this study because of no use of propensity score. However, there were the time-related changes in the indication for LC; it was thought that matching the backgrounds as closely as possible and comparing with OC was the most meaningful approach. The dropout rate increased because seven variables were matched.

The analysis of the short-term outcomes revealed that the morbidity rate was lower in the LC group than in the OC group. This result was similar to those of previous large-scale reports [21, 22]. However, there were no significant

Table 5 Five-year overall and disease-free survival rates at respective tumor locations for patients at all stages

Location		Laparoscopic (%)	Open (%)	*P*
Right-sided colon				
Stage I	5-year OS[a]	84.0	79.3	0.666
	5-year DFS[b]	84.0	79.3	0.666
Stage II	5-year OS	94.1	94.1	0.552
	5-year DFS	94.1	88.2	0.988
Stage III	5-year OS	71.1	55.6	0.663
	5-year DFS	44.4	66.7	0.959
Transverse colon				
Stage I	5-year OS	100	85.7	0.317
	5-year DFS	100	85.7	0.317
Stage II	5-year OS	100	75.0	0.317
	5-year DFS	75.0	75.0	0.919
Stage III	5-year OS	100	66.7	0.317
	5-year DFS	66.7	66.7	0.486
Left-sided colon				
Stage I	5-year OS	100	92.2	0.066
	5-year DFS	97.4	88.9	0.085
Stage II	5-year OS	96.3	96.0	0.964
	5-year DFS	92.6	91.4	0.927
Stage III	5-year OS	85.6	90.0	0.483
	5-year DFS	62.2	77.1	0.216
Rectum				
Stage I	5-year OS	93.6	100	0.146
	5-year DFS	94.6	92.7	0.995
Stage II	5-year OS	93.3	86.2	0.276
	5-year DFS	93.3	70.6	0.078
Stage III	5-year OS	77.2	78.9	0.993
	5-year DFS	75.4	65.2	0.598

[a] Overall survival rate

[b] Disease-free survival rate

differences in specific illnesses excluding the digestive symptoms. There were no differences in the outcomes of surgical site infections (9.7% vs. 8.5%, respectively). Intestinal obstruction (2.3% vs. 5.8%, respectively) is thought to have contributed to the overall illness rates. This corresponds to grade 2 in the Clavien system [23]. It is thought to be an important result, even though it was not a significant difference (p=0.072). The LC group showed better short-term outcomes, with the exception of operation time. However, during the later period, the operation time did not differ significantly owing to a learning curve effect. It seems that the learning effect in LC also improved OC outcomes because the short-term results of OC were improved at the latter term. Only the morbidity rate of the LC group did not improve during the later stage because the number of cases of rectal cancer or advanced cancer cases increased during this period.

Table 6 The initial recurrence pattern and the causes of death

	Laparoscopic	Open	*P*
Recurrent site			
Liver	13 (5.1%)	14 (5.5%)	1.000
Lung	7 (2.8%)	8 (3.2%)	1.000
Peritoneum	4 (1.6%)	3 (1.2%)	1.000
Local	3 (1.2%)	4 (1.6%)	1.000
Lymph node	3 (1.2%)	2 (0.8%)	1.000
Bone	2 (0.8%)	0 (0%)	0.449
Port site	1 (0.4%)	0 (0%)	1.000
Causes of death			0.261
Colorectal cancer death	11 (4.3%)	9 (3.6%)	
Other cancer death	3 (1.2%)	2 (0.8%)	
Other disease	7 (2.8%)	16 (6.3%)	

Several previous studies have reported on the efficacy of oncologic resection by lymph node harvesting in LC [24–26]. Tsikitis et al. reported that the total number of lymph nodes analyzed in stage III colon cancer was not a prognostic indicator of the cancer-specific and disease-free

Table 7 Patient's demographics for research of the health-related quality of life graphics

