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J Gastrointest Surg (2010) 14:500–505
DOI 10.1007/s11605-009-1105-2

ORIGINAL ARTICLE

Long-Term Outcome of Metachronous Rectal Cancer Following Ileorectal Anastomosis for Familial Adenomatous Polyposis

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Received: 19 July 2009 / Accepted: 9 November 2009 / Published online: 25 November 2009

Abstract
Background Total colectomy with ileorectal anastomosis (IRA) for familial adenomatous polyposis (FAP) carries a potential risk of metachronous cancer in the residual rectum. This study evaluated the risk of cancer development in the residual rectum.
Methods Ninety-six patients who underwent initial surgery for prevention and cure of FAP were studied, and a clinicopathologic comparison was conducted between 59 patients who underwent IRA and 24 who underwent total proctocolectomy.
Results The 5-year overall survival rates were 94% after IRA and 95% after total proctocolectomy with no significant difference. The incidence of dense-type rectal polyps (4/17, 24%) was significantly higher in patients who developed metachronous rectal cancer following IRA compared to that in patients who did not (1/39, 3%). Moreover, 60% of patients with dense-type colon polyps developed metachronous rectal cancer compared to 24% in patients without and 80% of those with dense type rectal polyps developed metachronous rectal cancer compared to 25% without. Endoscopic surveillance of the eight Tis or T1 patients was performed at intervals of 6 months to 1 year after IRA but was not performed in three T3 patients for more than 2 years.
Conclusions Effective IRA requires selection of patients without invasive rectal cancer and without dense rectal polyps in whom long-term postoperative follow-up of the residual rectum is possible.

Keywords Ileorectal anastomosis · Familial adenomatous polyposis · Metachronous rectal cancer

Introduction

The prevention of advanced colorectal cancer requires colectomy or proctocolectomy in patients with familial adenomatous polyposis (FAP) at a premalignant stage.[1] In Western countries, total proctocolectomy with ileal-pouch anal anastomosis (IPAA) is often indicated for preventive and curative resection, whereas total colectomy with ileorectal anastomosis (IRA) is more common in Japan. IPAA is an ideal strategy to reduce the risk of postoperative cancer in the residual rectum but often causes postoperative dyschezia[2,3] and deteriorated quality-of-life (QOL).[2–4] IRA provides superior postoperative bowel function compared to IPAA and is sometimes indicated in selected patients in Japan on this basis; however, the risk of cancer in the residual rectum is unavoidable after IRA, and prevention requires long-term endoscopic surveillance.

It has been suggested that IRA should be limited to patients with non-dense colorectal polyps;[5–8] patients with

A part of this paper was presented at the 2nd Biennial Scientific Meeting of International Society for Gastrointestinal Hereditary Tumors held between March 27 and 30, 2007 in Yokohama, Tokyo.

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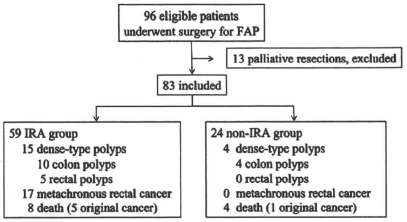

Figure 1 Study profile.

attenuated familial adenomatous polyposis;[9] young females who desire future pregnancy;[10] and patients for whom long-term follow-up can be conducted;[8] however, only a few studies have compared cancer recurrence and prognosis between IRA and IPAA. In this study, we examined these issues and identified risk factors for the development of metachronous cancer in the residual rectum following IRA.

Material and Methods

Ninety-six patients (male 62, female 34) who underwent initial surgery for prevention and cure of FAP at the National Cancer Center Hospital (Tokyo, Japan) between 1962 and 2007 were studied retrospectively. Patients who underwent palliative resections (partial colectomy, abdominoperineal resection, or ileostomy) were excluded. A clinicopathologic comparison was conducted between 59 patients who underwent IRA (IRA group) and 24 (non-IRA group) who underwent total proctocolectomy with ileoanal anastomosis (IAA) or IPAA, or total proctocolectomy with ileostomy. Age at the first operation, sex, surveillance period, density of polyps, presence of coexisting cancer, recurrence, overall survival, and relapse-free survival were examined in the two groups. More than 2,000 polyps in colon tissue samples were defined as dense-type polyposis and less than 2,000 polyps were defined as non-dense type. The number of polyps was counted roughly by the pathologist in charge. Rectal polyposis with more than 20 polyps on endoscopy was defined as a dense type, and less than 20 polyps were defined as a non-dense type. Clinicopathological factors were also compared between subgroups of patients who did and did not develop cancer in the residual rectum following IRA. Patients with intramucosal carcinoma were included in the subgroup who developed cancer in the residual rectum. Background and surgical data were obtained from a retrospective study of medical records. Since the study was a single-center observational design, approval by the institutional review board was not required in the present study.

Fisher's exact test and chi-square test were used for comparison between groups. Continuous nonparametric data were analyzed by the Mann–Whitney *U* test. Recurrence and survival rates were analyzed by the Kaplan–Meier method, and comparison of outcomes was conducted by log-rank test. A significant difference was assumed at $P<0.05$. Analyses were performed by using software (JMP, Version 7. SAS Institute Inc., Cary, NC).

Results

Figure 1 shows the study profile. Chronological changes in the operative procedure are shown in Table 1. IRA was performed in 42% patients (18/43) from 1962 to 1990 and in 77% (41/53) from 1991 to 2007.

The patient demographics are summarized in Table 2. Significantly more patients had coexisting rectal cancer in the non-IRA group; however, no significant differences were observed regarding the rate of patients with dense-type colorectal polyps between the two groups.

Prognosis was examined in all patients except for three Stage IV patients in the IRA group. The 5- and 10-year overall survival rates were 94% and 94%, respectively, in the IRA group, and 95% and 90%, respectively, in the non-IRA group, with no significant difference between groups (Fig. 2). There was also no significant difference in relapse-free survival rates between groups ($p=0.7111$; Fig. 3). There were eight deaths in the IRA group (five due to the original cancer and three of unknown cause) and four in the non-IRA group (one due to the original cancer, two due to other diseases, and one of unknown cause).

The patterns of cancer recurrence and metachronous cancer development in each group are shown in Table 3. Metachronous rectal cancer was detected in 17 patients in the IRA group.

A comparison of the 17 patients (30%) with metachronous cancer in the residual rectum and 39 patients (70%)

Table 1 Surgery for Familial Adenomatous Polyposis between 1962 and 2007

	1962–1990	1991–2007
IRA	18 (42)	41 (77)
IPAA	15 (35)	9 (17)
APR	5 (12)	1 (2)
Others	5 (12)	2 (4)
Total	43	53

Values in parentheses are percentages

IRA total colectomy with ileorectal anastomosis; *IPAA* total proctocolectomy with ileal-pouch anal anastomosis; *APR* abdominoperineal resection

Table 2 Patient Characteristics between IRA Group and Non-IRA Group

		IRA group (n=59)	Non-IRA group (n=24)	P value
Median age at operation (range)		30 (13–65)	31 (20–51)	0.9651
Sex	Male	35	19	0.1272
	Female	24	5	
Median follow-up (years)		8.9	16.1	0.1624
Colon polyps	Dense-type	10	4	1.0000
	Not dense-type	49	20	
Rectal polyps	Dense-type	5	0	0.3148
	Not dense-type	54	24	
Colon cancer	Present	30	7	0.0906
	Absent	29	17	
Rectal cancer	Present	5	7	0.0334
	Absent	54	17	
Pathological TNM stage for patients with cancer		31	11	
	0	12	2	0.5974
	I	5	2	
	IIA	1	0	
	IIB	0	0	
	IIIA	2	1	
	IIIB	5	4	
	IIIC	3	2	
	IV	3	0	

without cancer following IRA showed that cancer of the residual rectum occurred more frequently in patients with dense-type rectal polyps (p=0.0259; Table 4), and the incidence of dense-type rectal polyps (4/17, 24%) was significantly higher among those who developed metachronous rectal cancer following IRA compared to that in patients who did not (1/39, 3%). Moreover, 60% of patients with dense-type colon polyps developed metachronous rectal cancer compared to 24% in those without, and 80% of those with dense-type rectal polyps developed compared to 25% without.

