

## Clinical Characteristics of Rectal Cancer Involving the Anal Canal

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### Abstract

**Background** This study evaluates the clinical characteristics of rectal cancer involving the anal canal.

**Methods** A total of 346 consecutive patients with primary low rectal cancer located below the peritoneal reflection were reviewed in this study. Patients were divided into two groups according to whether the lower edge of the tumor came in contact with the anal canal (P group,  $n=78$ ) or not (Rb group,  $n=268$ ). Clinical and pathological parameters, recurrence rates, and survival rates were compared between the two groups.

**Results** The occurrence of uncommon histological types of tumor was significantly higher in the P group than in the Rb group. P group patients also had a significantly higher lateral pelvic node metastasis rate ( $p<0.001$ ), lower 5-year overall survival rate ( $p=0.0491$ ), and higher 5-year local recurrence rate ( $p=0.0171$ ) than Rb group patients. Multivariate analysis revealed that tumor location was a significant risk factor for local recurrence. In the P group, multivariate analysis showed that uncommon histological tumor types were a significant prognostic factor.

**Conclusion** Rectal cancer involving the anal canal should be treated with special care, considering the particularly high lateral pelvic lymph node metastasis rate and high local recurrence rate.

**Keywords** Rectal cancer · Local recurrence · Lateral pelvic node · Anal canal

### Introduction

The high incidence of local recurrence after curative operation leading to poor prognosis is the biggest problem when treating rectal cancer. Many studies have been conducted to reveal the risk factors of local recurrence in rectal cancer, such as positive circumferential resection margin, nodal positivity, and advanced T stage.<sup>1–3</sup>

Total mesorectal excision has played a major role in reducing the rates of local recurrence and improving

survival in rectal cancer.<sup>4,5</sup> One reason for this is the higher frequency of complete resection of the tumor together with its lymphatic and venous drainage that is achieved by complete removal of the mesorectum.<sup>6</sup> This procedure also increased the rate of sphincter-preserving surgery for low rectal cancer<sup>7</sup>; moreover, the recently developed surgical technique of intersphincteric resection has been proposed to offer sphincter preservation in patients with very low rectal carcinomas such as those involving the rectal canal.<sup>8</sup>

However, there still remains the question whether very low rectal cancer which involves the anal canal has the same clinical and pathological characteristics as cancer situated higher in the rectum. Whereas several studies have revealed that the distance from the anal verge was one of the risk factors for local recurrence, none of these reports addressed the clinical differences between very low rectal cancer involving the rectal canal and low rectal cancer which does not. In this study, we discuss the clinical characteristics of rectal cancer involving the anal canal in comparison to those with other types of low rectal cancer,

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**Table 1** Clinical characteristics

Characteristic		P group (n=78)	Rb group (n=268)	p value
Gender	Male	52	185	
	Female	26	83	N.S.
Age (range)		63 (39–85)	61 (28–87)	N.S.
CEA (ng/ml)		7.1	9	N.S.
Tumor size (mm)		49	44	N.S.
Tumor differentiation	Well/Mod	62	257	
	Others	16	11	<0.001
Lateral pelvic node metastasis	Negative	60	249	
	Positive	18	19	0.015
TNM T	T1	6	59	
	T2	18	77	
	T3	44	123	
	T4	10	9	N.S.
TNM N	N0	45	156	
	N1	18	81	
	N2	15	31	N.S.
TNM stage	Stage I	20	100	
	Stage IIA	23	52	
	Stage IIB	2	4	
	Stage IIIA	3	23	
	Stage IIIB	15	58	
	Stage IIIC	15	31	N.S.
Surgical procedure	Sphincter-preserving surgery	5	173	
	Others	73	95	<0.001

N.S. not significant

our goal being to define the optimum treatment strategy for this particular kind of rectal cancer.

## Materials and Methods

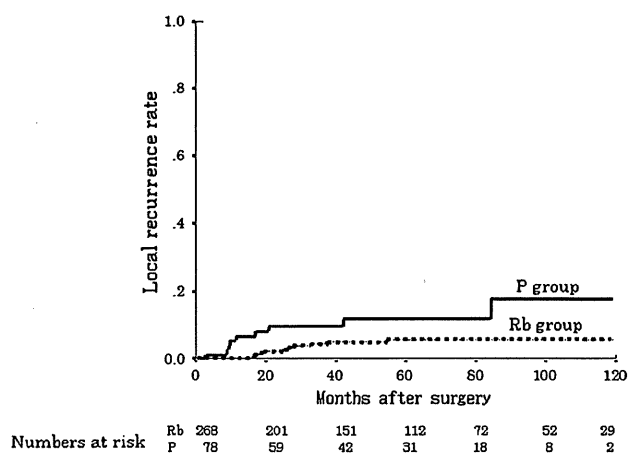
### Patients

A total of 346 consecutive patients with primary low rectal cancer located below the peritoneal reflection and who underwent curative resection at the Yokohama City Uni-

versity Hospital, Japan, between 1993 and 2003 were reviewed in this study. Tumor location was determined before surgery by digital rectal examination, endoscopy, barium enema, computed axial tomography (CAT scan), and magnetic resonance imaging. All rectal cancers were adenocarcinomas. Those carcinomas originating from squamous or transitional epithelium were excluded from study. The patients were seen at the outpatient clinic at 3-month intervals for 5 years and at 12-month intervals thereafter. Tumor markers were examined at every patient visit. CAT scan of the liver and lung or abdominal ultrasonography

**Table 2** Recurrence pattern

	P group (n=78)	Rb group (n=268)	p value
Liver	5	15	N.S.
Lung	6	16	N.S.
Local	9	11	<0.001
Inguinal lymph node	7	1	<0.001
miscellaneous	2	4	N.S.



**Fig. 1** Five-year local recurrence rate was 5.9% in the Rb group and 11.9% in the P group ( $p=0.0171$ )

with chest X-rays was performed at least every 6 months. Colonoscopy was performed every 12 months. Recurrences were clinically determined by colonoscopy or radiological images. Pathological stage III patients were given adjuvant chemotherapy with oral fluorinated pyrimidine.

#### Surgical Treatment

Total mesorectal excision (TME) was performed in all cases. In patients with T4 tumors, we performed a combined resection of those tissues and/or organs invaded by the cancer. At our institution, the diagnosis of stage II or III cancer is an indication of the need for lateral pelvic node dissection, which was performed on 231 patients in this study. In lateral pelvic node dissection, the fatty and connective tissues outside the pelvic plexus, around the internal iliac and common iliac vessels, and in the obturator cavity were removed, resulting in the iliac vessels becoming completely exposed, with or without pelvic autonomic nerve preservation. The surgical margin including radial margin was negative in all cases, as confirmed by histological examination. No patients underwent pre- and/or post-radiation therapy.

#### Clinical and Pathological Analysis

Patients were divided into two groups according to whether the lower edge of the tumor reached the anal canal (P group,  $n=78$ ) or not (Rb group,  $n=268$ ). To determine the location of the lower edge of the tumor, anoscopy and digital examination were performed in all cases, and when the distance between the lower edge of the tumor and the anal verge was within 3 cm, we defined that the tumor involved the anal canal. In this study, 73 out of 78 in the P group underwent abdominoperineal resection or total pelvic exenteration. In all those cases, it was histologically

confirmed that the lower edge of the tumor exceeded the anorectal ring.

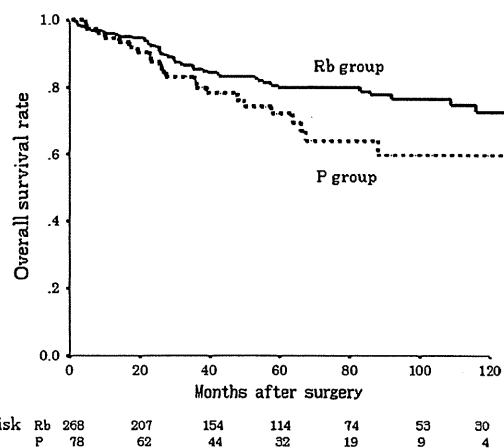
Standard oncological analysis was performed on all the patients and specimens in accordance with the TNM classification. Clinical and pathological parameters, recurrence rates, and survival rates were then compared between the two groups of patients.

#### Statistical Analysis

Local recurrence rates and survival rates were calculated by the Kaplan–Meier method and differences were compared statistically by the log-rank test. Cox's proportional hazards model was used for multivariate analysis. Data differences between groups were considered statistically significant at  $p<0.05$ .

