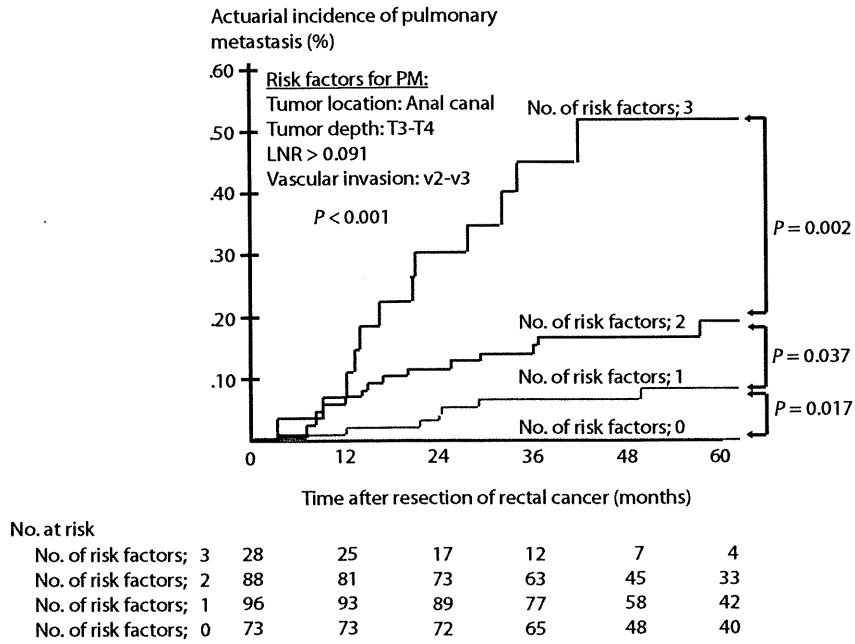

No. at risk

No. of risk factors; 3	28	25	17	12	7	4
No. of risk factors; 2	88	81	73	63	45	33
No. of risk factors; 1	96	93	89	77	58	42
No. of risk factors; 0	73	73	72	65	48	40

FIGURE 5. Kaplan-Meier curves for pulmonary metastases after R0 resection of rectal cancer according to the risk factors for pulmonary metastases, excluded 29 patients with lateral pelvic lymph node involvement. PM = pulmonary metastases; LNR = lymph node ratio.

CONCLUSION

The present study clearly demonstrated predictive factors for pulmonary metastases after R0 resection of rectal cancer without preoperative chemoradiotherapy. Actuarial incidence of pulmonary metastases was significantly related to the number of risk factors present. The data from the present study should facilitate the establishment of novel algorithms for predicting pulmonary metastases after resection of rectal cancer, which may lead to the appropriate surveillance strategies after rectal surgery.

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ORIGINAL CONTRIBUTION

The Association Between Anal Function and Neural Degeneration After Preoperative Chemoradiotherapy Followed by Intersphincteric Resection

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BACKGROUND: Preoperative chemoradiotherapy for rectal cancer is administered to improve local control, but it can also induce severe anal dysfunction after surgery.

OBJECTIVE: The goals of the study were to assess the influence of preoperative chemoradiotherapy on pathological findings and to examine the correlation of these findings with the cause of severe anal dysfunction after intersphincteric resection.

DESIGN: Peripheral nerve degeneration was evaluated histopathologically with the use of hematoxylin and eosin-stained sections of surgical specimens after intersphincteric resection, based on karyopyknosis, vacuolar degeneration, acidophilic degeneration of cytoplasm, denucleation, and adventitial neuronal changes. Each item was scored to quantify the level of neural degeneration, and the relationship between degeneration and anal function was examined at 12 months after closure of the stoma. Anal function was assessed by questionnaire, and incontinence was evaluated based on the Wexner score.

SETTING: This study was conducted at the National Cancer Center Hospital East from 2001 to 2006.

PATIENTS: The subjects were 68 patients with lower rectal cancer who underwent intersphincteric resection with (n = 47) or without (n = 21) preoperative chemoradiotherapy.

MAIN OUTCOME MEASURES: The findings in the 2 groups were compared to clarify the association between the degree of histological degeneration and postoperative anal function.

RESULTS: Neural degeneration was significantly higher in the chemoradiotherapy group, and the neural degeneration and Wexner scores had a significant correlation ($P = .003$, $r = 0.477$).

CONCLUSION: Preoperative chemoradiotherapy induced marked neural degeneration around the rectal tumor. The significant correlation between the degeneration score and postoperative anal function suggests that this score may be a useful marker to predict the influence of preoperative chemoradiotherapy on anal function after surgery.

KEY WORDS: Chemoradiotherapy; Internal sphincteric resection; Neural degeneration; Rectal cancer; Anal function.

Innovative treatment for lower rectal cancer has recently tended toward preservation of the anus. Low anterior resection with coloanal anastomosis[1] and intersphincteric resection (ISR)[2] are advanced anus-preserving operations for the treatment of low rectal cancer with avoidance of a colostomy. Anastomoses are made near to or under the dentate line in the anal canal, and the procedures have a tolerable and clinically acceptable local recurrence rate.[3,4] Preoperative chemoradiotherapy (CRT) or

Disclosures: None reported.

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radiotherapy is also thought to be necessary to decrease local recurrence following ISR.[5–7]

Investigations of functional outcome after ISR[6,8–11] have shown that satisfactory anal function is preserved in most patients, but some have severe dysfunction[11,12] and conversion to colostomy may be necessary as an additional treatment.[8,12] Preoperative CRT has been found to be most strongly associated with poor anal function after ISR, suggesting that patients with rectal cancer who undergo ISR after preoperative CRT are likely to experience incontinence.[13,14] Lim et al[15] reported that a conventionally fractionated 45-Gy dose of preoperative CRT caused poor anorectal function because of damage to the pudendal nerve. Rectal function may also be worsened by radiation-induced proctitis and induction of rectal compliance due to fibrosis of the rectal wall,[16,17] and direct radiation injury to the internal anal sphincter muscles can also cause anal sphincter dysfunction.[18]

Given this background, it is likely that pathological analysis of the anal sphincter muscle area may show an association with anal sphincter dysfunction. However, the relationship between histopathological findings and CRT in the anal sphincter muscle area has not been studied. Therefore, we examined the degree of tissue degeneration, with a particular focus on neural degeneration and tissue fibrosis, in surgical specimens resected from patients who underwent surgery with or without preoperative CRT. In previous reports[19,20] on esophageal carcinoma, toxicities such as neuropathy have been observed during CRT, suggesting that neuropathy may be based on neural degeneration. The aim of this study was to investigate neural degeneration pathologically, because this may cause anal dysfunction. Findings in patients with or without preoperative CRT were compared to clarify the association between the degree of histological degeneration and postoperative anal function.