Treatment after metachronous rectal cancer is demonstrated in Table 5. Initially, local therapy was performed for 10 of the 17 patients with cancer in the residual rectum, and surgery was performed on seven. Four of the 10 patients who initially received local treatment subsequently underwent radical surgery because of metachronous rectal cancer that could not be managed by endoscopic resection or pathological invasive cancer. Thus, surgery was required in 65% (11/17) of patients who developed cancer in the residual rectum. The surgery was performed at an average of 8.8 years after IRA (range 1.3–23.3 years).

Among the 11 patients who required radical surgery after IRA, eight with Tis-T1 invasion had undergone endoscopic surveillance at intervals of 6 months to 1 year after IRA, but the other three T3 patients did not undergo surveillance for more than 2 years before the second operation because of patient-related circumstances that had interrupted the

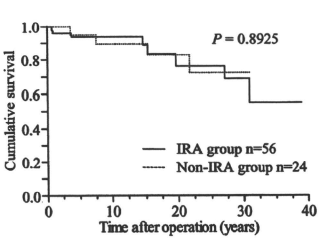

Figure 2 Overall survival rates in IRA and non-IRA groups.

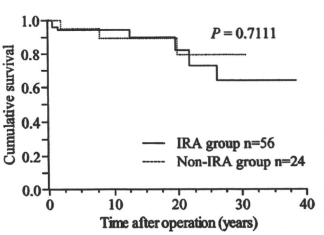

Figure 3 Relapse-free survival rates in IRA and non-IRA groups based on cancer recurrence.

Table 3 Pattern of Recurrence between IRA Group and Non-IRA Group

		IRA group (n=59)	Non-IRA group (n=24)
Metachronous cancer	Rectum	17	–
Recurrence	Liver	2	2
	Lung	0	0
	Small intestine	0	1
Total		19	3

postoperative surveillance. Regarding the surgical procedure of the 11 patients who required radical surgery after IRA, sphincter-preserving operations (IAA or IPAA) were performed in 88% (7/8) of patients with pathological Tis/T1 lesion, while 66.7% (2/3) of patients with pathological T3 lesion.

Discussion

A non-IRA procedure is ideal for preventive resection for patients with FAP to reduce the risk of metachronous cancer in the residual rectum, but IRA provides superior postoperative bowel function through alleviation of postoperative dyschezia and is sometimes indicated in Japan. Our findings demonstrate that IRA has no adverse effect on long-term prognosis, provided that appropriate surveillance is performed, despite the high risk of cancer development in the residual rectum. This suggests that IRA may be an option for selected patients who seem to be appropriately screened after IRA.

There have been several comparisons of IRA and non-IRA procedures, and IRA has been found to be superior to IPAA in that it provides a satisfactory level of postoperative defecation.[2,3] Some studies have reported improved QOL after IRA compared to IPAA,[2,3] but others have found no difference between these procedures based on findings from questionnaire surveys using the Short Form-36 Health Survey and the European Organization for Research and Treatment of Cancer Colorectal QoL Questionnaire.[4] Duijvendijk et al. had found no difference regarding QOL between the IRA and IPAA groups based on the responses to questionnaire surveys. Female fecundity has been found to deteriorate following IPAA compared with IRA,[10] which suggests that IRA might be superior in female patients who desire a future pregnancy, or IPAA should be performed after delivery. Meta-analysis by Aziz et al. of 12 reports published from 1991 to 2003 indicated that the development of adverse effects, such as bowel frequency, night defecation, and use of incontinence pads, was significantly lower after IRA than after IPAA, whereas fecal urgency was lower after IPAA.[11] Sexual dysfunction, dietary restriction, and postoperative complications did not differ between IRA and IPAA; however, the rate of reoperation within 30 days was significantly higher in patients who underwent IPAA than IRA (23.4% vs. 11.6%).[11]

The rate of cancer development in the residual rectum following IRA depends on the surveillance period and the

Table 5 Treatment for Metachronous Rectal Cancer

Procedure	Initial treatment	Final treatment
Operation	7	11 (65)
Proctectomy with IAA or IPAA	5	9[a]
APR	2	2
Local resection	10	6 (35)
EMR	9	5
Trans-anal resection	1	1

Values in parentheses are percentages

IAA total proctocolectomy with ileoanal anastomosis; *IPAA* total proctocolectomy with ileal-pouch anal anastomosis; *APR* abdominoperineal resection; *EMR* endoscopic mucosal resection

[a] One patient required total pelvic exenteration for the pelvic recurrence after IAA

Table 4 Patients Characteristics with or without Metachronous Rectal Cancer after IRA

		Metachronous rectal cancer		P value
		Present (n=17)	Absent (n=39)	
Colon polyps	Dense-type	6 (60)	4 (40)	0.0520
	Not dense-type	11 (24)	35 (76)	
Rectal polyps	Dense-type	4 (80)	1 (20)	0.0259
	Not dense-type	13 (25)	38 (75)	
Colon cancer	Present	6 (22)	21 (78)	0.2520
	Absent	11 (38)	18 (62)	
Rectal cancer	Present	2 (50)	2 (50)	0.5770
	Absent	15 (29)	37 (71)	
Length of residual rectum	<11 cm	9 (35)	17 (65)	0.5702
	≥11 cm	8 (27)	22 (73)	

Values in parentheses are percentages

age of the patient.[12,13] Studies with follow-up periods of 5 years or longer have reported rates of 7–37%.[6,8,12–20] The risk rate of postoperative rectal cancer in the residual rectum in our study was 30% over a surveillance period of 8.9 years. This relatively high rate may have been due to the inclusion of Tis patients in the analysis. If the six patients with Tis tumors are excluded, the rectal cancer rate in this group would be only 20% (11/59). Although Tis lesions are regarded as adenomas in Western countries, it cannot be rejected that patients with Tis lesion in the residual rectum require resection of the lesion, and if local resection fails, radical surgery is indicated; therefore, patients with Tis lesions were included in the present study. However, most of the noninvasive lesions can be managed by endoscopic resection, thus, not requiring resection of the remnant rectum. Moreover, postoperative rectal cancer developed more often in patients with dense-type colorectal polyps (p=0.0259); therefore, we recommend that IRA is not indicated for patients with many colon polyps or those with 20 or more rectal polyps.