Variable	Laparoscopic (n=35)	Open (n=27)	*P*
Mean age (years, mean ± SD)	65.7±9.0	63.7±9.7	0.424
Gender			
Female	18	12	0.618
Male	17	15	
American Society of Anesthesiologists score (mean ± SD)	1.66±0.54	1.63±0.56	0.846
Tumor location			0.503
Right-sided colon	9	6	
Transverse colon	2	2	
Left-sided colon	11	13	
Rectum	13	6	
Operative procedure			0.503
Right colectomy	9	6	
Transverse colectomy	2	2	
Left-sided colectomy	11	13	
Anterior resection of rectum	13	6	
TNM stage			0.915
0	0	0	
I	13	11	
II	9	8	
III	12	7	
IV	1	1	
Postoperative adjuvant chemotherapy	10 (28.6%)	7 (25.9%)	0.817
Research time of the health-related quality of life after surgery (months, mean ± SD)	17.6±3.7	18.2±3.6	0.509

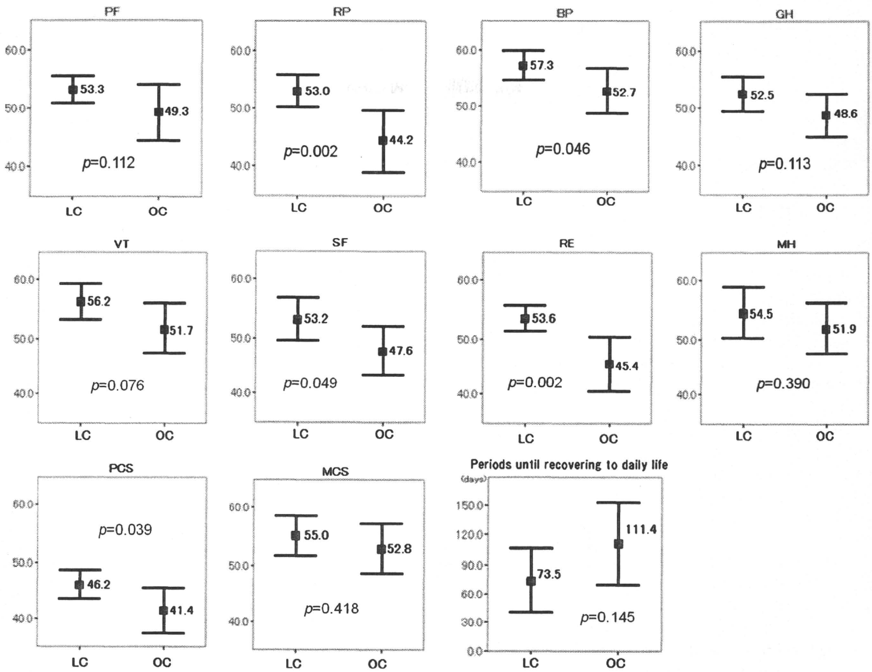

Fig. 3 Comparison of the health-related quality life scores. The *error bars* display 95% confidence interval of the mean value. There were significant differences in RP, SF, RE, and PCS scores between two groups. The scores of them in LC group were better than OC group. *PF* physical functioning, *RP* role physical, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social functioning, *RE* role emotional, *MH* mental health, *PCS* physical component summary, *MCS* mental component summary

survival rates [27]. The important factors appeared to be accurate staging, appropriate surgery, and the identification of lymph nodes in the colon cancer specimen. The surgical margin and the number of harvested lymph nodes seemed to be adequate for our comparison of LC with OC, and there appeared to be no oncological problems. In this study, the circumferential margins were negative in all patients. This may have been because the indication for LC was limited to T4 colon cancer and T2 lower rectal cancer without other internal organ infiltration.

The analysis of the long-term outcomes showed similar oncologic results for all stages, probably because numerous variables were matched in the current study. It was suggested that peritoneal metastasis may be increased due to being overlooked intraoperatively and the influence of carbon dioxide pneumoperitoneum in the laparoscopic surgery [28–31]. However, the peritoneum recurrence rate was 1.6% in LC and 1.2% in OC, and the difference was not significant. Peritoneal metastasis would be unlikely to increase if there was no inappropriate technique, such as touching of the tumor directly. There was no difference in the overall and disease-free survival of all stages. If the cancer stage and physical status of patients undergoing LC are equivalent to those of patients undergoing OC, both approaches can be seen to have similar survival benefits.