PATIENTS AND METHODS

Patients

Between 2001 and 2006, 68 patients underwent ISR for very low rectal cancer at the National Cancer Center Hospital East, Chiba, Japan. Of these patients, 47 received CRT before surgery and 21 underwent surgery alone (control group). For ISR cases from 2002 to 2004, CRT was performed for all patients who gave consent. The subjects examined before and after this period and ISR cases in which patients did not consent to CRT were examined as the surgery-only group. Cases in which infiltration in the external sphincter muscle was shown by MRI in the preoperative diagnosis of tumor depth were excluded from our indication for ISR. A diverting stoma was constructed in each patient, and the stoma was finally closed in all the patients. Questionnaires on postoperative anal function[8] were collected from 59 of the 68 patients at 12 months after closure of the stoma. Our operative indications for ISR were a tumor edge 5 cm above the anal verge or 3 cm above the dentate line; adenocarcinoma confirmed histologically by preoperative biopsy; and age less than 76 years.[8] Preoperative stage was determined according to the International Union Against Cancer classification.[21]

Surgical Procedure

ISR was performed as described previously.[8] First, dissection was performed by the abdominal approach until total mesorectal excision was complete. The outside layer of the internal sphincter muscle was then exposed and circumferentially divided from the puborectal muscle and the external sphincter. After the abdominal approach was completed, perianal resection was performed. The mucosa and the internal sphincter muscle were incised 1 to 2 cm distal to the tumor. If the tumor had invaded the external sphincter, ISR plus partial resection of the external sphincter was performed with preservation of at least the subcutaneous part of the external sphincter. The decision of whether to create a pouch (either a J-pouch or a transverse coloplasty pouch) was left to the discretion of the surgeon.

Preoperative Therapy

Forty-seven patients with clinical T3 tumors agreed to undergo CRT. Over a 5-week period, a dose of 45 Gy was administered along with intravenous infusion of 5-fluorouracil (250 $mg \cdot m^{-2} \cdot d^{-1}$) to increase the efficacy of radiotherapy. Nerve-sparing resection surgery was performed 2 weeks after completion of preoperative CRT.[22]

Pathological Evaluation

Hematoxylin and eosin-stained sections of the surgical specimens were used for pathological evaluation. The sections were evaluated by 2 authors (S.F. and Y.N.) who were blinded to the clinical information for the patients.

Pathological Examination of Nerves Near the Internal Sphincter Muscle

Before pathological evaluation, the numbers of nerves in the hematoxylin and eosin-stained sections were counted in low-power magnification fields (10 × 10). Ten nerves around the primary lesion were selected and photographed, and the consistency of features of the nerves in each photograph was evaluated. In this manner, pathological neural degeneration was evaluated for 10 nerves near to the tumor in each patient, based on the following features: karyopyknosis, vacuolar degeneration, acidophilic degeneration of cytoplasm, denucleation, and adventitial neuronal changes. To obtain a total degeneration score, the presence of the first 4 features was scored as 1 point each. Adventitial neuronal changes were evaluated based on a 3-point scale, with 1, 2, and 3 defined as perineurial hypertrophy, perineurial fibrosis, and intraneural fibrosis.

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Therefore, the degeneration score ranged from 0 to 7. The association between this score and anal function was examined at 12 months after surgery.

Fibrosis

The degree of fibrosis of the primary tumor was evaluated on a 4-point scale, with grades 0, 1, 2, and 3 reflecting <10%, 10% to 30%, 30% to 50% and ≥50% replacement of tumor tissue by fibrosis in the section with the maximum tumor diameter.[18]

Abscess Formation

The presence of an abscess in the tumor was examined based on aggregates of neutrophil infiltration (0, absence of abscess; 1, presence of abscess). An abscess was defined as an area of neutrophilic aggregation with a diameter larger than 500 μm observed microscopically.

Assessment of Anal Function

The functional outcome was assessed by the use of the continence score of Jorge and Wexner (Wexner score).[23] Questionnaires were collected from patients during consultation in the physician's office after the patient had filled out the questionnaire by themselves at home. Questionnaires to evaluate the Wexner score were given at 12 months after stoma closure. Thus, the relationship between the degree of degeneration and postoperative anal function was examined based on the Wexner score at 12 months after stoma closure. This score reflects the postoperative anal function, because gradual improvements in Wexner scores are seen from 3 to 6 months and further slight improvements occur between 6 and 24 months.[13]

Statistical Analysis

A Student *t* test and Fisher exact test were used to examine histological differences between the CRT and control groups. A Mann-Whitney *U* test was used to examine the relationship between CRT and Wexner scores. The Mann-Whitney *U* test was also used to examine the relationship between histological findings (karyopyknosis, vacuolar degeneration, acidophilic change, and denucleation) and Wexner scores. A Kruskal-Wallis test was used to examine the relationship between histological findings (adventitial neuronal changes, fibrosis, and abscess) and Wexner scores. Spearman analysis was used to examine the correlation between degeneration scores and Wexner scores. All statistical analyses were performed using SPSS for Windows, v.13.0 J (SPSS-Japan Inc., Tokyo, Japan). A *P* value of <.05 was considered to be significant.

RESULTS

The clinical characteristics of the 68 patients are shown in Table 1, including preoperative CRT, mean tumor distance from the anal verge, extent of excision of the internal sphincter muscle, resection of the external sphincter, and pathological stage. There were no significant differences between the CRT and control groups in age, sex ratio, and anal verge distance. Total ISR was used less frequently in the control group. Regarding the pathological stage, 66% of cases in the CRT group were stages I and II, whereas 58% of cases in the control group were stage III. There were no significant differences in clinical stage ($P = .70$) and pathology stage ($P = .12$) between the CRT and control groups. Many cases in the CRT group were stage I or II and total ISR was performed in some of these cases (Table 1).

TABLE 1. Clinical characteristics of the patients

	CRT group	*Control group*	*P*
Patients	47	21	
Median age (range)	56 (27–77)	60 (39–72)	.22
Sex, M:F	35:12:00	15:06	.79
Median AV (cm)	3.5 (0–5.0)	4.0 (2.5–5.5)	.66
Operative procedure (%)			
Total ISR	20 (43)	1 (5)	.03
Subtotal ISR	22 (47)	13 (62)	
Partial ISR	5 (11)	7 (33)	
PESR	13 (28)	7 (33)	.63
Clinical/pathology stage (%)			
I	9 (19)/25 (53)	4 (19)/4 (19)	.70/.12
II	16 (34)/6 (13)	8 (38)/5 (24)	
IIIa	9 (19)/5 (11)	5 (24)/6 (29)	
IIIb	11 (23)/8 (17)	3 (14)/6 (29)	
IV	2 (4)/2 (4)	1 (5)/0 (0)	
Postoperative complications (%)	14 (29)	9 (43)	.29
Anastomotic leakage	5 (11)	3 (14)	.67
Pelvic abscess	6 (12)	5 (24)	.25

AV = anal verge; ISR = intersphincteric resection; CRT = chemoradiotherapy; PESR = partial external sphincter resection.