#### Results

Clinical characteristics of the two groups are shown in Table 1. There were no differences in gender, age, serum CEA level, TNM T, TNM N, or TNM stage between the two groups. Average tumor size was 5 cm larger in the P group than in the Rb group; however, there was no significant difference. In the P group, there were three poorly differentiated adenocarcinomas, nine mucinous carcinoma, two endocrine cell carcinomas, and one anaplastic carcinoma, whereas in the Rb group, there were one poorly differentiated adenocarcinoma and ten mucinous carcinomas. The incidence of mucinous carcinoma and poorly differentiated carcinoma were 11.5% and 3.8% in the P group and 3.7% and 0.4% in the Rb group, respectively. The rate of occurrence of unusual histological tumor types was significantly higher in the P group than the Rb group ( $p<0.001$ ). P group patients also suffered



**Fig. 2** Overall 5-year survival rate was 80% in the Rb group and 72.2% in the P group ( $p=0.0491$ )

**Table 3** Uni- and multivariate analysis of local recurrence risk factors

	Univariate <i>p</i> value	Multivariate <i>p</i> value	Odds ratio	95% CI
Age (>60 vs. ≤60)	N.S.			
Sex (male vs. female)	N.S.			
CEA (>5.0 vs. ≤5.0)	N.S.			
Histology (well/mod vs. others)	N.S.			
Tumor size (>45 mm vs. ≤45 mm)	N.S.			
Lateral pelvic node metastasis (Negative vs. Positive)	0.033	N.S.		
TNM T (T1/T2 vs. T3/T4)	N.S.			
TNM N (N0 vs. N1/N2)	0.027	N.S.		
Group (Rb vs. P)	0.017	0.028	2.793	1.156–6.757

CI confidence interval

significantly more lateral pelvic node metastasis than Rb group patients (23.0% vs. 7.1%,  $p < 0.001$ ).

The recurrence pattern of the two groups is shown in Table 2. The rate of liver and lung metastases did not differ significantly between the two groups; however, local recurrence was significantly higher in P group compared with Rb group patients. Moreover, most inguinal lymph node metastases were observed in P group patients, with the exception of one Rb group case.

The 5-year local recurrence rate was significantly higher in P group compared with Rb group patients (11.9% vs. 5.9%,  $p = 0.0171$ ; Fig. 1), while the 5-year overall survival rate was significantly higher in Rb group compared with P group patients (80% vs. 72.2%,  $p = 0.0491$ ; Fig. 2).

Uni- and multivariate analyses of the risk factor for local recurrence were conducted to examine clinical factors. The presence of lateral pelvic node metastasis, TNM N, and tumor location were shown to be statistically significant risk factors for local recurrence by univariate analysis, while multivariate analysis found tumor location to be the only significant risk factor for local recurrence (Table 3).

The risk factor for local recurrence and prognostic factor in the P group were examined. No significant risk factor for local recurrence was detected in this study, while the histological types of the tumor (well/mod vs. others,  $p = 0.237$ , odds ratio = 2.330) seemed to most affect the outcome.

Of these factors, univariate analysis found that histology, lateral pelvic node metastasis, and TNM N were significant

prognostic factors in the P group, while multivariate analysis revealed histology to be significant (Table 4).

**Discussion**

This study found several characteristics typical of rectal cancer involving the anal canal compared to other low rectal cancer. First, a significantly higher occurrence of different kinds of histological tumor types occurred; in particular, mucinous carcinomas and poorly differentiated adenocarcinomas were observed in 15.4% of P group patients compared with 4.1% of Rb group patients ( $p < 0.001$  for all unusual tumor types). This supports the hypothesis that mucinous carcinomas arising in the anorectal region are associated with anal glands or fistula in anus.<sup>9</sup> Moreover, poorly differentiated adenocarcinoma has a potentially high invasive tendency that leads to involvement of the anal canal.

Second, the rate of lateral pelvic lymph node metastasis was higher in rectal cancers involving the anal canal, which agrees with the finding of Ueno et al.<sup>10</sup> that the lower the tumor location, the higher the risk of lateral nodal involvement. The rate of lateral nodal metastasis in T3/T4 low rectal tumors below 8 cm was 17%, but this varied according to location from the anal verge: 42% at 0–2.0 cm and 10.5% at 6.1–8.0 cm. Division of the rectum into two zones was proposed in 1895 by Gerota and supported in 1904 by Poirier and colleagues.<sup>11,12</sup> They described lateral

**Table 4** Multivariate analysis of prognostic factor of the P group

	<i>p</i> value	Exp(B)	CI
Histology (well/mod vs. others)	0.014	3.09	1.264–8.048
Lateral pelvic node metastasis (negative vs. positive)	0.218	1.916	0.680–5.396
TNM N (N0 vs. N1/N2)	0.671	1.282	0.407–4.049

lymphatic channels consisting of three pedicles: anterior, running along the prostate and bladder to end at nodes near the external and internal iliac vessels; lateral, along the middle rectal vessels; and posterior, along the middle and lateral sacral vessels. The result of this study suggested the possibility that the main lymphatic drainage channel to the lateral region may be located more closely to the sphincter muscle or that the existence of the channel along the inferior rectal artery pass through Alcock's canal to the lateral region.

In the present study, the local recurrence rate was significantly higher in P group patients, while multivariate analysis showed that anal involvement was the factor that most affected the likelihood of local recurrence. In this series, the surgical margin was negative in all cases, which was confirmed by histological examination.<sup>13</sup> Moreover, TNM N and presence of lateral pelvic lymph node metastasis were not significant factors by multivariate analysis, though these were significant by univariate analysis. Several studies showed that clinical N stage, gender, CRM, and distance from anal verge were independent risk factors for local recurrence.<sup>14,15</sup> Our study suggests that lateral pelvic node metastasis is another reason for the observed high frequency of local recurrence. In this way, our observations indirectly support the findings of other investigators; for example, Sugihara et al.<sup>16</sup> reported that positive lateral lymph node was the strongest predictor in both patient survival and local recurrence. Although radiation therapy is regarded as an essential option for advanced low rectal cancer in the western world,<sup>17,18</sup> we do not perform pre- and/or post-radiation therapy, whereas lateral pelvic node dissection is performed in stage II and stage III cancers, as is the common practice in many Japanese institutions.<sup>19,20</sup> As discussed above, lateral pelvic node metastasis is a risk factor for local recurrence, so lateral pelvic node dissection would be expected to reduce this risk. We are currently undertaking a clinical trial to compare TME with TME and lateral pelvic lymph node dissection (JCOG0212; ClinicalTrials.gov Identifier: NCT00190541).

In this study, however, we observed a 5-year cumulative local recurrence rate of 11.9% in patients with rectal cancer involving the anal canal. Though there are no previous reports which specifically mention the local recurrence rate of anal canal involving rectal cancer, our results cannot be expected to be better in comparison to other investigations of TME plus radiation therapy. For instance, Rullier et al.<sup>21</sup> found that after a median follow-up time of 40 months, the rate of local recurrence was 2%. This previous study concluded that preoperative radiochemotherapy allowed sphincter-saving resections to be performed, resulting in good local control and functional results in patients with T3 low rectal cancers that would have otherwise required abdominoperineal resections. This suggests that when it

comes to cases of anal canal-involving rectal cancer, treatment with TME plus lateral pelvic node dissection is insufficient, so we should consider performing preoperative chemoradiation therapy.

In this series, we could not find the significant risk factor of local recurrence in the P group mainly because of the relatively small sample size. However, according to the clinical characteristics of the P group, uncommon histological types of tumor and high frequency of lateral pelvic node metastasis may be the relevant risk factors for local recurrence.

Finally, we used multivariate analysis to find independent prognostic factors, which were revealed as uncommon histological tumor types. The rate of uncommon histological tumor type was about 21%. These histological types are associated with less response to chemoradiation and poorer prognosis.<sup>22</sup> Therefore, the development of a new preoperative chemoradiation regimen which is effective for poorly differentiated adenocarcinoma is necessary. We believe that this will improve the prognosis of an otherwise difficult care of anal canal-involving rectal cancer.

## Conclusion

Rectal cancer involving the anal canal should be treated with special care, considering the particularly high lateral pelvic lymph node metastasis rate and high local recurrence rate. Development of an effective chemoradiation regimen for uncommon histological tumor types is necessary for a better prognosis.