The correlation between the density of polyps and the rate of cancer development has been examined at a genetic level. Nieuwenhuis et al.[21] suggested that the severity of colonic polyposis may depend on the position of a mutation in the APC gene, with mutations between codons 1250 and 1464, and especially those at codon 1309, contributing to the severity of colonic polyposis. Other studies have proposed that mutations localized at the ends of the gene and in the alternatively spliced region of exon 9 cause a mild form of FAP, and it has been recommended that IRA should be limited to patients for whom a genetic diagnosis indicates a mild form of FAP.[6,9] Besides the density of polyps, development of a desmoid tumor should be considered in determining the indication for IRA, since a secondary proctectomy may be difficult to perform if cancer develops in the residual rectum in association with a desmoid tumor. Therefore, it has been proposed that IPAA should be selected for patients with a family history of desmoid tumor and those with a mutation located distal to codon 1444 in the APC gene.[1]

The stage at which cancer develops in the residual rectum clearly has a strong influence on prognosis. Vasen et al.[22] have reported that Dukes B, C, and D colon cancers account for 76% of cancers in the residual rectum, with most being detected at an advanced stage. In the present study, most patients were detected at an early stage, and Dukes B, C, and D colon cancers accounted for 29% (5/17). Detection at an early stage was arguably achieved by performing periodic endoscopic surveillance at intervals of 6 months to 1 year following surgery. Indeed, for the three T3 patients out of 11 patients who required further surgery, no endoscopic surveillance had been performed for 2 years or more before cancer was diagnosed; therefore, there may be no difference in prognosis after IRA and non-IRA procedures provided that appropriate surveillance is performed. Previous studies have shown that the main causes of death following IRA are cancer in the residual rectum, duodenal cancer,[23] and desmoid tumor;[24] however, duodenal and desmoid cancers may develop independently of the type of operative procedure. Therefore, IRA has no effect on overall survival when indicated appropriately in selected patients and with long-term periodic endoscopic surveillance to detect cancer in the residual rectum at an early stage. Vasen et al.[1] recommended intervals of 3 to 6 months for endoscopic follow-up of the rectum after IRA and suggested an indication for proctectomy in patients with multiple large (>5 mm) rectal adenomas with a high degree of dysplasia. Further acquisition of data is required to establish the appropriate interval for surveillance colonoscopy and to determine whether endoscopic resection is applicable following IRA.

Conclusion

Selection of an appropriate operative procedure for FAP requires consideration of a variety of factors, including the density of the colon or rectal polyps, whether future pregnancy is desired, the patient has a high risk of desmoid tumor, and the position of the mutation in an APC gene. Strict screening of patients will result in no difference in prognosis after IRA and non-IRA surgery, and we consider that the results demonstrated in the present study are essential in selecting suitable patients for IRA. Thus, IRA may be indicated for selected patients without invasive rectal cancer and without dense rectal polyps for whom frequent surveillance of the residual rectum can be performed over their lifetime.

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Surg Endosc (2010) 24:2850–2854
DOI 10.1007/s00464-010-1063-5

Accelerated learning curve for colorectal resection, open versus laparoscopic approach, can be attained with expert supervision

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Received: 3 December 2009 / Accepted: 19 March 2010 / Published online: 5 May 2010

Abstract
Background Laparoscopic colorectal resection (LCR) is gaining popularity. Nonetheless, open surgery remains an important technique. Thus, surgeons should be technically proficient in both open and laparoscopic surgery. One question however remains unanswered: Can training for open and LCR occur simultaneously? The objective of this paper is to review the learning curve for open and laparoscopic colon resection of one surgeon who underwent a rigorous training program.
Methods A review of consecutive patients who underwent surgery for colon and rectosigmoid junction cancers by one trainee surgeon was performed. This surgeon had completed his basic surgical residency but had limited experience in colorectal cancer surgery. In total, 75 patients were included in this study. All operations were supervised by at least one staff surgeon with experience of more than 300 LCR cases. The trainee surgeon was allowed to train in both laparoscopic and open colorectal resection simultaneously.
Results Forty-three patients underwent laparoscopic resection, while 32 patients underwent open surgery. Age, gender, mean body mass index (BMI), preoperative risk, and history of past abdominal surgery showed no significant difference between laparoscopic and open groups. There were no differences in tumor stage [International Union against Cancer (UICC)] or tumor size ($p = 0.068$ and 0.228, respectively). The morbidity rate for open and laparoscopic surgery was 3.1% (1/32) and 4.7% (2/43), respectively ($p = 0.484$). Operation time decreased with increasing experience, and plateaued after 25 cases in the laparoscopic group and 22 cases in the open group. The learning curve for open cases was 11 cases, and 7 for laparoscopic surgery.
Conclusions Surgeons who have completed a basic surgical residency but have limited colorectal surgery experience can learn both open and laparoscopic colorectal surgery simultaneously in an effective manner under supervision by well-experienced surgeons.

Keywords Laparoscopic colorectal resection · Learning curve · Trainee surgeon

Laparoscopic colorectal resection (LCR) is gaining popularity. Prospective randomized control studies have revealed some benefits of LCR for colorectal cancer compared with open surgery [1–5]. Nonetheless, open surgery remains an important technique. Thus, surgeons should be technically proficient in both open and laparoscopic surgery.

LCR is believed to be technically more difficult than open surgery and thought to require more intensive training to ensure safe and oncologic operation [6, 7]. There are many reports regarding the learning curve for performing LCR [7–15]. The learning curve is generally accepted to be approximately 30 procedures based on decline in operative time, intraoperative complications, and conversion rate. One question however remains unanswered: Can training for open and LCR occur simultaneously?

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We hypothesized that surgeons who have finished a basic 4-year surgical residency program according to the Japanese system can learn both open and laparoscopic colorectal cancer resection efficiently simultaneously as long as they are well supervised. The objective of this study is to review the learning curve for open and laparoscopic colon resection of one surgeon who underwent a rigorous training program.

Patients and methods

A review of consecutive patients who underwent surgery for colon and rectosigmoid junction cancers from May 2005 to December 2007 by one trainee surgeon at Jichi Medical University Saitama Medical Center was performed. This surgeon had completed his basic surgical residency but had limited experience in colorectal cancer surgery and D3 dissection. Prior to commencement of the colorectal training, this surgeon had performed 350 cases of general surgery operations as first surgeon, including 80 cases of appendectomy, 62 cases of hernia repair, 46 cases of laparoscopic cholecystectomy, 10 cases of gastrectomy, and 21 cases of colectomy. Colectomies included five cases of ileocecal resection, nine cases of sigmoid colectomy, and seven cases of right hemicolectomy. He had also been an assistant in more than 1,000 other cases during a 4-year surgical residency program in Japan.

Because this study was designed to investigate the learning curve for laparoscopic and open colorectal surgery under supervision by experts, difficult cases were excluded from this study. Exclusion criteria were as follows: (1) patients who underwent combined procedures such as cholecystectomy, hepatectomy, and hysterectomy, (2) tumor located near the splenic flexure or in the rectum, and (3) T4 tumors that directly invaded adjacent organs or structures. In total, 75 patients were included in this study. All operations were supervised by at least one staff surgeon with experience of more than 300 LCR cases. The trainee surgeon was allowed to train in both laparoscopic and open colorectal resection simultaneously. When the surgeon performed more than 80% of the procedure, it was credited to this surgeon. Patient characteristics and oncological outcomes were analyzed.