Postoperative complications occurred in 14 subjects (29%) in the CRT group (anastomotic leakage in 5 (11%) and pelvic abscess in 6 (12)), and in 9 subjects (43%) in the control group (anastomotic leakage in 3 (14%) and pelvic abscess in 5 (24%)). There was no significant difference in the rate of postoperative complications between the 2 groups. The average time between the primary operation and closure of the stoma was 227 days (range, 80–665 days) in the CRT group and 247 days (range, 85–558 days) in the control group.

Tissue fibrosis of grade 2 or 3 was observed in 73% of cases in the CRT group, whereas fibrosis of grade 0 or 1 accounted for 86% of cases in the control group. The incidence of more severe fibrosis was significantly higher in the CRT group ($P < .001$). No intratumor abscess was present in 79% of cases in the CRT group, but abscesses were observed in 52% of cases in the control group, giving a significantly higher incidence of abscess formation in the control group ($P = .010$).

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TABLE 2. Pathologic findings

	CRT group (n = 47)	*Control group (n = 21)*	*P*
Fibrosis grade: 0/1/2/3, n (%)	2/11/13/21 (4/23/28/45)	16/2/2/1 (76/10/10/5)	<.001
Abscess grade: 0/1, n (%)	37/10 (79/21)	10/11 (48/52)	.010
Karyopyknosis, n (%)	19 (40)	0 (0)	.001
Vacuolar degeneration, n (%)	32 (68)	4 (19)	<.001
Acidophilic degeneration of cytoplasm, n (%)	15 (32)	0 (0)	.002
Adventitial neuron change: 0/1/2/3, n (%)	2/25/7/13 (4/53/15/28)	17/4/0/0 (81/19/0/0)	<.001
Denucleation, n (%)	26 (55)	0 (0)	<.001

Karyopyknosis, vacuolar degeneration, acidophilic degeneration of cytoplasm, adventitial neuron change, and denucleation were evaluation items of neurodegeneration.
CRT = chemoradiotherapy.

The incidence of neural degeneration was significantly higher in the CRT group and the incidence of vacuolar degeneration (68%) was particularly high in the CRT group compared with the control group. In the adventitia and perineurium of neurons, only perineurial hypertrophy (grade 1) occurred in the control group, whereas perineurial and intraneural fibrosis (grades 2 and 3) was found in 43% of cases in the CRT group, indicating a significantly higher frequency of severe effects in the CRT group ($P \leq .001$ to $P = .01$) (Table 2). Representative histopathological findings for neurons are shown in Figure 1.

Association with Anal Function 12 Months After Surgery

No patient had a Wexner score of ≥2 preoperatively, and none had problems with preoperative anal function. The median values of the Wexner scores at 12 months after stoma closure in the CRT and control groups were 8.0 and 5.0, indicating that function was significantly poorer in the CRT group ($P = .018$ by Mann-Whitney U test) (Fig. 2).

In a comparison of Wexner scores based on background factors in the CRT group, sex, age, type of resection (partial, subtotal, total ISR), and partial resection of the external sphincter were not associated with poor anal function after ISR. Postoperative anal dysfunction did not show a significant association with each feature of neural degeneration or with Wexner score in the CRT group (karyopyknosis, $P = .05$; vacuolar degeneration, $P = .298$; acidophilic change, $P = .090$; denucleation, $P = .067$; and adventitial neuronal changes, $P = .081$). However, there was a significant correlation between the total degeneration score and the Wexner score ($P = .003$, $r = 0.477$ by Spearman analysis) (Fig. 3).

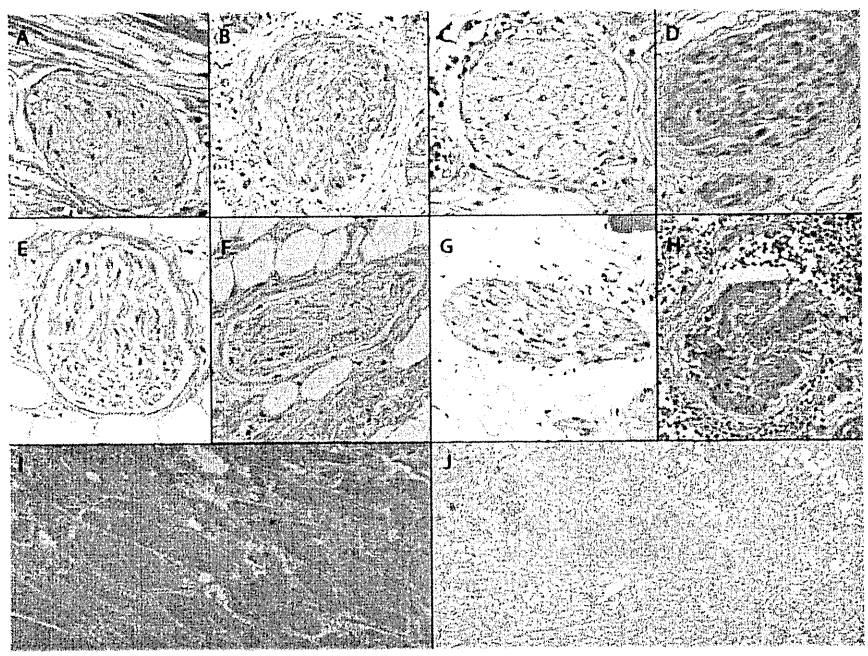

FIGURE 1. Pathological evaluation. The hematoxylin and eosin sections were assessed under a standard light microscope at low-power magnification (×100). The nerve evaluation items are (A–H): A, Normal. B, Karyopyknosis. C, Vacuolar degeneration. D, Acidophilic degeneration of cytoplasm. E, Denucleation. F, Adventitial neuron change grade 1. G, Adventitial neuron change grade 2. H, Adventitial neuron change grade 3. The degree of fibrosis was evaluated by grades: I, grade 1; J, grade 3.

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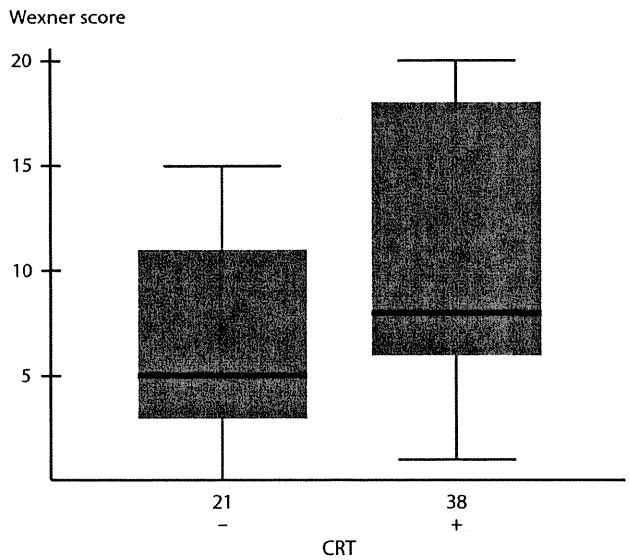

FIGURE 2. Relationship between CRT and Wexner score. Wexner score comparison at 12 months after stoma closure between the CRT and control groups resulted in median values of 8.0 and 5.0 (P = .018 by Mann-Whitney U test). CRT = chemoradiotherapy.