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## Analysis of Lymph Node Metastatic Pattern according to the Depth of In-Growth in the Muscularis Propria in T2 Rectal Cancer for Lateral Lymph Node Dissection

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### Key Words

Rectal cancer · Muscularis propria · Lateral pelvic lymph node · Growth pattern

lect cases in which resection of the lateral pelvic lymph node is required for the treatment of rectal cancer invading the muscularis propria (pT2).

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### Abstract

**Background/Aims:** The biological behavior of rectal cancers that invade the muscularis propria (pT2) has not been well studied. We retrospectively studied the pattern of lymph node metastases in patients with T2 rectal cancer. **Methods:** We enrolled 88 patients who had undergone curative resection of T2 colorectal cancer through mesorectal excision and lateral pelvic lymph node dissection; we microscopically estimated the maximum depth of muscularis propria invasion and classified the results into 3 groups representing distinct growth patterns. **Results:** In cases of pT2 colorectal carcinomas, lateral pelvic lymph node metastases depended on the degree of muscularis propria invasion, and the frequency of metastasis increased with the depth of muscularis propria invasion. Lateral pelvic lymph node metastases were not observed when the depth of muscularis propria invasion was less than half of the thickness of the inner circular layer. **Conclusions:** These findings suggest that lateral pelvic lymph node metastasis of pT2 colorectal cancer depends on the depth of vertical invasion, which is analogous to the findings in pT1 and pT3 cancers. This information will be useful in se-

### Introduction

In Japan, lateral lymph node dissection is generally indicated if the lower margin of the primary cancer is located below the peritoneal reflection or anal canal with invasion into the muscularis propria or deeper [1–4].

However, in rectal cancer cases showing invasion into the muscularis propria (pT2), the incidence of perirectal lymph node metastases ranges from 24.3 to 29.7%, and the incidence of lateral pelvic lymph node metastases ranges from 5.5 to 8.2% in patients who undergo lateral pelvic lymph node dissection of rectal cancer [5, 6].

The depth of rectal cancer invasion into the muscularis propria varies widely, i.e. from minimal vertical invasion near the submucosal layer (pT1) to very deep vertical invasion near the subserous layer (pT3).

The biological behavior of submucosal cancer (pT1) in the colorectum has been well studied. Under conditions of lymphatic invasion, vascular invasion, poorly differentiated adenocarcinoma and budding, the depth of vertical

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invasion is  $\geq 1,000 \mu\text{m}$ , and perirectal lymph node metastases are present in about 10% of these cases [7].

In cases of subserous layer cancer (pT3), the prognosis is influenced by the depth of rectal cancer invasion. Thus, the prognosis worsens as the depth of invasion increases [8, 9].

However, the biological behavior of cancers invading the muscularis propria (pT2) has not been well studied.

In this study, we retrospectively estimated the incidence of lateral pelvic lymph node metastases in rectal cancers invading the muscularis propria (pT2).

### Patients and Methods

Between January 1980 and December 2001, 920 patients with rectal cancer underwent curative resection with mesorectal excision and lateral pelvic lymph node dissection at the Department of Gastroenterological Surgery, Aichi Cancer Center Hospital (Nagoya, Japan). Among these, 88 patients who had undergone curative resection of T2 colorectal cancer were enrolled in this study.

Lateral lymph node dissection was indicated if the lower margin of the primary cancer was located below the peritoneal reflection or anal canal with invasion into the muscularis propria or deeper.

The average patient was 55 years of age (range: 24–76), and the study group included 49 men and 39 women.

Anterior resections were performed on 36 patients (40.9%), Hartmann's procedure was performed on 1 patient (1.1%) and abdominoperineal resections were performed on 51 patients (38.0%). In total, 61 patients (69.3%) were negative and 27 patients (30.7%) were positive for lymph node metastasis; furthermore, 19 patients (21.6%) were positive for mesorectal lymph node metastasis only, 3 patients (3.4%) were positive for lateral pelvic lymph node metastasis and 5 patients (5.7%) were positive for both mesorectal and lateral pelvic lymph node metastasis (table 1).

Lateral pelvic lymph node dissection refers to the complete dissection of the lymph nodes up to the aortic bifurcation, the common iliac lymph nodes, the internal iliac lymph nodes, the external iliac lymph nodes, the middle rectal root lymph nodes and the obturator lymph nodes.

The upper margin of the mesenteric lymph node dissection is the root of the inferior mesenteric artery. The distance from the anal margin should be  $\geq 2$  cm when total mesorectal excision is performed.

The resected specimens were fixed with 10% formalin for several days, and the tumor-containing tissue samples were sliced into 4-mm sections at the part with the deepest tumor invasion. Histopathological diagnoses were established by hematoxylin and eosin staining using standard procedures without specific immunostaining.

Using a microscope, the maximum depth of muscularis propria invasion was estimated, and the results were used to classify the cases into 3 groups representing different growth patterns, as explained below (fig. 1).

'Type mp slight' indicates that the maximum depth of the muscularis propria invasion is within half of the thickness of the inner circular layer (fig. 2a). 'Type mp moderate' indicates that the maximum depth of the muscularis propria invasion is more than

**Table 1.** Clinicopathological findings of 88 T2 rectal cancers

Age	55.3 $\pm$ 10.5
Range	24–76
Gender	
Male	49 (55.7)
Female	39 (44.3)
Macroscopic tumor configuration	
Protruded type	11 (12.5)
Ulcerative type	77 (87.5)
Tumor size, cm	4.0 $\pm$ 1.5
Histological type	
Well-differentiated and moderately differentiated types	82 (93.2)
Other types (poorly differentiated, mucinous and Signet-ring cells)	6 (6.8)
Lymphatic invasion	
Negative	37 (42.0)
Positive	51 (58.0)
Vascular invasion	
Negative	50 (56.8)
Positive	38 (43.2)
Operative procedure	
Anterior resection	36 (40.9)
Hartmann	1 (1.1)
Abdominoperineal resection	51 (58.0)
Lymph node metastasis	
Negative	61 (69.3)
Positive	27 (30.7)
Only mesorectum lymph node positive	19 (21.6)
Only lateral pelvic lymph node positive	3 (3.4)
Both mesorectum and lateral pelvic lymph node positive	5 (5.7)

Values are means  $\pm$  SD or n (%), unless otherwise indicated.

half of the thickness of the inner circular layer, with no invasion into the outer longitudinal layer (fig. 2b). 'Type mp massive' indicates that the maximum depth of the muscularis propria invasion is in the outer longitudinal layer (fig. 2c).

From hospital records, we obtained information on a number of variables, including patient age and sex, the operative procedure, macroscopic tumor configuration, and tumor size within the colorectum. On the basis of the data for macroscopic tumor configuration, the tumors were classified as protruded type or ulcerative type. All cases were evaluated by endoscopic ultrasound (EUS), not MRI.

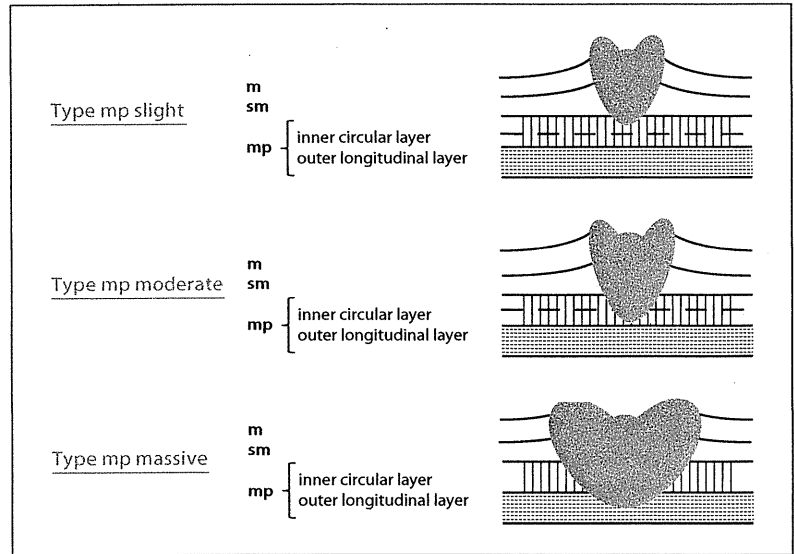
Histological type, lymphatic invasion, venous invasion and the presence or absence of lymph node metastases were investigated using hematoxylin and eosin-stained specimens.