Standardized procedures were performed for all cases. For left-sided lesions, medial-to-lateral approach was performed in laparoscopic surgery, while lateral-to-medial approach was done in open surgery. Laparoscopic left-sided colon resection began with ligation of proximal vascular pedicles, followed by mobilization and resection of bowel with anastomosis. For right-sided lesions, both procedures were performed using lateral-to-medial approach, which began with mobilization of the bowel, followed by exploration of the retroperitoneum, ligation of vascular pedicles, and resection of bowel with anastomosis. D3 dissection (exposure of the root of the feeding vessels) was performed when indicated.

Quality assessment and analysis of learning curve was performed by plotting cumulative summation (CUSUM) curves, and the moving average method was used to assess changes in operation time for both laparoscopic surgery and open surgery. CUSUM curve has emerged as a popular tool to monitor quality of surgery [16]. CUSUM allows one to judge whether a given variation in performance is acceptable, or whether the variation is greater than could be expected from random variation and thus may be a concern. As previous report utilized CUSUM to assess the learning curve for surgical treatment, CUSUM (S_n) was defined as $S_n = \Sigma(X_i - X_0)$, where X_i is an individual attempt and X_0 is the predetermined acceptable failure rate for the procedure, with X_i assigned a score of 0 for success and 1 for failure [13, 14]. The acceptable failure rate was defined such that, when the target success rate was set at 90%, the acceptable failure rate was 10% (X_0 was set at 0.1). For the CUSUM curve we defined "failure" has occurring when any of the following occurred: (1) perioperative major morbidity and mortality, (2) intraoperative blood loss >1,000 ml, or (3) long operative time more than two standard deviations above the department average (>240 min for open surgery, >270 min for LCR).

The moving average method was also used to assess changes in operation time for qualification of the learning curve. Creating an average of values that moves with the addition of new data results in smoothing of the value of the variable being analyzed.

Statistical analysis was performed using SPSS version 17.0 (SPSS Inc., Chicago, IL) for Windows. The chi-square test or Fisher's exact test was used for comparison of categorical variables as appropriate, and Student's *t*-test was used for comparison of continuous variables. Values of $p < 0.05$ were regarded as statistically significant.

Results

A total of 75 patients were included in this study. The choice of surgical procedure was basically determined by patient preference, with LCR performed as default. Consequently, 43 patients underwent laparoscopic resection, while 32 patients underwent open surgery. Patient characteristics are presented in Table 1. Age, mean BMI, American Society of Anesthesiologists (ASA) score, and history of past abdominal surgery showed no significant difference between laparoscopic and open groups.

Tumor characteristics are listed in Table 2. There were no differences in tumor stage (UICC) or tumor size

Table 1 Patient demographics: comparison between laparoscopic and open cases

Factor	Laparoscopic, $N = 43$	Open, $N = 32$	p
Mean age (years)	66.1 ± 8.8	69.9 ± 10.5	0.095
Male sex	21	22	0.085
Mean BMI (kg/m^2)	22.7 ± 2.69	23.8 ± 4.48	0.187
ASA ≥ 3	3	4	0.451
Past abdominal surgery	9	7	0.921

($p = 0.068$ and 0.194, respectively). Extent of lymph node involvement or distant metastasis did not show significant difference. There were a significantly larger number of harvested lymph nodes in the laparoscopic group ($p = 0.012$). Operative outcomes are listed in Table 3. In laparoscopic surgery, operative time was significantly longer, while estimated blood loss was significantly less. The morbidity rate for open and laparoscopic surgery was 3.1% (1/32) and 4.7% (2/43), respectively ($p = 0.484$). Morbidities were small bowel obstruction for open surgery, and major leakage and bleeding that required blood transfusion for laparoscopic surgery. Mortality rate was 0% in both groups during this study. There were three cases of conversion to open surgery from initially performed laparoscopic surgery during this study; reasons for conversion were severe small bowel adhesion to abdominal wall due to previous laparotomy for duodenal ulcer in one case, and two cases of bleeding which were difficult to control by laparoscopic operation.

Table 2 Tumor characteristics: comparison between laparoscopic and open cases

Factor	Laparoscopic, $N = 43$	Open, $N = 32$	p
Location			
Cecum	3	7	
Ascending colon	14	2	
Transverse colon	3	7	
Descending colon	0	3	
Sigmoid colon	17	7	
Recto sigmoid	6	6	
Tumor stage			
T0 and 1	13	6	
T2	9	4	
T3	21	22	0.068
N stage ≥ 1	17	14	0.714
M stage 1	1	3	0.179
Mean maximum diameter (mm)	33.1 ± 18.8	38.8 ± 21.4	0.228
Mean lymph nodes harvested	20.9 (7–42)	15.9 (2–31)	0.015

Table 3 Operative outcomes

Factor	Laparoscopic, $N = 43$	Open, $N = 32$	p
Type of colon resection			
Ileocecal resection	4	2	
Right colectomy	15	12	
Left colectomy	0	3	
Sigmoid colectomy	18	8	
Anterior resection	6	6	
Operative time (median)	224 (120–350)	150 (85–335)	<0.01
Estimated blood loss (ml)	64.7 ± 96.5	210.6 ± 203.2	<0.005
Conversion rate	7.0% (3/43)	–	

The moving average of the operation time for open and laparoscopic surgery is shown in Fig. 1. For both groups, operation time decreased with increasing experience, and plateaued after 25 cases in the laparoscopic group and 22 cases in the open group.

CUSUM curves are shown in Fig. 2. In the laparoscopic group, surgical morbidity was observed in two cases, and operative time was longer than 270 min in five cases. In the open group, surgical morbidity occurred in one case, and operative time exceeded 240 min in three cases. There were no cases exceeding 1,000 ml blood loss in either approach. The learning curve for open cases was 11 cases and 7 for laparoscopic surgery.

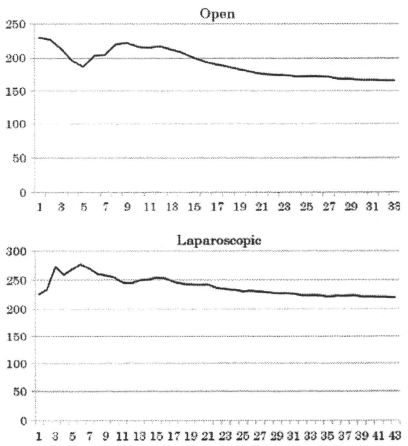

Fig. 1 Moving average of the operating time

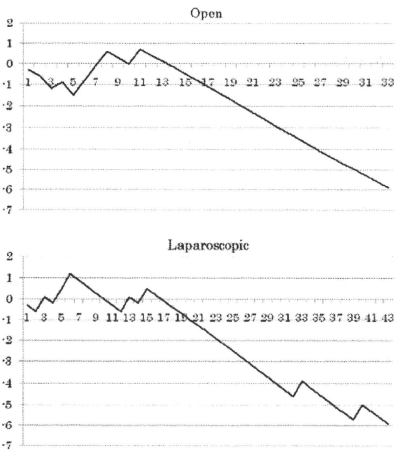

Fig. 2 Cumulative summation (CUSUM) score; upward slopes indicate that at least one failure was recorded in the case index number. Case was scored as +0.9 for failure or −0.3 otherwise, then the score was sequentially added

Discussion

The 4-year basic surgical residency program in Japan involves attainment of basic surgical skills. Basic surgical residents start with basic procedures such as appendectomy, cholecystectomy, and hernia repair [17–21]. They then progress to open colorectal cancer surgery. LCR is learned later, after proficiency in open colorectal resections. With efforts to standardize LCR technique and supervision from expert surgeon in LCR, it has become easier for a trainee surgeon to learn the technical skills of LCR. We thus hypothesized that LCR could be learned simultaneously with open colorectal surgery.