DISCUSSION

The results of the study showed that preoperative CRT had a negative effect on anal function regardless of the surgical method. This suggests that it is important to examine neural degeneration around the internal sphincter muscle for prediction of anal dysfunction. Many cases were of pathological stages I and II because of downstaging by CRT, but total ISR was performed in some of these cases. This approach was used because we were unable to judge the position of the tumor edge on the anal side before preoperative CRT, which prevented maintenance of a clear distal margin. However, this had no influence on the analysis of the Wexner score because the comparison of this score with anal dysfunction was performed only within the CRT group. Moreover, of the factors investigated, preoperative CRT had the greatest effect on anal dysfunction after ISR, and total ISR was more strongly associated with anal dysfunction than either subtotal or partial ISR. Therefore, a negative effect of preoperative CRT on anal function was found regardless of the extent of internal sphincter muscle preservation.[13]

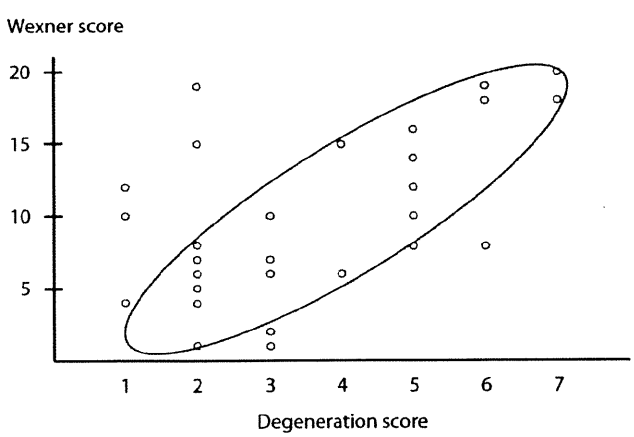

FIGURE 3. Association between the degeneration score and Wexner score. The correlation between the original score (range, 0–7) and the Wexner score was investigated. Correlation was significant with P = .003 and a correlation coefficient of r = 0.477 by Spearman analysis.

The cause of the negative effect of conventionally fractionated CRT on anorectal function is still unclear. Lim et al[15] suggested that poor anorectal function after preoperative CRT was due to damage to the pudendal nerve, and rectal function may also be worsened by radiation-induced proctitis and reduced rectal compliance.[16,17] Moreover, anal sphincter dysfunction may be caused by direct radiation injury to the internal anal sphincter muscles.[18] Our results showed a significantly higher incidence of neural degeneration and fibrosis in the CRT group. In this study, we did not include cases treated with radiation therapy only. However, in another series, we found that treatment with radiation alone caused tissue degeneration, including neural degeneration similar to that caused by CRT. We also evaluated another 8 patients with colorectal cancer who received preoperative folinic acid/fluorouracil/oxiliplatin (FOLFOX) treatment. The incidence of neural degeneration was significantly higher in the CRT group than in the FOLFOX cases. There were no differences in any items of neural degeneration between the FOLFOX cases and control groups, suggesting that radiation may exert a critical damage on tissue damage. In the pathological evaluation, patients treated with preoperative chemotherapy alone had no neural degeneration, with results similar to those in the control group. These results suggest that radiation plays a critical role in tissue damage.

The tissue and nerves were evaluated in surgical tissue specimens, but these specimens and the left internal and external sphincter muscles were similarly affected by CRT, which suggests that the histological changes in the analyzed specimens were also present in the body. The nerve examined in the study is an autonomic nerve that is distributed longitudinally in the intestine and innervates the internal sphincter muscle. After surgery, the somatic and pudendal nerves are involved in anal function and mainly innervate the external sphincter muscle of the anus. Although their origins are different, examination of these 2 nerves may be appropriate for assessment of neural degeneration, because neuronal failure of these nerves may cause anal dysfunction. In this study we evaluated tissue degeneration in the neural range affected by CRT, including the sphincter muscle, and these results are important for prediction of anal function after surgery.

In the CRT group, surgery was performed within 2 to 3 weeks after completion of preoperative CRT, and the investigated histological changes occurred during this period. Anal function improved with the postoperative course in some cases, suggesting that nerves and tissue including muscle can regenerate and result in improved anal function. However, an investigation of anal function after ISR in patients who underwent surgery at our hospital suggested that functional recovery cannot be expected in cases with unfavorable function at 6 to 12 months after surgery.[13] Because CRT-induced early-phase tissue degeneration is associated with anal function at 12 months after surgery (as found in this study), tissue degeneration early after CRT may have a long-term effect on anal function.

Various factors may exert an influence on anal function, and this makes it difficult to predict postoperative anal function before surgery. However, the results of this study showed a significant correlation between the degeneration score defined in the study and the Wexner score in the Spearman analysis. Furthermore, there was no significant relationship between each histological finding and Wexner score, and no significant association between each item for evaluation of neural degeneration and Wexner score in multivariate regression. These results suggest that tissue degeneration should be evaluated by examining various items, rather than based on only a single item, because neural degeneration associated with anal dysfunction may be reflected by several critical items. A further study is needed to identify these important items.

Postoperative maintenance of anal function is important after ISR and further research is necessary to develop a compensatory treatment for maintenance of function (for example, reconstruction of functional muscles) for CRT cases with functional failure. Simultaneous management of therapeutic benefit and anal function is required following ISR, and we intend to examine approaches to maintenance of the therapeutic benefit of preoperative CRT in a future study. For example, preoperative chemotherapy alone may be appropriate based on the improvement of colorectal cancer observed with this approach.

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Original article

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The indications for a diverting stoma in low anterior resection for rectal cancer: a prospective multicentre study of 222 patients from Japanese cancer centers

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Abstract

Aim The aim of the study was to determine the present state of diverting stoma construction in Japanese cancer centres and to investigate the relationship between symptomatic leakage and diverting stoma after low anterior resection for rectal cancer.

Method Two hundred and twenty-two consecutive patients undergoing low anterior resection for rectal cancer located within 10 cm from the anal verge were investigated in a prospective, multicenter study.

Results The overall leakage rate was 9.0% (20/222). Of 31 cases with an anastomosis within 2.0 cm from the anal verge, 22 (71%) had a diverting stoma. Of cases anastomosed within 5.0 cm, the absence of a diverting stoma and tumour size were significantly related to an increased rate of leakage [leakage in 13 (12.7%) of 102 cases without a diverting stoma; in three (3.8%) of 80 cases with a diverting stoma]. Among anastomoses within 2.0 cm from the anal verge, leakage occurred in four (44.4%) of nine cases without and in none (0%) of 22 cases with a diverting stoma.