### Statistical Analysis

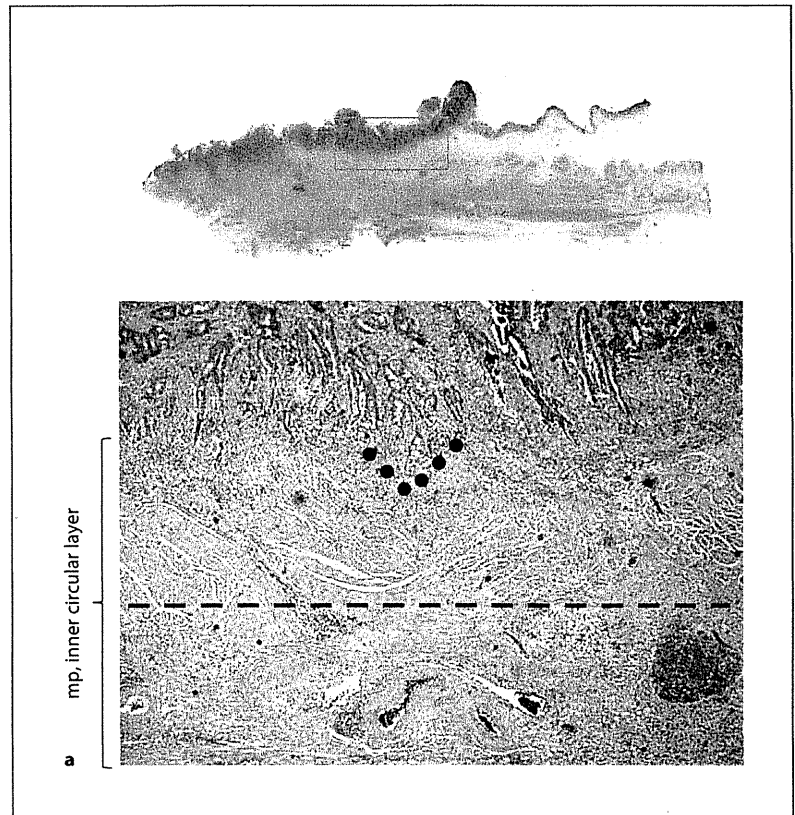
All data are expressed as means  $\pm$  SD. The  $\chi^2$  test, Fisher's exact probability test and the Mann-Whitney U test were used as appropriate. The multivariate Cox proportional hazards model analysis was then performed. log-rank tests were used to compare survival according to each prognostic factor. A level of  $p < 0.05$  was regarded as statistically significant, and CIs were determined at the 95% level.



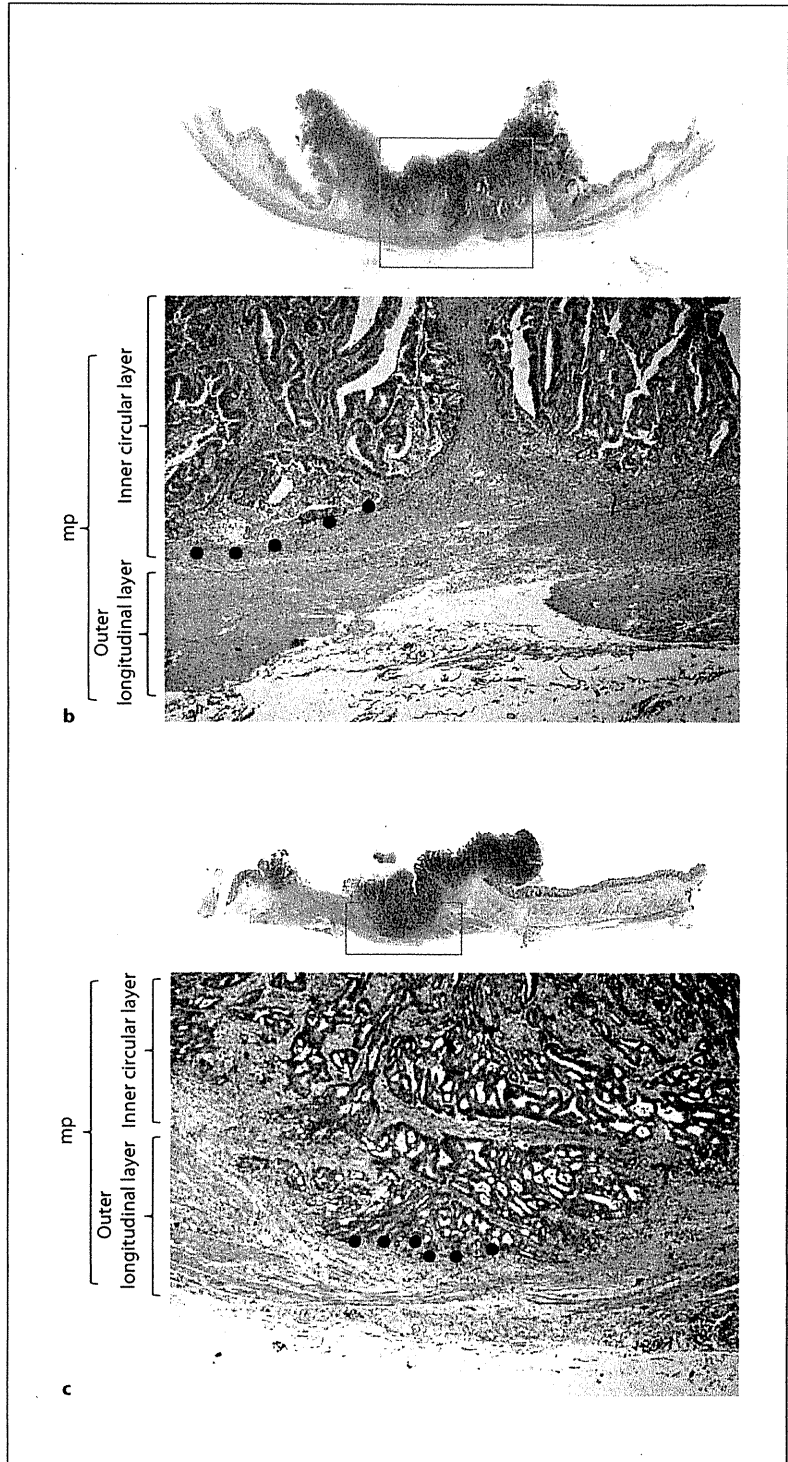
**Fig. 1.** The greatest depth of the vertical muscularis propria invasion was estimated, and the invasion was classified into 3 growth patterns. The black dashed line indicates the midportion of the inner circular layer of the muscularis propria. 'Type mp slight': the greatest depth of the muscularis propria is within half of the inner circular layer. 'Type mp moderate': the greatest depth of the muscularis propria is beyond half of the inner circular layer, but not in the outer longitudinal layer. 'Type mp massive': the greatest depth of the muscularis propria is the outer longitudinal layer.



**Fig. 2. a** Hematoxylin and eosin staining for a 'type mp slight' case. The black dots indicate the greatest depth of the tumor and the black dashed line indicates the midportion of the inner circular layer of the muscularis propria. The greatest depth of the muscularis propria is within half of the inner circular layer (the original magnification of the upper figure is  $\times 2$  and the original magnification of the lower figure is  $\times 40$ ).



**Fig. 2. b** Hematoxylin and eosin staining for a 'type mp moderate' case. The black dots indicate the greatest depth of the tumor. The greatest depth of the muscularis propria is beyond half of the inner circular layer but not in the outer longitudinal layer (the original magnification of the upper figure is  $\times 2$  and the original magnification of the lower figure is  $\times 40$ ). **c** Hematoxylin and eosin stain of a 'type mp massive' case. The black dots indicate the greatest depth of the tumor. The greatest depth of the muscularis propria is in the outer longitudinal layer (the original magnification of the upper figure is  $\times 2$  and the original magnification of the lower figure is  $\times 40$ ).