In this study, we excluded tumors that were located near the splenic flexure, at the descending colon, and the rectum, as these locations are technically more difficult and may not be suitable for operation by trainee. Cases of tumors that were invading adjacent organs were also excluded for similar reasons.

Previous reports evaluating the learning curve of laparoscopic colorectal surgery included some different factors from those utilized herein [7, 9, 13, 22, 23]. To evaluate quality of LCR, we did not include number of lymph nodes harvested, as standard D2 or D3 operations for early and advanced tumors, respectively, were performed in all cases. Extent of dissection was ensured by the supervisor in every case. Conversion to open surgery was also not included in this study. In our previous study, trainee surgeon did not cause more conversion in LCR if they were well supervised [24]. So, we do not believe that conversion to open surgery is a good indicator to assess quality of LCR under good supervision. Besides, conversion rate should be evaluated as proficiency of laparoscopic surgery only. We considered blood loss more than 1,000 ml and long operative time as failure, as our previous study showed that these were independent predictors of poorer outcome (data to be published in the *American Journal of Surgery*).

Monitoring quality in surgical treatment has been a topic of interest for many. Direct observation by a supervisor and graphical representation of the learning curve are two common ways of assessing individual competence, but both are likely to be subjective [25, 26]. Assessment of surgeon competency should be dynamic and enable quantitative and continuous evaluation of surgeon performance. CUSUM allows continuous monitoring of surgical performance using clearly defined situations of failure and provides objective evaluation. CUSUM has emerged as a popular tool for performance monitoring in surgery since its first application to evaluate surgical outcomes by de Leval et al. [27]. CUSUM methodology has been applied to describe quality in colorectal surgery in several studies [8, 13, 14]. In this study, the CUSUM curve demonstrated downward slope after 11 cases in open group and 7 cases in laparoscopic group, which implies that the surgeon had acquired sufficient skills for index procedures.

The moving time average stabilized after 25 cases for laparoscopic colorectal surgery and 22 cases for open surgery, which implies that a further 18 and 11 cases were required to stabilize operation time in laparoscopic and open surgery, respectively. These patterns suggest that the trainee surgeon was able to perform the procedure safely at an early stage, and this was then followed by reduction in operative time when technical skills were further improved.

The learning curve for LCR in our study was similar to one previous report [13], while other reports demonstrated larger number of cases for the learning curve [7, 10, 12, 15]. The accelerated learning curve demonstrated herein is likely to be a result of the following: Firstly, the trainers in this series were extremely experienced in both laparoscopic and open colorectal surgery. Each of the trainers had carried out more than 300 cases of LCR. With this experience, it was possible for them to impart a technique for both open and laparoscopic surgery that has already been well established and standardized. This enabled easier learning, as the trainee did not have to contend with different techniques of different supervising surgeons. Secondly, the ever-present supervision of the experienced staff surgeons enabled the trainee to commit fewer mistakes intraoperatively, especially in identification of anatomical structures

and planes of dissection. Furthermore, the radicality of oncologic surgery was maintained [24].

Conclusions

Surgeons who have completed basic surgical residency but have limited colorectal surgery experience can learn both open and laparoscopic colorectal surgery simultaneously in an effective manner under supervision by well-experienced surgeons.

Disclosures Authors Maeda, Tan, Konishi, Tsujinaka, Mizokami, Sasaki, and Kawamura have no conflicts of interest or financial ties to disclosure.

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Surg Today (2010) 40:97–101
DOI 10.1007/s00595-009-4133-3

SURGERY TODAY

Review Articles

Long-Term Results of Laparoscopic Colorectal Cancer Resection: Current Knowledge and What Remains Unclear

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Abstract
Laparoscopic colorectal cancer resection has advanced considerably since it was first described in 1991. It is becoming increasingly popular, and earlier concerns about its oncologic safety are being dispelled by long-term data, which have emerged over recent years, suggesting that laparoscopic colorectal cancer surgery is not inferior to open surgery. This article reviews our current knowledge of the long-term results of laparoscopic colorectal cancer resection, and addresses what remains unknown and needs to be elucidated.

Key words Laparoscopic · Colorectal cancer · Long term · Survival · Recurrence

Introduction

Laparoscopic colorectal surgery was first performed in Japan in 1992, very soon after its initial description by Jacobs et al.[1,2] Through the leadership of the pioneers of laparoscopic colorectal surgery in Japan, the field of laparoscopic colorectal surgery in Japan has progressed in leaps and bounds. The number of laparoscopic colorectal cancer operations is steadily increasing,[2] not only for early cancers, but also for advanced and invasive cancers.[3] During the 1990s, there were concerns about port-site metastasis, but these were subsequently proven to be unfounded. However, questions remain about whether laparoscopic colorectal cancer surgery is in fact less radical, and despite reported superior short-term outcomes, laparoscopic colorectal surgery is still not considered standard treatment. It is only recently that follow-up after laparoscopic colorectal cancer resections has matured to allow analysis of oncologic outcome; thus, the long-term outcomes of laparoscopic colorectal surgery have become very topical. As laparoscopic colorectal surgeons, we must become familiar with the current data available on the long-term outcomes of colorectal cancer resections. Only then can we be certain that we are justified in performing laparoscopic colorectal resections in preference to conventional open surgery. This article summarizes the best data we could find and looks at what remains unclear. It is not, however, intended to be an exhaustive review.

Reprint requests to: F. Konishi
Received: December 24, 2008 / Accepted: February 20, 2009

Long-Term Results of Laparoscopic Surgery Versus Open Surgery for Colon Cancers

There are numerous reports on the long-term results of laparoscopic surgery for colon cancer. The most conclusive data come from a few large randomized controlled trials, most of which began during the 1990s. These data have only recently matured, with reports of long-term outcomes emerging in the last few years. The most important data are summarized in Table 1.[4–7] These randomized studies provide robust information on long-term outcomes as they have been conducted efficiently. All studies had sample size calculations, preoperative randomization, intention to treat analysis, and allocation concealment. The COST study,[4] CLASSIC[5] study, and the study by Liang et al.[6] concluded that laparoscopic colorectal cancer surgery was not inferior to open surgery. The study by Lacy et al.[7] arrived at a similar conclusion, and suggested further that laparoscopic surgery was superior for stage III disease. There have since been two reviews that pooled available data. The first was performed by the Transatlantic Laparoscopically Assisted vs Open Colectomy Trials Study Group.[8] Data were pooled from the study of Lacy et al.,[9] the COST study,[4] and the CLASSIC study,[10] and also from unpublished information from the COLOR study[11] con-

Table 1. Randomized trials comparing laparoscopic and open surgery for right, left, and sigmoid colon cancers