Conclusion We recommend a diverting stoma for an anastomosis within 5.0 cm of the anal verge and strongly recommend it for a very low anastomosis within 2.0 cm.

Keywords Rectal cancer, low anterior resection, anastomotic leakage, diverting stoma, defunctioning stoma

What is new in this paper

Recently, a DS construction is recommended for a low anastomosis in LAR, but the definition of a low anastomosis is not clear. In the present study, we focused on the relationship between the anastomotic level and leakage.

Introduction

With advances in surgical procedures and adjuvant treatment, sphincter-preserving surgery has become the standard operation for most patients with rectal cancer. Anastomotic leakage is, however, still an important complication. A temporary diverting stoma (DS), which is often constructed in many cases of low anterior resection (LAR), aims to divert the faecal stream. However, it remains unproven whether this in itself can prevent clinical leakage. Recent randomized control studies [1–4] and meta-analyses [5,6] have shown that a DS does reduce the incidence of symptomatic leakage in LAR for rectal cancer, but the evidence is still limited and the definition of a low anastomosis is not clear.

The aim of this prospective study was to determine the present state of DS construction in Japanese cancer centres and to investigate the relationship between symptomatic anastomotic leakage and DS. This is the first prospective, multicenter, large-scale study from Japanese colorectal cancer centres.

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Method

Patients

The design was a prospective, multicenter study. Data were collected from nine participating cancer centres involved in the 'Studies on the standardization for diagnosis, treatment, and follow up of colorectal cancer patients', sponsored by Grant-in-Aid 21-2 for Cancer Research from the Ministry of Health, Welfare and Labour of Japan. The study was approved by the local ethics committee of each hospital and informed consent was obtained.

From January 2008 to May 2009, 222 consecutive patients with primary rectal cancer underwent LAR. This was performed for patients with rectal cancer in which the lower edge of the tumour was within 10 cm from the anal verge and all anastomoses were carried out using circular staplers. Patients having a sutured colo-anal anastomosis were excluded. Cases having laparoscopic anterior resection, subtotal colectomy, total proctocolectomy, abdominoperineal resection, Hartmann's procedure or pull-through procedures were also excluded. No patient received neoadjuvant radiotherapy or chemoradiotherapy. The decision to construct a DS and the choice of ileostomy/colostomy were made by the individual surgeon in each case. When a DS was constructed, each surgeon reported the primary reason for the decision.

Anastomotic leakage

Anastomotic leakage was defined by the emission of gas, pus or faeces from the drain or wound or the vagina or the discharge of pus *per anum*. All clinically suspicious leakages were confirmed by one or more of the following techniques: contrast enema radiography, computed tomography scan and endoscopy. When there was no abnormal communication of the intraluminal and extraluminal compartments due to a dehiscence of intestinal wall integrity, the patient was said to have a pelvic abscess and not anastomotic leakage.

Analysis of variables

Variables recorded included age, sex, body mass index (BMI), neoadjuvant therapy, bowel obstruction, tumor location, UICC-TNM stage, level of IMA ligation, mobilization of splenic flexure, lateral lymph node dissection, types of reconstruction (including straight, colonic J-pouch, transverse coloplasty, or other), completeness of doughnuts, intra-operative blood loss, operating time, DS construction, synchronous resections of other organs (hepatectomy for simultaneous liver metastasis or extended surgery to adherent organs, or additional cancer resection for synchronous cancers), tumour size, the distal resection margin of the specimen, level of the anastomosis from the anal verge, and use of a pelvic or intraluminal drain.

Bowel obstruction was defined as stenosis preventing the passage of a fibrescope. The level of the lower border of the tumour from the anal verge was measured just before the operation under general anesthesia and the lithotomic position using an anoscope. Clinical stage was classified preoperatively according to the UICC-TNM classification (6th edition) [8]. Tumour size and distal resection margin were measured on the specimen before fixation with formalin. The level of anastomosis from the anal verge was measured by digital examination just after completing the reconstruction, with the patient in the lithotomy position.

Statistical analysis

In the univariate analysis the χ^2 and the Mann–Whitney U-test were used. After univariate analysis, variables with a P value ≤ 0.1 were selected for multivariate analysis. A multivariate analysis was performed using a binary logistic regression model. This was performed using IBM SPSS Statistics software version 18 (SPSS Inc., an IBM company, Chicago, Illinois, USA). All P values < 0.05 were considered statistically significant.

Results

Patient characteristics

From January 2008 to May 2009, 222 consecutive patients with primary rectal cancer who underwent LAR were included in this prospective, multicentre study. They included 144 (65%) males. The mean age was 62.2 ± 10.1 years, the mean body mass index (BMI) was 22.5 ± 3.4 kg/m^2, the average distance of the tumour from the anal verge was 6.7 ± 1.8 cm and the average level of the anastomosis was 4.0 ± 1.5 cm. Neoadjuvant chemotherapy was performed in five patients only. Neoadjuvant radiotherapy or chemoradiotherapy was not performed in this series. All anastomoses were performed using the circular stapling instrument by the double staple technique in 221 patients. Most patients (202) had a straight anastomosis and 20 underwent a side-to-end anastomosis. No colonic J pouch or transverse coloplasty was constructed. Twenty-one synchronous resections included nine extended resections for direct invasion of adjacent organs; eight hepatectomies for liver metastasis, three resections of double primary cancers and one adrenalectomy for adrenal metastasis were carried out. There was no mortality.

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Diverting stoma

In the initial LAR, 80 (36.0%) of the 222 patients received a diverting stoma (DS). Ileostomy was chosen in 70 (87.5%) patients and a transverse colostomy in 10 (12.5%).

The primary reasons stated by the surgeons for the decision to construct a DS included low level of anastomosis (41 cases) and low tumour location (16 cases). Other reasons are listed in Table 1.

Clinical factors associated with DS construction included neoadjuvant chemotherapy, low tumour location, low anastomotic level, long operating time, massive intra-operative bleeding, mobilization of splenic flexure, and incompleteness of doughnuts. As shown in Table 2, no DS construction was performed in patients whose anastomosis was more than 5.1 cm from the anal verge.

Table 1 Primary reason for diverting stoma construction (n = 80).

	No.	Rate (%)
Anastomotic level was too low	41	51.3
Tumour location was too low	16	20.0
Synchronous resections of other organs	4	5.0
History of diabetes or previous steroid abuse	4	5.0
Tumour size was too large	2	2.5
Incomplete anastomotic ring	1	1.3
Incomplete bowel preparation	1	1.3
Operating time was too long	1	1.3
Poor blood supply to anastomotic site	1	1.3
Intra-operative leakage test was positive	1	1.3
History of previous angina pectoris	1	1.3
Multiple firings during rectal division	1	1.3
Injury to vaginal wall	1	1.3
Others	5	6.3

Table 2 Relationship between the anastomotic level and diverting stoma construction rate.