**Table 2.** Analysis of the correlation between systemic lymph node metastases and clinicopathological findings

	Negative (n = 61)	Positive (n = 27)	Univariate p	Multivariate	
				p	HR
Macroscopic tumor configuration					
Protruded type	7 (11.5)	4 (14.8)	0.664	0.538	0.568 (0.094–3.430)
Ulcerative type	54 (88.5)	23 (85.2)			
Tumor size, cm	4.1 ± 1.8	3.5 ± 1.1	0.089	0.185	0.743 (0.479–1.153)
Histological type					
Well-differentiated and moderately differentiated type	60 (98.4)	22 (81.5)	0.004	0.119	7.331 (0.559–89.694)
Other types (poorly differentiated, mucinous and Signet-ring cells)	1 (1.6)	5 (18.5)			
Lymphatic invasion					
Negative	31 (50.8)	6 (22.2)	0.013	0.608	1.680 (0.232–12.186)
Positive	30 (49.2)	21 (77.8)			
Vascular invasion					
Negative	41 (67.2)	9 (33.3)	0.003	0.390	2.536 (0.422–15.247)
Positive	20 (32.8)	18 (66.7)			
Growth pattern					
Type mp slight	17 (27.9)	3 (11.1)	0.010	0.009	3.119 (1.328–7.323)
Type mp moderate	29 (47.5)	10 (37.0)			
Type mp massive	15 (24.6)	14 (51.9)			

Values are means ± SD or n (%), unless otherwise indicated.

## Results

The average number of retrieved lymph nodes was 46.3 (range: 10–92), and the average number of metastases was 0.7 (range: 0–15). The average number of retrieved lateral pelvic lymph nodes was 27.4 (range: 1–57), and the average number of metastases was 0.16 (range: 0–5).

Tables 2, 3 and 4 show the results of the univariate and multivariate analyses of the 88 cases with pT2 colorectal carcinomas.

Table 2 shows the results of the analysis of systemic lymph node metastasis status in the 88 patients. While the 'type mp slight' and 'type mp moderate' growth patterns account for more than half of the cases with negative lymph node metastasis, the 'type mp massive', 'type mp moderate' and 'type mp slight' growth patterns accounted for 51.9, 37.0 and 11.0%, respectively, of the cases with positive lymph node metastasis. Multivariate analysis revealed that the growth patterns showed a significant correlation with the presence of lymph node metastasis ( $p = 0.009$ ).

Table 3 shows the results of the analysis of the correlation of mesorectal lymph node metastasis with pT2 colorectal carcinoma. Multivariate analysis revealed that the correlation was not statistically significant.

Table 4 shows the results of the analysis of the correlation between lateral pelvic lymph node metastasis and pT2 colorectal carcinomas. Growth patterns and lymphatic invasion were determined to be significant factors influencing this correlation. Of the cases with lateral pelvic lymph node metastasis, 75.0% were 'type mp massive', 25.0% were 'type mp moderate' and none were 'type mp slight.' Conversely, of the cases without lateral pelvic lymph node metastasis, 71.2% were 'type mp slight' or 'type mp moderate', and 28.8% were 'type mp massive'. Multivariate analysis revealed that the growth patterns showed a significant correlation with lymph node metastasis ( $p = 0.006$ ).

Growth patterns are a statistically significant risk factor of lateral pelvic lymph node metastases. In pT2 colorectal carcinomas, the 'type mp slight' to 'type mp massive' classifications describe the depth of muscularis propria invasion, and the frequency of mesorectal and lateral pelvic lymph node metastases increases gradually.

Figure 3 shows the overall survival rate after surgery and the disease-free survival rate after radical surgery. Although there were no significant differences in the survival rates between patients with different growth patterns, the overall survival rate after surgery and the disease-free survival rate after radical surgery increased in the following order: 'type mp slight' > 'type mp moderate' > 'type mp massive'.

**Table 3.** Analysis of the correlation between mesorectal lymph node metastases and clinicopathological findings

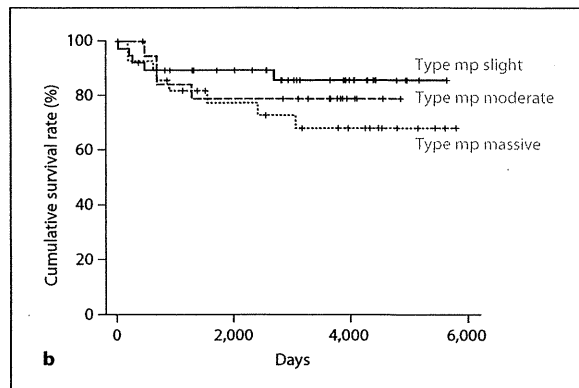
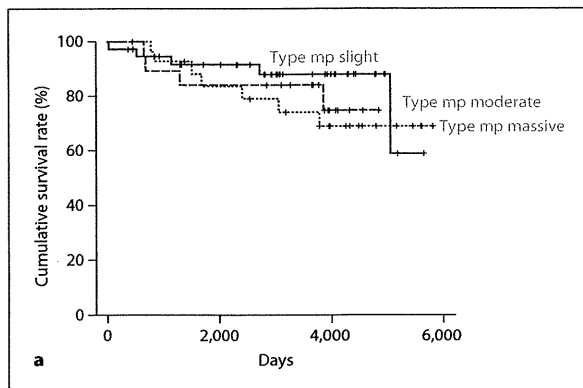
	Negative (n = 64)	Positive (n = 24)	Univariate P	Multivariate	
				p	HR
Macroscopic tumor configuration					
Protruded type	7 (10.9)	4 (16.7)	0.472	0.402	0.482 (0.087–2.660)
Ulcerative type	57 (89.1)	20 (83.3)			
Tumor size, cm	4.1 ± 1.6	3.6 ± 1.2	0.207	0.316	0.803 (0.523–1.233)
Histological type					
Well-differentiated and moderately differentiated type	62 (96.9)	20 (83.3)	0.026	0.254	3.450 (0.411–28.959)
Other types (poorly differentiated, mucinous and Signet-ring cells)	2 (3.1)	4 (16.7)			
Lymphatic invasion					
Negative	32 (50.0)	5 (20.8)	0.014	0.935	1.090 (0.136–8.724)
Positive	32 (50.0)	19 (79.2)			
Vascular invasion					
Negative	43 (67.2)	7 (29.2)	0.001	0.126	4.292 (0.663–27.764)
Positive	21 (32.8)	17 (70.8)			
Growth pattern					
Type mp slight	17 (26.6)	3 (12.5)	0.074	0.085	2.007 (0.908–4.434)
Type mp moderate	29 (45.3)	10 (41.7)			
Type mp massive	18 (8.1)	11 (45.8)			

Values are means ± SD or n (%), unless otherwise indicated.

**Table 4.** Analysis of the correlation between lateral pelvic lymph node metastases and clinicopathological findings

	Negative (n = 80)	Positive (n = 8)	Univariate P	Multivariate	
				p	HR
Macroscopic tumor configuration					
Protruded type	10 (12.5)	1 (12.5)	1.000	0.975	1.058 (0.032–35.013)
Ulcerative type	70 (87.5)	7 (87.5)			
Tumor size, cm	4.0 ± 1.5	3.3 ± 1.2	0.131	0.124	0.485 (0.193–1.218)
Histological type					
Well-differentiated and moderately differentiated type	76 (95.0)	6 (75.0)	0.033	0.812	1.533 (0.045–51.737)
Other types (poorly differentiated, mucinous and Signet-ring cells)	4 (5.0)	2 (25.0)			
Lymphatic invasion					
Negative	36 (45.0)	1 (12.5)	0.077	0.050	36.479 (0.998–1,338.062)
Positive	44 (55.0)	7 (87.5)			
Vascular invasion					
Negative	47 (58.8)	3 (37.5)	0.250	0.250	0.206 (0.014–3.044)
Positive	33 (41.2)	5 (62.5)			
Growth Pattern					
Type mp slight	20 (25.0)	0 (0.0)	0.009	0.006	14.578 (2.194–96.874)
Type mp moderate	37 (46.3)	2 (25.0)			
Type mp massive	23 (28.8)	6 (75.0)			

Values are means ± SD or n (%), unless otherwise indicated.



**Fig. 3.** Prognosis. **a** Overall survival rate after surgery. 'Type mp slight' vs. 'type mp moderate',  $p = 0.395$ ; 'type mp slight' vs. 'type mp massive',  $p = 0.339$ ; 'type mp moderate' vs. 'type mp massive',  $p = 0.680$ . **b** Disease-free survival rate after radical surgery. 'Type

mp slight' vs. 'type mp moderate',  $p = 0.563$ ; 'type mp slight' vs. 'type mp massive',  $p = 0.153$ ; 'type mp moderate' vs. 'type mp massive',  $p = 0.490$ .