	COST 2007[4] Lap vs Open	CLASICC 2007[5] Lap vs Open	Liang et al., 2007[6] Lap vs Open	Lacy et al., 2008[7] Lap vs Open
No. of patients	435:428	273:140	135:134	106:102
Year	1994–2001	1996–2002	2000–2004	1993–1998
Age (years)	70:69	69:69	64:64	68:71
Exclusion	TNM:T4 and M1	TNM:M1	TNM:T4, Right and proximal transverse colon, AJCC Stage I and IV	TNM:T4 and M1
	Transverse colon	Transverse colon		Transverse colon
AJCC Stage				
0	5%:8%	Stage not given Presented T, N and M separately	0:0	0:0
I	35%:26%	16.7%:16.4%	0:0	25.4%:17.6%
II	31%:34%	34.6%:36.9%	50.4%:47.8%	39.6%:47.1%
III	26%:28%	36.1%:34.7%	49.6%:52.8%	34.9%:35.3%
IV	4%:2%	Not reported	0:0	4.7:5.9%
No. of lymph nodes	12:12	12:13.5	Not reported	11.1:11.1
Conversion	21%	25%	3%	11%
30-day mortality	<1%:1%	4%:5%	Not reported	Not reported
Median follow-up	7 years	36.8 months	40 months	95 months
Cancer outcomes				
Overall recurrence	19.4%:21.8%		17.0%:21.6%	18%:28%
Locoregional recurrence		7.3%:6.0%	No locoregional recurrence	7.5%:13.7%
Distant recurrence		11.3%:12.5%	14.8%:18.7%	6.6%:9.8%
Cancer-related mortality	11.0%:14.3% (2004 data)	22.7%:19.3%		16%:27%
Overall mortality	23.6%:25.4%	28.8%:32.2%		36%:49%
Methodology	Adequate	Adequate	Adequate	Adequate

AJCC, American Joint Committee on Cancer; TNM, tumor, node, metastasis

ducted by Europeans, the long-term results of which have yet to be published. Only 3-year survival data were analyzed in this meta-analysis, and these revealed that laparoscopic surgery and open surgery had similar overall and disease-free survival at 3 years' follow-up. The following year, a Cochrane review pooled more available data, which also concluded that laparoscopic surgery was not inferior to open surgery for colon cancer.[12]

It is noteworthy that these trials were started before laparoscopic colorectal surgery was well established. Conversion rates for the COST[4] and CLASSIC[5] studies were over 20%, testifying to the infancy of the procedure when the trials were conducted. There were many exclusion criteria, but the main ones were transverse colon cancer, advanced cancer, and elderly patients. As such, it can be said that these randomized trials comprised operations that could be performed easily by open surgery or laparoscopically. Thus, the long-term results of more complex resections of transverse colon and advanced colorectal cancer remain unclear.

A number of randomized trials have yet to report their long-term 5-year results (Table 2).[11,13,14] Among these, the European COLOR trial[11] will give some noteworthy results as it is a large and relatively well conducted study. Although its 3-year data were used in a pooled analysis,[8] this group has yet to report its individual long-term data; however, its impact will not be unlike that of those already published (Table 1), as the type of pathology and operations is not dissimilar.

The trial that is likely to have more impact is the Japanese Clinical Oncology Group (JCOG) 0404 trial,[14] because it includes more locally advanced cases of only T3 and T4 colorectal cancers. Furthermore, it was started when surgeons had become experienced in laparoscopic colorectal surgery and the quality control for the operations performed is very stringent. Thus, conclusions can be made about the more complex aspects of laparoscopic colon resection. With an accrual approaching more than 1000 patients, this will no doubt be one of the landmark studies of our time.

Can laparoscopic colorectal surgery be superior to open surgery in terms of long-term outcome? Although Lacy et al.[7] suggested this and Law et al.[15] made similar suggestions based on their nonrandomized data, we cannot answer this question yet. No other randomized trials were able to prove any superiority of laparoscopic surgery, and none were actually powered to show supe-

Table 2. Long-term results of ongoing randomized trials of laparoscopic versus open surgery for colorectal cancers

	COLOR[11]	COLOR II	Hasegawa et al., 2003[13]	JCOG 0404[14]	LAPKON II
Type	Multicenter	Multicenter	Single	Multicenter	Multicenter
Inclusions (according to TNM staging)	M0	M0	T2 or T3, M0	T3 or T4, M0	M0
Tumor site	Colon	Rectum	Colon up to rectosigmoid	Colon up to rectosigmoid	Colon and rectum
Primary endpoint	DFS at 3 years	Locoregional recurrence	OS and DFS	OS	Locoregional recurrence, OS at 5 years
Secondary endpoints		DFS at 3 and 5 years, distant metastasis		DFS	
Start date of accrual	1997	2003	1998	2004	1998
End date of accrual		Ongoing	2000	To be completed 2009	2004
Sample size	1248		59	Target 1000	477 (Target 900)

JCOG, Japan Clinical Oncology Group; DFS, disease-free survival; OS, overall survival

riority, just noninferiority. Thus, the oncologic superiority of laparoscopic surgery remains speculative.

Long-Term Results of Laparoscopic Surgery Versus Open Surgery for Rectal Cancers

Laparoscopic rectal surgery has not developed as quickly as laparoscopic colon surgery because the techniques involved are more complex and technically demanding. Furthermore, the techniques for open resection are still evolving, and there is still no consensus on the optimal adjuvant treatment regime and handling of lateral nodes.

As such, there have not been many good-quality studies comparing laparoscopic and open surgery for rectal cancers. The available randomized trials for rectal cancers are summarized in Table 3.[5,16–18] One study from Hong Kong[16] focuses only on rectosigmoid lesions and it is not surprising to find results similar to that for colon surgery. Among the other trials on rectal cancer, the CLASICC trial had a relatively high conversion and morbidity rate[10] and thus, maturity of the technique of laparoscopic rectal resection was not obtained during the period of the trial. The trial by Braga et al.[17] included some rectal cancers, but there was no specific mention of the stage of the cancers included, and only locoregional recurrence was reported. The study by Zhou et al.[18] reported very good short-term results; however, the methodology of the study was unclear and the follow-up was extremely short so no conclusion could be drawn. Thus, the long-term outcomes of laparoscopic versus open rectal resection remain unclear and good-quality trials are still required. Of particular interest are the COLOR II and LAPKON II trials, which may provide some of the information that is required. However, accrual for the LAPKON II trial was terminated at $n = 477$ before the target of $n = 900$ was reached, so this trial may be weak.

In Japan, a phase II prospective, nonrandomized trial is being conducted on the feasibility of laparoscopic rectal resections for early (Stage 1) rectal cancers, with the primary short-term outcome measure being anastomotic leakage and the long-term measure, disease-free survival.[19] The target sample size is 350 and the inclusion and exclusion criteria are strict, with good quality control. The results of this trial will be eagerly awaited; however, it will be some time before the long-term results of laparoscopic resection for more advanced rectal cancers can be evaluated in Japan. The main hurdle is the existence of lateral lymph nodes in more advanced low rectal cancers. Laparoscopic lateral node dissection is still only in the experimental stage, so conducting a trial on laparoscopic resection of advanced low rectal cancers remains impossible. Whether laparoscopic low rectal cancers can be combined with neoadjuvant chemoradiation is still a matter of debate among Japanese surgeons. Perhaps in the future, with increasing expertise in laparoscopic surgery, laparoscopic lateral node dissection will become readily available. In that situation, many potential trials will come to the fore. Some potential trials should include laparoscopic rectal resection with lateral node dissection vs open resection with node dissection, and laparoscopic rectal resection with lateral node dissection vs neoadjuvant chemoradiation followed by laparoscopic resection.