Anastomotic level from AV (cm)	DS rate (%)	Leakage rate Without DS	Leakage rate With DS
1.0–2.0	71.0	4/9 (44.4%)	0/22 (0%)
2.1–3.0	41.5	3/31 (9.7%)	1/22 (4.5%)
3.1–4.0	52.6	3/27 (11.1%)	2/30 (6.7%)
4.1–5.0	14.6	3/36 (8.3%)	0/6 (0%)
5.1–6.0	0	3/24 (12.5%)	0/0 (0%)
6.1–7.0	0	0/10 (0%)	0/0 (0%)
7.1+	0	1/5 (25.0%)	0/0 (0%)

AV, anal verge; DS, diverting stoma.

Table 3 Multivariate analysis of leakage risk factors.

	P-value	Odds ratio (95% CI)
Intra-operative bleeding (ml)	0.12	1.0 (1.00–1.00)
Tumour size (cm)	0.02	1.3 (10.5–1.62)
Diverting stoma	0.04	4.2 (1.04–16.6)

Most of the patients (22 of 31; 71.0%) whose anastomosis was within 2.0 cm from the anal verge received DS. Of the patients whose anastomosis was within 2.1–5.0 cm from the anal verge, 38.4% (58 of 151) received a DS (Table 2).

Anastomotic leakage

The overall rate of anastomotic leakage was 9.0% (20 of 222). This was 12.0% (17 of 142) in patients without a DS compared with 3.8% (3 of 80) of cases with a DS ($P < 0.05$). Every pelvic abscess was accompanied by anastomotic dehiscence.

Clinical variables were analysed to investigate the risk factors for anastomotic leakage. Patients whose anastomosis was above 5.1 cm were excluded. Among patients whose anastomosis was within 5.0 cm, the absence of a DS and tumour size were significantly related to an increased leakage rate ($P < 0.05$) on univariate analysis. In this subgroup, 13 (12.7%) of 102 cases without DS had leakage, whereas three (3.8%) of 80 cases with DS had leakage. On multivariate analysis, the absence of a DS had a significantly high leakage rate (Table 3).Furthermore, among cases with an anastomosis, within 2.0 cm from the anal verge, four (44.4%) of nine cases without DS had leakage, whereas none (0%) of 22 cases with DS had leakage. ($P < 0.05$) (Table 2).

Three (3.8%) of 80 patients who underwent LAR with DS experienced leakage. All were treated conservatively. Of the 17 (12%) patients who had leakage without a DS, 14 needed urgent surgery and only three were treated conservatively. The need for reoperation was significantly increased in patients without DS compared with those with DS ($P = 0.018$).

Discussion

This prospective study has confirmed that the indication for DS construction in Japanese cancer centres is limited to patients having an anastomosis within 5.0 cm from the anal verge. In patients with an anastomosis at this level, DS was significantly associated with a reduced rate of clinically relevant anastomotic leakage. Our data further identified that DS construction for patients with

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an anastomosis within 2.0 cm from the anal verge had a marked association with reduced leakage. This is the first prospective, multicentre study regarding DS construction in rectal cancer surgery from Japanese cancer centres.

Symptomatic anastomotic leakage has been reported to occur in 5–20% of cases [9–17]. When it occurs, the associated risk of postoperative mortality is increased to between 6% and 22% [17]. Theoretically, DS is constructed to divert the faecal stream to protect the healing anastomosis. However, it is unproven whether diverting the faecal stream in itself directly prevents anastomotic dehiscence.

Several retrospective or nonrandomized prospective studies have shown that the absence of a DS is a risk factor for leakage after LAR [12,16,18,19], but others have disputed this [20,21]. Four randomized control studies have investigated the association between DS and leakage [1–4]. Matthiessen *et al.* [3] reported the results following intra-operative randomization of patients undergoing LAR for rectal cancer within 15 cm from the anal verge and anastomosed within 7 cm. Leakage occurred in 10.3% (12 of 116) of patients with a defunctioning stoma compared with 28.8% (33 of 118) of patients without a stoma. They concluded that a defunctioning stoma significantly decreased the rate of symptomatic leakage and therefore recommended it in cases of LAR. In a trial by Chude *et al.* [1], 256 patients were randomized into two arms. Anastomotic leakage developed in 2.2% (3 of 136) of patients with a defunctioning stoma and in 10.0% (12 of 120) of patients without ($P < 0.05$). Thus, they also recommended a DS in surgery for low rectal cancer. Two meta-analyses were reported recently [5,6]. Both concluded that a DS reduces the rate of clinically relevant anastomotic leakage.

Despite these studies there is less information on the effect of DS related to a detailed analysis of the level of the anastomosis. In the present study, therefore, we focused on the relationship between the anastomotic level and leakage. Matthiessen *et al.* [3] recommended that a DS was indicated for patients whose anastomosis was within 7 cm. In the light of the present study, this would appear to be too broad a generalization. When the level is divided in distances of 1 cm from the anal verge, as in the present study, it is clear that the risk increases steadily the lower the anastomosis is performed. It is also noteworthy in our study that no patient with an anastomosis above 5 cm received a stoma and in these patients the incidence of leakage was 10.3%, which is the same as that reported by Matthiessen *et al.* in defunctioned patients. This raises the question of whether a stoma is necessary for an anastomosis above 5 cm, which is well below the level of anastomosis of many patients who would have undergone a stoma on the advice of Matthiesson *et al.* It seems that the definition of 'low anastomosis' for Japanese surgeons was more selective.

In the study by Chude *et al.* [1], their inclusion criterion consisted of rectal cancer located 5 cm above the anal verge but the level of the anastomosis ranged from 5 to 6 cm from the anal verge, which when allowing for an adequate distal clearance [22] would put the level of the tumour at a level well above 5 cm. Furthermore, some tumours within 5 cm of the anal verge may need an intersphincteric dissection, especially in some males with a narrow pelvis [23]. Thus not all of such patients would be able to have a standard low anterior resection.

There are many other reported risk factors for leakage, such as male sex [10,12,14,17], previous radiation therapy [10,14], poor bowel preparation [9], blood transfusion [9] and low anastomotic level. Interestingly, in our study, DS tended to be constructed in patients in whom there was considerable anticipated risk to the anastomosis. Despite this selection bias in our nonrandomized study, although paradoxical, the leakage rate was lower in patients with DS compared with patients without. This may prove that DS is preventative for anastomotic leakage.

The indication for DS in the present study was applied to selected patients with a low anastomosis and was more limited than in the controlled trials. There may be an explanation based on differences in the patient populations between Japan and western countries. First, preoperative radiation therapy is considered to be a risk factor by some authors [10,14]. Although randomized multicentre trials have shown that it does not increase postoperative morbidity [24,25], Peeters *et al.* [16] retrospectively analysed risk factors from the database of the Dutch Colorectal Cancer Group [24], and reported that a defunctioning stoma was constructed more often in patients who had received radiation, and that the absence of a DS was significantly associated with a higher leakage rate. In Japan, particularly in our study group, preoperative therapy (including chemoradiotherapy) for resectable rectal cancer was not standard [7,26], whereas it was so in western countries. This may be one reason for the limited number of DSs.