### Discussion

To the best of our knowledge, this is the first report to histopathologically classify T stages in pT2 rectal cancer cases in great detail. Pollheimer et al. [10] previously reported on pT2 rectal cancer cases, but they made only 2 classifications, and the classifications themselves were not detailed. The main finding of this retrospective study is that the lateral pelvic lymph node metastasis of pT2 colorectal cancer depends on the depth of vertical invasion, and this is analogous to the findings obtained for pT1 and pT3 cancers.

Several studies have reported the biological behavior of pT1 and pT3 colorectal cancers. In pT1 colorectal cancer, pericolorectal lymph node metastasis is noted when the vertical depth of submucosal invasion exceeds 1,000  $\mu\text{m}$ , poorly differentiated adenocarcinoma is the main histological type and is at the deepest invasive portion, and tumor budding is present [7]. Merkel et al. [8] reported that the pT3 type was subdivided into the following groups according to the histological measurements of the maximal tumor invasion beyond the outer border of the muscularis propria: pT3a (up to 5 mm) and pT3b (more than 5 mm); the prognosis of the former is better than that of the latter. They also reported that of pT3 cancer, cases with a depth of invasion less than 1 mm had better 5-year survival rates than those with a depth of invasion greater than 15 mm.

Our study suggests that the deeper the invasion in the muscularis propria, the higher the frequency of perirectal

and lateral pelvic lymph node metastases. It also suggests that the biological behavior of pT2 is analogous to that of pT1 and pT3 in that lymph node metastasis is affected by the depth of vertical invasion. This biological behavior is especially similar with respect to lateral pelvic lymph node metastases. In pT1 cases, the vertical depth of the submucosal invasion was  $<1,000 \mu\text{m}$ , and there was no lymph node metastasis. Similarly, in pT2 cases, the vertical depth of the submucosal invasions was within half of the thickness of the inner circular layer, and there were no lateral pelvic lymph node metastases.

In Western countries, total mesorectal excision with chemoradiotherapy has now become the standard treatment for advanced rectal cancer. In Japan, however, extended lymphadenectomy with lateral dissection has been aggressively employed for pT2 or more extended rectal cancers located at or below the peritoneal reflection since the late 1970s [1, 3, 11]. There have been no randomized and controlled studies on the usefulness of pelvic sidewall dissections in patients with rectal cancer; therefore, a universal understanding of lateral pelvic lymph node dissection in advanced rectal cancer has not been well established, and the definitive efficacy of pelvic sidewall dissection remains unclear [3].

In other studies, the rates of positive lateral pelvic nodes ranged from 10 to 30% [3]. In particular, with regard to T stage, lateral pelvic lymph node metastases occur in 13–14.9% of rectal cancers localized in the lower rectum below the peritoneal reflection [2]; these metastases also occur in 5.4% of pT1 cancers, 8.2% of pT2 cancers, 16.5% of pT3

cancers and 37.2% of T4 cancers [5]. In other studies, lateral pelvic lymph node metastases occurred in 5.5% of pT2 cases, 16.7% of pT3 cases and 23.1% of T4 cases [6]. According to a previous study [5, 6], only a few lateral pelvic lymph node metastases are indicated in pT2 cases. Therefore, a large number of unnecessary extended lymphadenectomies with lateral dissections were carried out in the past. It is essential to establish the selection criteria for an extended lymphadenectomy with lateral dissection.

Our study established that muscularis propria invasion with maximum depth of less than half of the thickness of the inner circular layer in lateral pelvic lymph node metastasis is not an indication. However, if the maximum depth of the muscularis propria extends to the outer longitudinal layer, the frequency of lateral pelvic lymph node metastasis is high. Additionally, the greater the depth of the vertical invasion into the muscularis propria, the higher the frequency of lateral pelvic lymph node metastasis.

Therefore, our retrospective study will shed light on this question of selection criteria. In the near future, if the depth of vertical invasion into the muscularis propria can be accurately measured at the time of preoperative diagnosis, e.g. by EUS, then it will be possible to select cases with a high risk of lateral pelvic lymph node metastasis.

More recently, Puli et al. [12] reported that EUS should be preferably used for the detection of T stage rectal cancers because it has high sensitivity and specificity. The sensitivity of EUS is higher for advanced disease than for early disease. EUS should be strongly considered for T staging of rectal cancers [12]. Mezzi et al. [13] concluded that EUS and MRI are accurate imaging techniques for staging rectal cancer.

If the preoperative diagnosis can be made on the basis of techniques such as EUS and MRI, pT2 cases could be subdivided for T staging, i.e. 'type mp slight', 'type mp moderate' and 'type mp massive' in rectal cancer, and the findings of our study would make it possible to confirm the positive cases of lateral pelvic lymph node metastases.

## Conclusions

The results of this study suggest that the biological behavior of pT2 is affected by the depth of vertical invasion. Our findings are useful for the selection of cases in which it is necessary to resect the lateral pelvic lymph nodes for the treatment of rectal cancer invading the muscularis propria (pT2).

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## Evaluation of factors affecting the difficulty of laparoscopic anterior resection for rectal cancer: “narrow pelvis” is not a contraindication

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### Abstract

**Background** This study aims to evaluate the clinical and anatomical factors, particularly pelvic dimensions that influence the difficulty of performing laparoscopic anterior resection for rectal cancer.

**Methods** We studied 50 consecutive patients who underwent laparoscopic anterior resection with double-stapling technique (DST) anastomosis for rectal cancer between January 2006 and February 2010. Staging was performed by computed tomography. Five pelvic dimensions (anteroposterior and transverse diameters of pelvic inlet and outlet, and pelvic depth) were measured using three-dimensional volume-rendering images. We also examined a number of other clinical characteristics, including gender, history of laparotomy, body mass index (BMI), operator, tumor location, tumor depth, nodal involvement, and tumor diameter. Univariate and multivariate analyses were performed to determine the predictive significance of these variables on surgical difficulty based on operative time and intraoperative blood loss.

**Results** Males had significantly shorter pelvic inlets and outlets and significantly greater pelvic depth than females. However, gender did not significantly affect surgical outcomes, although males did tend to experience greater blood loss. Maximum tumor diameter ( $p = 0.014$ ), BMI

( $p = 0.001$ ), operator ( $p < 0.001$ ), and tumor location ( $p = 0.009$ ) were independent predictors of operative time, which, in turn, was related to intraoperative blood loss ( $p < 0.001$ ).

**Conclusions** Maximum tumor diameter, BMI, operator experience, and tumor location can be used to predict the operative time required to complete laparoscopic anterior resection with DST anastomosis for rectal cancer, with no correlations between pelvic dimensions and operative time. The difficulty of the procedure was not related to patients' pelvic dimensions, which led us to conclude that “narrow pelvis” is not a contraindication for this surgery. Based on these results, we suggest that laparoscopic anterior resection should be performed by experienced surgeons in patients with large tumors, high BMI, and/or extraperitoneal rectal cancer.

**Keywords** Laparoscopic anterior resection · Rectal cancer · Body mass index · Pelvic dimension · Narrow pelvis · Volume-rendering image

Laparoscopic procedures for rectal cancer have been reported to be safe and effective for a number of reasons, including relatively low levels of pain and blood loss, early resumption of bowel movement, and short postoperative hospital stay [1–6]. Additionally, randomized studies have shown that laparoscopic total mesorectal excision (TME) and lymph node dissection are productive surgical techniques with survival and recurrence rates comparable to those of open procedures [4, 6–8]. However, while laparoscopic surgery is the standard treatment for colon cancer, it is not commonly performed in cases of rectal cancer because it is technically challenging and may be associated with disadvantages such as long

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operative time [1, 2, 4] and increased rate of positive surgical margins [9].

Rectal surgery is performed through a narrow and funneling bony inlet, which makes access and visualization difficult in the deep pelvis. Even in the relatively simpler open approach, it is difficult to maintain a clear surgical field, to recognize precise anatomy, and to accurately perform rectal mobilization and excision while preserving urogenital functions. Recent studies have suggested that the quality of open rectal surgery is influenced not only by the surgeon's skill but also by the patient's clinical and anatomical factors, such as gender, tumor height, and pelvic size [10–12]. Similar relationships possibly influence the outcomes when using the laparoscopic approach, but evaluation of the influence of such clinical and anatomical factors on laparoscopic rectal surgery has been limited [13, 14]. The purpose of this study is to evaluate the influence of various clinical and anatomical factors, particularly pelvic dimensions, on operative time and intraoperative blood loss, which were selected as dependent variables to represent the level of difficulty in performing laparoscopic anterior resection with double-stapling technique (DST) anastomosis for rectal cancer.