However, the current study was limited because it was not a randomized trial. A high-quality large-scale RCT is necessary to obtain stronger evidence. The JCOG 0404 multicenter randomized study of laparoscopic versus open surgery for T3/4 colon cancer is currently ongoing, with results expected imminently [18]. We greatly anticipate a large-scale multicenter randomized study of the long-term results in advanced cancer. Additionally, the current analysis of tumor locations was less effective for lower rectal cancer and transverse colon cancer. Analyzing long-term outcomes in a single-center study appears to be difficult for tumors of the transverse colon cancer due to the relatively small number of patients. A phase II multicenter study in stage 0 or I disease of rectal cancer was started under the direction of the Japan Society of Laparoscopic Colorectal Surgery beginning in 2008 [32]. Another multicenter study of transverse colon cancer is scheduled to begin soon by this society. The results of these clinical studies are expected to clarify the effectiveness of laparoscopic surgery.

There are few large-scale multicenter randomized studies of HRQOL after laparoscopic and open resection (OC) for colorectal cancer [5, 13, 14]. The Clinical Outcome of Surgical Therapy (COST) group analyzed HRQOL in 428 patients at 2 days, 2 weeks, and 2 months after surgery using 13 scoring items. They reported that physical pain in the hospital and HRQOL 2 months postoperatively were superior in LC compared with OC [13]. Braga analyzed HRQOL in 391 patients at 12, 24, and 48 months after surgery using the SF-36 and reported that GH, PF, and SF at 12 months and SF at 24 months were better in LC [14]. The UK Medical Research Council Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer trial (CLASCC) Group analyzed HRQOL in 696 patients at 2 weeks and 3, 18, and 36 months after surgery using the EORTC QOL-C30 [33] and QLQ-C30 [34]. They reported no significant difference between LC and OC. In another randomized study, HRQOL at 4 months after surgery in LC was better than in OC [35]. In a retrospective study of benign bowel disease, there was no significant difference in HRQOL between LC and OC at 39 months [36]. Thus, short-term HRQOL of LC is thought to be excellent; however, the superiority of mid/long-term HRQOL of LC is controversial. Our data showed that RP, BP, SF, RE, and PCS scores in LC were significantly better than in OC. Five other items and the period until full recovery to daily life did not differ significantly; however, all mean values in LC exceeded those in OC. Moreover, nine of ten items in LC were better than the Japanese national reference value, but five were better in OC. These results suggest that mid-term QOL with LC is better than that with OC. Chiefly, physical items and mental functions were influenced because the RE score was better.

In this study, SF-36 scores were normalized to the Japanese National Reference values published in 2002 [15]. This normalization makes it easy to compare scores. Moreover, a self-administered questionnaire form was used. The response rates might lower with this type of questionnaire than with the interview type, but this method is preferred to reduce possible biases in response [14].

This study never denies high-quality RCT. We would like to send our data to a more refined research group such as COST [4]. In this study, the results obtained in a single institute, according to almost the same procedure, were compared, matching a lot of variables and matching the background. It is smaller than the RCT of the multicenter with regards to the number of cases. However, there are a lot of numbers of cases with examination in single facilities in the past case-matched report. It is thought that the conclusion is more detailed because a lot of corresponding variables were able to be put out.

Conclusion

This study demonstrated that LC outperformed OC with regard to short-term outcomes and mid-term HRQOL, with the exception of the operation time. Moreover, LC had no adverse effects in respect to long-term outcomes. LC was therefore shown to be a suitable therapy for colorectal cancer in this single-center case-matched study. However, a large-scale multicenter study is necessary for transverse colon and lower rectal cancer.

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大腸癌に対する腹腔鏡手術と開腹手術の術後中期健康関連 QOL の比較

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COMPARISON OF THE POST-OPERATIVE MID-TERM HEALTH RELATED QUALITY OF LIFE BETWEEN LAPAROSCOPIC AND OPEN SURGERY FOR COLORECTAL CANCER

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