Secondly, our low mortality rate may have influenced the limited indication for DS. In the present series, there was no mortality, even in cases of leakage without DS. This reflects our low leakage rate in cases without DS (12%; 17 of 142), which is comparable to that reported by Matthiessen *et al.* [3] in cases with DS (10.3%; 12 of 116). Chude *et al.* [1] reported two deaths in their patients who did not receive a DS.

Ulrich *et al.* [27] also conducted a randomized controlled trial of patients undergoing low anterior

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resection. The symptomatic anastomotic leakage rate in the groups with and without a DS were 5.5% and 37.5% ($P = 0.02$) and the study was terminated prematurely as a result.

There are four main limitations of the present study. First, the clinically unapparent leakages might have been missed in either group because no systematic assessment of the anastomosis for clinically stable patients was performed. Second, the study was not randomized. Certainly, a randomized clinical trial is the best methodology to determine this evidence. But Matthiessen *et al.* [3] stated that the proportion of eligible patients in their randomized study was less than one-third (28.5%) of all patients who would have been eligible owing to intraoperative adverse events and patient refusal to participate. Consent is one of the main difficulties of a randomized clinical trial. Third, the level of the tumour was measured by anoscopy, but the level of the anastomosis in the present study was measured by digital examination performed by the operating surgeon. Fourthly, we did not investigate operating surgeon as a risk factor for leakage.

In conclusion, the indication of DS construction in our group was limited to anastomoses below 5 cm from the anal verge, lower than that recommended in a recent randomized study. Leakage was less in patients with DS compared with patients without and this was related to the distance of the anastomosis from the anal verge. We therefore recommend DS construction where the anastomosis is within 5.0 cm of the anal verge and strongly recommend it for a very low anastomosis within 2.0 cm.

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ORIGINAL ARTICLE

Male sexual dysfunction after rectal cancer surgery

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Abstract
Purpose The aims of the study were to determine the extent of male sexual dysfunction after surgical treatment of rectal cancer and to examine the outcome of postoperative treatment with sildenafil.
Methods A prospective study was performed in patients who underwent attempted curative total mesorectal excision (TME) for low rectal cancers. Sexual function scores were determined by questionnaire preoperatively and at 3 and 12 months postoperatively. Outcomes were examined in patients who were sexually active preoperatively.
Results From 2000 to 2007, 207 patients underwent TME at our institution, of whom 49 (24%) were sexually active preoperatively. Erectile dysfunction and ejaculatory problems were present in 80% and 82%, respectively of the 49 patients at 3 months postoperatively, and in 76% and 67%, respectively at 12 months. Lateral lymph node dissection was a strong risk factor for postoperative sexual dysfunction. The impotency rate was 37% and 47% of patients were unable to ejaculate. Sildenafil was administered to 16 patients who requested the drug during follow-up, and sexual dysfunction was improved in 11 of these patients (69%).
Conclusion Sexual dysfunction occurs frequently after rectal cancer treatment and is mainly caused by surgical damage in lateral lymph node dissection. Sildenafil may be effective for the treatment of sexual dysfunction.

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Keywords Male sexual dysfunction · Rectal cancer · Sildenafil · Total mesorectal excision

Introduction

The past two decades have witnessed substantial improvement in survival from rectal cancer due to earlier diagnosis, improved efficacy and delivery of radiotherapy and advances in surgical techniques such as total mesorectal excision (TME) [1, 2]. The degree of autonomic nerve preservation in surgery for rectal cancer is an important factor associated with postoperative sexual and urinary functions. Sexual dysfunction occurs due to intraoperative nerve injury, and preservation of pelvic autonomic nerves such as the pelvic plexus and superior hypogastric plexus seems to lower the incidence of sexual morbidity. In particular, damage to the cavernous nerves of the penis distributed in the nerve-vascular bundle is directly associated with postoperative sexual dysfunction.

The incidence of erectile dysfunction after surgery for rectal cancer has been reported to be 20–70% [3–7], and ejaculation dysfunction occurs in 20–60% of cases with erectile ability [3–5, 8].A high rate of sexual function can be maintained by autonomic nerve preservation [9, 10], but the incidence of dysfunction has varied among reports. Surgeon-related factors are also important in treatment of rectal cancer, both for achieving local control and for preserving function [11]. Sexual dysfunction is an important postoperative issue, but the relationship between differences in surgical procedures and the incidence of postoperative sexual dysfunction has not been examined. Moreover, reduced function and functional impotence have not been investigated separately, and the severity of dysfunction has not been evaluated in previous studies of sexual function after surgery for rectal cancer.

At our hospital, we perform a prospective questionnaire-based survey of functions (defecation, urination and sexual function) after surgery for rectal cancer. In this study, we investigated the items concerning sexual function in this survey. Data on sexual function were obtained, patients who were sexually active before surgery were identified and postoperative sexual function was investigated in these patients. Oral sildenafil was administered to patients in whom sexual dysfunction occurred after surgery and the outcome was also investigated.

Methods

Prospective questionnaire-based study of sexual function

The subjects were 207 patients who underwent TME for rectal cancer at our hospital between 2000 and 2007. The treatment was given with curative intent in all cases. Hospital records were analyzed to obtain details of the surgical procedures related to the degree of nerve preservation in all patients. Questionnaires on anal, sexual and urinary functions were completed by patients who gave informed consent, and the answers were accumulated prospectively. Sexual function scores were determined preoperatively and at 3 and 12 months postoperatively based on the questionnaires, and the preoperative level of sexual activity was analyzed.

Among patients who completed the questionnaire on sexual function, those who provided answers to items concerning ejaculation and erection before and after surgery were regarded as eligible for the study. Those without sexual function before surgery were excluded. Sexual function outcome was assessed using questions related to pre- and postoperative libido, erection, stiffness for penetration, ejaculation and orgasm, as measured by the International Index of Erectile Function (IIEF) scale [12–15]. Patients with active sexual function preoperatively were selected based on an answer of one or two to both of the following questions on the IIEF questionnaire. What is your condition of erection? [1. Normal erection 2. Slightly reduced 3. Almost no erection 4. No erection 5. Not indicated]. What is your condition of ejaculation? [1. Normal ejaculation 2. Slightly reduced 3. Almost no ejaculation 4. No ejaculation 5. Not indicated 6. Retrograde ejaculation]. The results of questionnaires given at 3 months and 1 year after surgery were analyzed for the patients who met this criterion.

Postoperative urinary function was also investigated. Residual urine was measured after removal of a urethral catheter after surgery. A residual urine volume of ≥100 mL was regarded as residual urine-positive, and early urinary dysfunction was defined as three consecutive residual urine-positive measurements. Long-term urinary dysfunction was defined based on the results of a questionnaire given on urinary dysfunction at 6 months after surgery. Urinary dysfunction was defined as a reduction in urinary function compared to the preoperative condition.