## Patients and methods

### Patients

We studied 50 consecutive patients who underwent laparoscopic anterior resection with DST anastomosis for rectal cancer located below the inferior edge of the S2 vertebra between January 2006 and February 2010.

The indications for laparoscopic surgery were rectal cancer without involvement of the lateral lymph nodes or invasion of the adjacent organs, as determined by computed tomography (CT) and pelvic magnetic resonance imaging (MRI) during preoperative examinations. An additional indication was evidence of metastatic disease that could not be curatively resected using open surgery.

In Japan, preoperative radiotherapy or chemotherapy is not routinely administered in the treatment of rectal cancer; it is currently being used in clinical trials or mainly in patients with locally advanced, very low tumors to increase the chance of sphincter-preserving surgery. In this study, no patients underwent preoperative radiotherapy or chemotherapy.

Data for age, gender, history of laparotomy, body mass index (BMI), tumor location, tumor size, tumor staging, operative time, amount of blood loss, conversion to open surgery, pathology, 30-day morbidity, and mortality were collected prospectively. Tumors were staged according to the sixth tumor–node–metastasis (TNM) classification of

the International Union against Cancer (UICC) on the basis of the histological findings of the surgical specimens.

### Surgical procedures

The surgeries were performed by an experienced expert surgeon (T.Y.) or by trainees with 3–6 years of experience, operating under the expert's supervision.

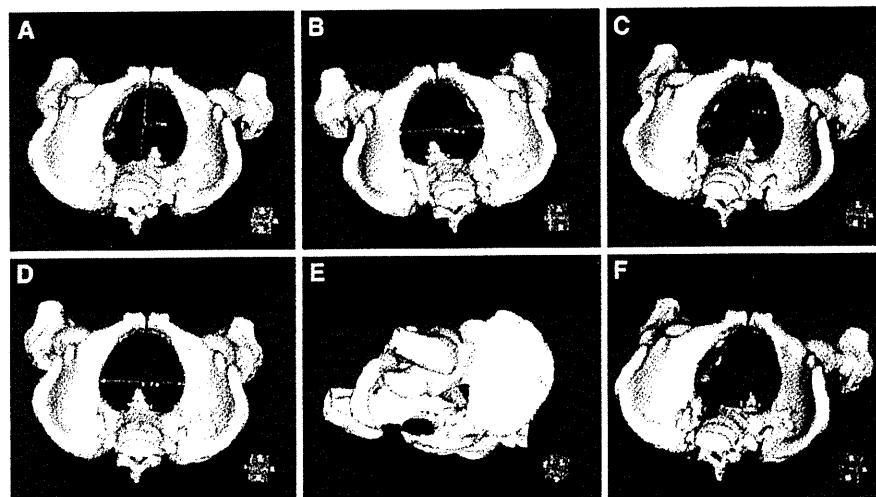
Anterior resection is used for the treatment of early cancer located just above the dentate line and advanced cancer located >1 cm above the dentate line; these criteria enable the acquisition of adequate distal margin after rectal transection. Here, patients were placed in Lloyd–Davis position with the head and right side of the bed lowered. First, a 12-mm camera port was inserted below the umbilicus using the open method. After creation of a pneumoperitoneum, four working ports were inserted: a 5-mm port in the right and left upper abdominal quadrants each, and a 12-mm port in the right and left lower abdominal quadrants each. The mesocolon was mobilized using the mediolateral approach, and the inferior mesenteric artery was divided near its origin in order to achieve wide lymphadenectomy. This permitted TME, except in cases of intraperitoneal rectal cancer, where tumor-specific mesorectal excision (TSME) was performed instead. The rectum was transected intracorporeally using an Endo-Cutter (Ethicon Endo-Surgery, Cincinnati, OH, USA) and anastomosed with DST. No diverting stoma was created.

### Pelvimetry

All patients underwent abdominopelvic CT (Aquilion 16; Toshiba Medical Systems Corporation, Tochigi, Japan). In most cases, the slice interval was adjusted to 5 mm. Sequences were volume-rendered using a DICOM 3D viewer, INTAGE Realia (KGT Inc., Tokyo, Japan). Volume-rendering (VR) images were obtained from the extracted volume data using INTAGE Volume Player (KGT Inc., Tokyo, Japan). A single observer (S.O.) blinded to all clinical information regarding the patients made all measurements in the VR images. Five pelvic dimensions were measured: anteroposterior and transverse diameters in the pelvic inlet (the axis from the superior aspect of the pubis symphysis to the sacral promontory and the longest lateral axis in the iliopectineal line), anteroposterior and transverse diameters in the pelvic outlet (the axis from the inferior aspect of the pubis symphysis to the tip of the coccyx and the distance between the tips of the ischial spines, i.e., interspinous distance), and the pelvic depth (the distance between the sacral promontory to the tip of the coccyx) (Fig. 1).



**Fig. 1** Anteroposterior (A) and transverse (B) diameters in the pelvic inlet, anteroposterior (C) and transverse (D), E) diameters in the pelvic outlet, and length of pelvic depth (F) were measured using three-dimensional VR images



### Statistical analysis

The sample size was calculated to detect moderate correlation (correlation coefficient:  $|r| = 0.4$ ) with  $\alpha$  of 0.05 (two-sided) and  $\beta$  of 0.2 (power of 80%), suggesting a total study population of 47 patients. All statistical analyses were performed using SPSS version 15.0 (Statistical Package for Social Sciences™; SPSS, Inc., Chicago, IL, USA). Statistical significance was defined as  $p < 0.05$ . Where appropriate, we used Fisher's exact test, chi-square test, Student's  $t$  test, Welch's test, or Pearson's product-moment correlation coefficient to investigate relationships between patients' clinical and anatomical characteristics and surgical difficulties. Multivariate analysis was performed using a multiple linear regression model with a stepwise method (significance level to enter = 0.05; significance level to stay = 0.1).

To assess intraobserver variation, measurements of the pelvic dimensions of 10 patients were repeated after an interval of 4 weeks, with the observer blinded to the initial results [10, 14]. According to the Pearson's product-moment correlation coefficient, the intraobserver variation was 0.946. The two sets of measurements were highly correlated ( $p < 0.001$ ), indicating that they accurately described pelvic anatomy.

### Results

Patient and tumor characteristics are summarized in Table 1. Anastomosis height was significantly greater in males than in females ( $p = 0.014$ ). All five pelvic dimensions differed significantly between male and female patients. Females had significantly longer measurements for the pelvic inlet and outlet (all  $p < 0.003$ ), while males

had significantly greater pelvic depth ( $p < 0.001$ ). Overall, this indicated that male pelvises were significantly narrower and deeper than female pelvises.

Although males tended to experience more blood loss during surgery ( $p = 0.11$ ), there were no significant differences between the genders in surgical outcomes (Table 2). In no case was there conversion to open surgery, death or positive circumferential resection margins (CRM). Complications were identified in two male patients: one wound infection and one anastomotic leakage. The overall morbidity rate was 4%, and the anastomotic leakage rate was 2%.

Univariate analysis showed that age ( $p = 0.012$ ), BMI ( $p = 0.009$ ), operator ( $p = 0.006$ ), and maximum tumor diameter ( $p = 0.003$ ) were significantly associated with operative time (Table 3). Although operative time tended to increase as anteroposterior pelvic inlet diameter decreased ( $p = 0.151$ ) and pelvic depth increased ( $p = 0.103$ ), these relationships were not significant.

Stepwise linear regression analysis showed that the optimal model for predicting operative time included maximum tumor diameter, BMI, operator, and tumor location ( $p < 0.001$ , Table 4). Operative time increased as maximum tumor diameter and BMI increased, but decreased with an expert performing the operation and for intraperitoneal tumor location. Operative time, in turn, was the only factor significantly associated with blood loss ( $p < 0.001$ ); no other variables had any relationship with blood loss.