Noteworthy Long-Term Results from Japan

Some noteworthy results are shown in Table 4. The study from Jichi Medical School[20] is the only

Table 3. Randomized trials comparing laparoscopic and open surgery for rectosigmoid and rectal tumors

	Leung et al., 2004[16] Rectosigmoid Lap vs Open	CLASICC 2007[5] Lap vs Open	Braga et al., 2005[17] Lap vs Open	Zhou et al., 2004[18] Lap vs Open
No. of patients	203:200	253:128	68:68	82:89
Year	1993–2002	1996–2002	Not reported	2001–2002
Age (years)	67:67	69:69	65:67	44:45
Exclusion (according to TNM staging)	T4, M1	M1	T4	T4, M1
APR	0	26%:13%	0	0
TME	NA	79%:67%		100%
Site in rectum	NA	Not reported	Not reported	1.5–8cm from dentate line
AJCC Stage				
I	15.3%:14.0%	16.7%:16.4%	27.4%:28.4%	6.1%:6.7%
II	35.5%:36.5%	34.6%:36.9%	28.9%:21.9%	11.2%:9.0%
III	31.5%:34.5%	36.1%:34.7%	33.7%:38.3%	76.8%:76.4%
IV	17.7%:15.0%	Not reported (Individual data for rectal lesions unavailable)	10%:11.4% (Individual data for rectal lesions unavailable)	4.9%:8.5%
No. of lymph nodes	11.1:12.1	12:13.5	13:14	Not reported
Conversion	23.2%	34%	4.2%	Not reported
30-day mortality	0.6%:2.4%	4%:5%	Not reported	0%:0%
Median follow-up	52.7 months	36.8 months	36 months	Range 1–16 months
Cancer outcomes				
Locoregional recurrence	6.6%:4.1%	9.9%:9.4%	7.4%:8.8%	0%:3.4%
Distant recurrence	18.0%:15.3%	18.6%:16.4%	Not specifically reported	0%:0%
Cancer-related mortality	15.6%:11.8%	12.6%:18.0%	Not specifically reported	0%:0%
Overall mortality	22.8%:23.5%	Not specifically reported	Not specifically reported	0%:0%
Methodology	Adequate	Adequate	Adequate	Unclear

APR, abdominoperineal resection; TME, total mesorectal excision

Table 4. Long-term results of Japanese studies on rectal cancer surgery

	Jichi University, Tochigi 2004[20] Lap vs Open	Keio University, Tokyo 2003[21]	Sendai Medical Center, Sendai 2008[22]	Miyajima et al., Multicenter 2008[23]
Type	Retrospective comparative	Retrospective Noncomparative	Retrospective Noncomparative	Multicenter retrospective
n	118:163	226	121	1057
Tumor site	C, A, S	Colorectal	C, A, T, D, S, R	Ra & Rb
Stage	II and III	T1 and T2	II and III	All
Conversion	8.5%		4.1%	7.3%
30-day mortality	0%			0%
Median follow-up	58 months	43 months	29.6 months	29.8 months
Lymph node harvest	16.5:14.0		25.3	15
Overall recurrence	12.1%:14.0%	T1: 2.0% T2: 3.9%	14.9%	6.6%
Local recurrence				1.1%
Distant recurrence	8.6%:11.5%			4.3%
Estimated 5-year DFS	87.8%:85.5%	T1: 97.6% T2: 93.4%	II: 75.6% IIIA/B: 80.1% IIIC: 66.8%	I: 94.6% II: 82.1% III: 79.7% (3 year)

C, caecum; A, ascending colon; T, transverse colon; D, descending colon; S, sigmoid colon; R, rectum; Ra, upper rectum; Rb, lower rectum

comparative study, and its good mid-term results for stage II and II cancers will probably be validated soon with the results from the JCOG 0404 study. The other studies are noncomparative,[21-23] but also show similar good mid-term results. Of particular interest are the pooled data of rectal resection that were published this year.[23] The overall operative mortality was 0% in over 1000 patients, and the conversion rate was only 7%. These results are indeed testimony of the technical excellence of Japanese surgeons, and the world no doubt awaits results from their prospective trials.

Conclusion

Laparoscopic colorectal surgery for cancer has come a long way since 1991. The current data show that laparoscopic resection for colon cancer is not inferior to open surgery in terms of oncologic outcomes. The oncologic safety of laparoscopic rectal resection is much less defined, especially for locally advanced cancers. Quality trials are being conducted in Japan to investigate some of the issues that need to be clarified.

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Ann Surg Oncol (2010) 17:973–980
DOI 10.1245/s10434-009-0849-y

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – COLORECTAL CANCER

Is Total Mesorectal Excision Always Necessary for T1–T2 Lower Rectal Cancer?

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ABSTRACT

Background. The goal of this multicenter study was to clarify the determinants of local excision for patients with T1–T2 lower rectal cancer.

Methods. Data from 567 consecutive patients who underwent radical resection for T1–T2 lower rectal cancer at 12 institutions between 1991 and 1998 were reviewed. Rates of lymph node metastasis were investigated using a tree analysis, which was hierarchized using independent risk factors for nodal involvement.

Results. The independent risk factors for lymph node metastasis were female gender, depth of tumor invasion, histology other than well-differentiated adenocarcinoma, and lymphatic invasion. According to the first three parameters that can be obtained preoperatively, only 0.99% of the patients without risk factors had lymph node metastasis. On the other hand, even if the lower rectal cancer was at stage T1, women with histological types other than well-differentiated adenocarcinoma had an approximately 30% probability of having lymph node metastasis. Lymphatic invasion was most useful to predict nodal involvement among patients with T2 lower rectal cancer. The rates of lymph node metastasis in T2 patients with and without lymphatic invasion were 32.9% and 9.1%, respectively.

Conclusions. Gender is one of the most important predictors for lymph node metastasis in patients with early distal rectal cancer. Three parameters, including depth of tumor invasion, histology, and gender, are useful determinants for local excision. Additional studies are required to establish the minimum optimal treatment for T2 lower rectal cancer.

Total mesorectal excision (TME) has recently achieved excellent oncological outcomes for patients with rectal cancer.[1] The oncological outcome of rectal cancer is usually worse than that of colon cancer; one reason for this is the higher local recurrence rate after curative resection for rectal cancer.[2] Although TME has decreased the risk of local recurrence, some patients with rectal cancer undergo abdominoperineal resection (APR) followed by permanent colostomy. Some patients develop complications after radical resection for rectal cancer, despite sphincter-sparing procedures.

Local excision is an important treatment option for early distal rectal cancer, because complications can arise after

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First Received: 23 June 2009;
Published Online: 1 December 2009

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radical resection. However, one of the problems associated with local excision for rectal cancer is the unsatisfactory oncological outcome. The reported local recurrence rates after local excision for T1 and T2 tumors range from 6.6% to 18% and from 17% to 37%, respectively.[3–7] A recent study found that patients with T1 rectal cancer treated by local excision have a threefold to fivefold higher risk of tumor recurrence than those treated by radical resection.[3]

Criteria for local excision to treat early rectal cancer have not been established. In this study, the indication of local excision for patients with T1–T2 lower rectal cancer was examined using a model hierarchized with independent risk factors for lymph node metastasis.