### Discussion

In this study, multivariate analysis showed that larger maximum tumor diameter, higher BMI, trainee performing

**Table 1** Patients' clinical and anatomical characteristics

	Male ( <i>n</i> = 30)	Female ( <i>n</i> = 20)	<i>p</i> Value
Age (years)	66 (60, 79)	70 (58, 75)	0.93
Previous laparotomy (no.)	9	9	0.43
BMI (kg/m <sup>2</sup> )	21.5 (18.7, 22.6)	21.4 (18.0, 23.4)	0.87
Operator			0.82
Expert (no.)	17	12	
Trainee (no.)	13	8	
Tumor location of lower edge			0.20
Intraperitoneal (no.)	19	9	
Extraperitoneal (no.)	11	11	
Tumor depth			0.81
Tis/T1/T2 (no.)	19	12	
T3/T4 (no.)	11	8	
Nodal involvement			0.75
N0 (no.)	22	13	
N1/N2 (no.)	8	7	
Maximum tumor diameter (cm)	4.0 (1.8, 5.2)	3.3 (2.0, 4.1)	0.38
Procedure			0.72
High anterior resection (no.)	2	1	
Low anterior resection (no.)	28	19	
Anastomosis height from anal verge (cm)	6.0 (4.0, 6.8)	4.0 (4.0, 5.0)	<b>0.014</b>
Pelvic dimensions			
Inlet			
Anteroposterior (cm)	11.0 (10.3, 11.8)	11.9 (11.5, 12.7)	<b>&lt;0.001</b>
Transverse (cm)	12.3 (11.9, 12.7)	12.9 (12.4, 13.3)	<b>0.002</b>
Outlet			
Anteroposterior (cm)	10.0 (9.4, 10.3)	10.6 (10.1, 11.4)	<b>0.003</b>
Transverse (cm)	9.7 (9.1, 10.0)	11.1 (10.7, 11.9)	<b>&lt;0.001</b>
Depth (cm)	12.4 (11.4, 12.7)	11.2 (10.0, 11.8)	<b>&lt;0.001</b>

All continuous variables are described as median (first quartile, third quartile)

Bold font in table means that the *p*-values were statistically significant

**Table 2** Surgical outcomes in relation to gender

	Male ( <i>n</i> = 30)	Female ( <i>n</i> = 20)	<i>p</i> Value
Operative time (min)	305 (271, 325)	277 (254, 333)	0.26
Blood loss (ml)	25 (8, 58)	5 (0, 23)	0.11
Complication (no.)	2	0	0.66
Anastomotic leakage (no.)	1	0	0.84
Conversion (no.)	0	0	na
Mortality (no.)	0	0	na
Positive CRM (no.)	0	0	na

CRM circumferential resection margin

the operation, and extraperitoneal tumor location were significantly associated with longer operative time in laparoscopic anterior resection with DST anastomosis for rectal cancer, while pelvic dimensions had no correlations with operative time. Furthermore, operative time was the only factor significantly associated with intraoperative blood loss. The present findings are valuable in suggesting

that pelvic dimensions were not definitive factors as compared with maximum tumor diameter, BMI, operator experience, and tumor location in predicting the difficulty of performing this procedure.

Interest in pelvimetry began with attempts to predict cephalopelvic disproportion in pregnant women prior to labor. Pelvimetry has been utilized for patients with rectal cancer, using MRI [10–12] and CT [13, 14] images; in these cases, measurements were made on two-dimensional reconstructed (axial and sagittal) images. However, these cross-sectional images only permit measurement of distances between points that exist in the same orthogonal coordinate axis. We preferred the use of three-dimensional VR images, because they allow precise measurements along any axis and can be especially beneficial in cases with anatomically strained pelvis or mismatched alignments between patients and imaging devices. The precision and sensitivity of this technique were demonstrated by its ability to correctly indicate that male pelvises are narrower and deeper than female pelvises, as well as by the strong correlation between the two sets of

**Table 3** Correlations between operative time and operative parameters

Variable	<i>p</i> Value
Gender (male versus female)	0.131
Age	<b>0.012</b>
Previous laparotomy	0.430
BMI	<b>0.009</b>
Operator (expert vs. trainee)	<b>0.006</b>
Tumor location (intraoperative versus extraperitoneal)	0.338
Tumor depth (T1/T2 vs. T3/T4)	0.247
Nodal involvement (N0 vs. N1/N2)	0.471
Maximum tumor diameter	<b>0.003</b>
Anastomosis height from anal verge	0.338
Pelvic dimensions	
Inlet	
Anteroposterior	0.151
Transverse	0.250
Outlet	
Anteroposterior	0.481
Transverse	0.324
Depth	0.103

Bold font in table means that the *p*-values were statistically significant

**4** Variables included in the final stepwise linear regression model explaining variations in operative time

	<i>B</i>	$\beta$	<i>p</i> Value
Intercept	190.871		<0.001
Maximum tumor diameter (cm)	8.075	0.289	0.014
BMI (kg/m <sup>2</sup> )	6.828	0.382	0.001
Operator (expert)	-66.755	-0.576	<0.001
Tumor location (intraoperative)	-42.945	-0.373	0.009

$R^2 = 0.463$   
Model utility test:  $p < 0.001$

measurements in the intraobserver variation test ( $r = 0.946$ ,  $p < 0.001$ ).

In this study, we chose to evaluate cases of rectal cancer that underwent laparoscopic anterior resection with DST anastomosis, because intracorporeal rectal transection and anastomosis is one of the most difficult procedures in laparoscopic rectal surgery and therefore should be considered separately from cases that undergo abdominoperitoneal resection or intersphincteric resection with transanal hand-sewn anastomosis. We selected operative time and intraoperative blood loss as dependent variables representing technical difficulties during this procedure. Other variables, including complications, anastomotic leakage, conversion, mortality, and positive CRM, occurred at such low rates that they could not be analyzed. This indicates

that the procedure can be performed safely and without morbidity or conferring any oncologic disadvantage.

It is not immediately clear why anastomosis height was significantly greater in males than in females. Unlike previous authors [13, 15], we did not find that operative outcome differed significantly between the two genders. These results may partly be explained by the fact that pelvic procedures can be completed more easily in wider and shallower female pelvises, but may also be disrupted by the presence of the uterus.

Patients in this study had BMI ranging from 12.0 to 27.8 kg/m<sup>2</sup>; these values are lower than those in Western populations. Nevertheless, our results agreed with previous reports that found a positive association between operative time and BMI [14]. This is likely associated with greater mesorectal volume, which restricts the pelvic working space for the procedures. Therefore, visceral fat may be an even better predictor of surgical difficulty than BMI [16, 17]. Further, larger maximum tumor diameter reflects larger tumor volume, which again restricts the pelvic working space. Space can also be restricted by the location of tumors; i.e., when tumors are positioned extraperitoneally, surgeons have a narrower space in which to perform rectal dissection, transection, and anastomosis, since the pelvic width becomes narrower as one approaches deeper into the pelvis. Thus, cumulatively, higher BMI, larger maximum tumor diameter, and extraperitoneal tumor location impact operative time by limiting pelvic free space for the procedures and reducing visibility, maximum retraction, and access to the depths of the pelvis via the pelvic inlet.

In keeping with our previous finding, operative time was longer when procedures were performed by trainees [18]. Pelvic space cannot be expanded by pneumoperitoneum, as can be done in the upper abdomen, and limited working space directly affects the difficulty of safe and quick access, required to optimize visibility and retraction. We presume that these issues do not present as great a problem to expert surgeons because they have more experience in creating an appropriate surgical field and obtaining a good view for identifying and dissecting anatomical structures even in a limited pelvic working space.

Although pelvic depth tended to correlate with operative time, we did not find any significant patterns linking pelvic dimensions with operative outcomes. These results are contrary to those previously reported elsewhere [13, 14]. We hypothesize that this is because BMI, maximum tumor diameter, and tumor location have greater effect on pelvic working space than do pelvic dimensions. Additionally, this study included cases of both intraoperative and extraperitoneal rectal cancer, while a similar previous study focused only on extraperitoneal rectal cancer [14]. Furthermore, the procedures in our study were performed by both experts and trainees, rather than experts only [14].

Thus, these differences in inclusion criteria may explain why we did not detect any significant correlations between pelvic dimensions and operative time.

Our study has certain limitations. The sample size of this study was small, although the study was not statistically underpowered. However, future examinations with larger sample size would elucidate our results further. Additionally, other variables, including complications, anastomotic leakage, conversion, mortality, and positive CRM, should be examined to generalize the present findings.

In summary, our results indicate that “narrow pelvis” is not a contraindication for laparoscopic resection of rectal cancer. We also recommend that this procedure be performed by experienced surgeons in patients with large tumors, high BMI, and/or extraperitoneal rectal cancer.

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