PATIENTS AND METHODS

We enrolled 567 patients with T1–T2 lower rectal cancer who underwent curative resection at 12 institutions (all members of the Japanese Society for Cancer of the Colon and Rectum) between 1991 and 1998. The local ethics committee of each institution approved this study. Lower rectal cancer was defined as the distal margin of tumor located below the peritoneal reflection. All patients received tumor-specific mesorectal excision (TSME), meaning that the rectum and mesorectum were removed with an appropriate distal resection margin of >2 cm. Patients who underwent transanal local excision or endoscopic mucosal resection were excluded from this study. Other exclusion criteria were cancers associated with ulcerative colitis, Crohn's disease, or familial adenomatous polyposis.

Preoperative investigations included barium enema examination, colonoscopy, endoscopic ultrasonography, chest x-ray, ultrasonography (US), and/or computed tomography (CT) of the liver, as well as blood tests for carcinoembryonic antigen (CEA). Five- to 10-year postoperative follow-up at most of the participating institutions comprised serum tumor marker measurements every 3 months for the first 3 years and every 6 months for the next 2 years, hepatic imaging (US and/or CT) and chest x-rays every 3 to 6 months, and annual or biennial pelvic CT and colonoscopy.

We analyzed the risk factors for lymph node metastasis in 567 patients who underwent radical resection. To determine the criteria for local excision in patients with T1–T2 lower rectal cancer, the rates of lymph node metastasis were compared according to the number of risk factors for lymph node metastasis.

STATISTICAL ANALYSIS

Data were statistically analyzed using the StatView 5.0 statistical package (Abacus Concepts, Inc., Berkeley, CA). All data are expressed as median ± standard deviation. Associations between each parameter and lymph node metastasis were analyzed using the χ^2 test. Independent risk factors for lymph node metastasis were determined using logistic regression analysis. Differences in numbers of lymph node metastases were analyzed using the Mann–Whitney U test between two groups and by the Kruskal–Wallis test among three or more groups. The actuarial survival of the patients was calculated using the Kaplan–Meier method, and overall survival rates in all groups were compared using the log-rank test. Statistical significance was established at $P < 0.05$ for all results.

RESULTS

Table 1 shows the characteristics of the participating patients. Surgical procedures, tumor size, histology of the primary rectal tumor, rate of lymph node metastasis, and lymphatic and venous invasion significantly differed between patients with T1 and T2 rectal cancer.

Risk Factors for Lymph Node Metastasis

The rates of lymph node metastasis in patients with T1 and T2 lower rectal cancer were 8.6% and 25.7%, respectively. Parameters, such as gender, age, tumor size and histology, T-factor, lymphatic invasion, and venous invasion, were analyzed as potential risk factors for lymph node metastasis in 567 patients with T1–T2 lower rectal cancer scheduled for radical resection. Univariate analysis revealed that female gender ($P = 0.0006$), histology ($P < 0.0001$), T factor ($P < 0.0001$), lymphatic invasion ($P < 0.0001$), and venous invasion ($P < 0.0001$) were risk factors for lymph node metastasis (Table 2). Multivariate analysis revealed that female gender ($P = 0.0009$), histology ($P = 0.017$), T-factor ($P = 0.0085$), and lymphatic invasion ($P < 0.0001$) were independent risk factors for lymph node metastasis in patients with early lower rectal cancers (Table 2).

Tree Analysis of the Rate of Lymph Node Metastasis

The 567 patients with T1–T2 lower rectal cancer were hierarchized for tree analysis according to preoperatively ascertainable T-factor, gender, and histology (in that order) among the independent risk factors for lymph node metastasis (Fig. 1). The rates of lymph node metastasis according to the number of risk factors were 0.99%, 10.6–15.5%, 26.3–30.4%, and 37.3% in patients with zero, one, two, and all three risk factors, respectively. Only 1 of 101 patients without any factors had lymph node metastasis. On the other hand, even if women had T1 lower rectal cancer, 30.4% of those with histological types other than well-differentiated adenocarcinoma had lymph node metastasis.

TABLE 1 Clinicopathologic characteristics of 567 patients with T1–T2 lower rectal cancer

Parameters	T1 (%)	T2 (%)	*P* value
Gender			
Male	144/346 (41.6)	202/346 (58.4)	NS
Female	89/221 (40.3)	132/221 (59.7)	
Age (yr)			
<61	118/288 (41.0)	170/288 (59.0)	NS
≥61	115/278 (41.4)	163/278 (58.6)	
Unknown		1	
Surgical procedure			
APR	28/141 (19.9)	113/141 (80.1)	<0.0001
Hartmann	3/9 (33.3)	6/9 (66.7)	
LAR	202/417 (48.4)	215/417 (51.6)	
Size (cm)			
≤2	128/173 (74.0)	45/173 (26.0)	<0.0001
>2	98/386 (25.4)	288/386 (74.6)	
Unknown	7	1	
Histology			
Well-differentiated Adenocarcinoma	167/327 (51.1)	160/327 (48.9)	<0.0001
Others	64/238 (26.9)	174/238 (73.1)	
Unknown	2		
Lymph node metastasis			
Absent	213/461 (46.2)	248/461 (53.8)	<0.0001
Present	20/106 (18.9)	86/106 (81.1)	
Lymphatic invasion			
Absent	142/241 (58.9)	99/241 (41.1)	<0.0001
Present	86/320 (26.9)	234/320 (73.1)	
Unknown	5	1	
Venous invasion			
Absent	169/317 (53.3)	148/317 (46.7)	<0.0001
Present	59/244 (24.2)	185/244 (75.8)	
Unknown	5	1	

APR abdominoperineal resection, *LAR* low anterior resection, *Others* moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, or mucinous adenocarcinoma

Multivariate analysis revealed that female gender, histological type other than well-differentiated adenocarcinoma, and venous invasion were independent risk factors for lymph node metastasis in patients with T1 lower rectal cancer (Table 3). Lymphatic invasion and gender were independent risk factors for nodal involvement among patients with T2 lower rectal cancer (Table 4). Figure 2 shows a tree analysis of the lymph node metastasis rate, including lymphatic invasion as a risk factor. The rate of lymph node metastasis in patients without lymphatic invasion was 9.1%.

Number of Lymph Node Metastases

We examined a median of 19 lymph nodes in 87 (15.3%) and 20 (3.5%) patients with N1 and N2 metastases, respectively. The numbers of lymph node metastases in 567 patients with T1–T2 lower rectal cancer and zero, one, two, and three risk factors (Fig. 3) were 0 ± 0.1 (0–1), 0 ± 1.1 (0–11), 0 ± 1.8 (0–13), 0 ± 3.2 (0–26), respectively. The number of lymph node metastases significantly differed among the four groups according to the number of risk factors ($P < 0.0001$) but not between patients with two and three risk factors.

Recurrence in Patients with T1–T2 Lower Rectal Cancer

During a median follow-up period of 4.9 ± 2.3 years, the local recurrence rates among patients with T1 and T2 lower rectal cancer were 2.1% (5/233) and 6.0% (20/334), respectively. Among these 25 patients, 12, 1, 3, 3, and 4 of them underwent curative resection, palliative resection, radiotherapy, and chemoradiotherapy together with chemotherapy, respectively. Two patients did not receive any treatment. The median survival after recurrence was 19