Surgical treatment

TME was performed up to the level of exposing the levator ani muscle. The application of TME was used as a criterion for selection of low rectal cancer cases. Patients in whom TME was performed using a detailed Operation Record Form were initially selected. When the pelvic autonomic nerves were injured during surgery or partial/combined resection was performed, the patients were included with a description of the procedure. However, cases of combined resection of multiple organs and total resection of the pelvic autonomic nerves were excluded. Lateral lymph node dissection was performed in patients with suspected lateral metastasis and those with lower rectal cancer of clinical stage II or III receiving standard therapy. Anastomosis methods such as the double stapling technique and colo-anal anastomosis were disregarded on the condition that TME was performed, and abdominoperineal resection (APR) cases, which were colostomized, were also included. The anastomosis method and the presence or absence of a pouch was described in the Operation Record Form. Use of temporary colostomy was determined by the attending physicians.

Postoperative adjuvant chemotherapy

Postoperative chemotherapy was initiated for cases of pathological stage III diagnosed histopathologically in which lymph node metastasis was positive, after confirming that the patient met the criteria for adjuvant chemotherapy. The time and duration of this therapy were not examined in the study.

Treatment of sexual dysfunction

Oral sildenafil was administered to patients who developed sexual dysfunction during outpatient follow-up and requested treatment. An informed consent was obtained concerning the potential adverse effects of the drug. The patients received 25 mg of sildenafil and 5 mg of vardenafil, or 50 mg of sildenafil and 10 mg of vardenafil. Sexual function was surveyed by questionnaire after initiation of oral treatment and the outcome was investigated.

Protection of privacy

The study design was approved by the ethics committee of our institution and all patients provided informed consent

prior to participation in the study. The privacy of the patients was strictly protected. Patients were identified with a registration number, initials, birth date and a medical history number. Physicians (investigators) participating in the study followed the study protocol to ensure that the safety and human rights of the patients were protected. The study was performed within the ethical standards of the 1964 Declaration of Helsinki.

Statistical analysis

A Student's *t* test and a Fisher's exact test were used to examine differences in erection, ejaculation and urinary dysfunction between the groups of patients with and without sexual dysfunction. All statistical analyses were performed using SPSS for Windows, v.13.0 J (SPSS-Japan Inc., Tokyo, Japan). A p value <0.05 was considered to be significant.

Results

Patient background

Of the 207 patients who underwent TME between 2000 and 2007, 149 (72%) answered the questions concerning sexual function, and preoperative sexual function was identified in 49 cases (24%). The median age of the 49 patients was 58 years old, and 28 were ≤60 years old. The tumour size was ≤5 cm in 21 patients. One patient had undergone preoperative chemoradiotherapy. The clinical tumour stage was T3 in 40 cases (Table 1). The surgical procedures were very low anterior resection in 19 cases (39%), low anterior resection in 12 (25%), APR in 1 (2%) and intersphincteric resection (ISR) in 17 (35%). A stoma was prepared during surgery in 21 patients (43%). No stoma was closed within 3 months after the surgery. The stoma was closed in 13 patients by 12 months after surgery but remained open in eight patients (16%).

Table 1 Patient characteristics (n=49)

Procedure	Number of cases
Age (years)	
Median	58
Range	36–76
<60	28
>60	21
Tumour size (cm)	
Median	6.0
<5	21
>5	28
Clinical tumour stage	
T1	1
T2	8
T3	40
Preoperative radiotherapy	1

Bilateral lateral lymph node dissection was performed in 32 cases (65%). Of 35 patients who underwent lateral lymph node dissection, lateral lymph node metastasis was observed in four (11%) and lymph node metastasis, including that to regional lymph nodes (i.e. pathological stage III), was observed in 17 (35%).

Unilateral resection of the hypogastric nerves was performed in four (8%) and partial resection of the pelvic plexus in six (12%). Laparoscopic surgery was performed in two cases (Table 2).

Erectile dysfunction and ejaculatory problems occurred in 80% and 82%, respectively of the 49 patients at 3 months after the operation and in 76% and 67%, respectively at 12 months. Impotence was present in 37% and failure to ejaculate occurred in 47%.

Sexual dysfunction

A preoperative IIEF score of ≤21, which suggests erectile dysfunction, was not found in any patient. Sexual dysfunction after surgery was compared with the preoperative status, with the following results. Erectile and ejaculation functions were reduced in 39 (80%) and 40 (82%) patients, respectively at 3 months after surgery, and in 37 (76%) and 34 (67%), respectively at 12 months, including 18 patients (37%) with no erection and 23 (47%) who were unable to ejaculate. There were no significant differences in the incidences of erectile or ejaculation dysfunction by age, surgical procedure, tumour factors, the presence or absence of a stoma, preservation of the hypogastric nerve, or preservation of the pelvic plexus or splanchnic nerves at 3 or 12 months based on the questionnaire. However, these incidences were significantly higher at 12 months in cases treated with lateral lymph node dissection ($p \leq 0.01$), although no significant differences were noted at 3 months (Tables 3). Therefore, lateral node dissection appeared to be the main risk factor for postoperative sexual dysfunction. Erectile and ejaculation functions improved from 3 to 12 months after surgery in two (5%) and six (18%) cases, respectively. The autonomic hypogastric nerve, pelvic plexus and splanchnic nerve were totally preserved in all of these cases. Each of these items was analyzed in cases with no erection or ejaculation, but no significant differences were found (Table 4).

Urinary dysfunction

Early urinary dysfunction occurred in 18 cases (37%) and long-term dysfunction at 6 months postoperatively was

Table 2 Treatment characteristics (n=49)

Procedure	Number of cases
Type of resection	
LAR (low anterior resection)	12
vLAR (very low anterior resection)	19
ISR (intersphincteric resection)	17
APR (abdominoperineal resection)	1
Laparoscopy	2
Stoma	21
Lateral lymph node dissection	35
Hypogastric nerves	
Total preservation	45
Unilateral resection	4
Pelvic plexus	
Total preservation	43
Partial resection	6

noted in two cases (4%). Lateral lymph node dissection was significantly associated with the incidence of early urinary dysfunction ($p \leq 0.01$) (Table 4).

Treatment of postoperative sexual dysfunction

Sildenafil tablets were administered to 16 patients (mean age 54.7 years old) who requested treatment during follow-up. These cases included eight (50%) that underwent lateral lymph node dissection and two (13%) that received partial resection of the pelvic splanchnic nerves. Sexual function was improved in 11 (69%) of the 16 cases based on a questionnaire after initiation of oral drug treatment, but no functional improvement was achieved in the two cases with partial resection of the pelvic splanchnic nerves (Table 5). Anal function was additionally improved in one case after ISR.

Discussion

Investigation of surgery-associated sexual dysfunction alone is difficult after surgery for rectal cancer because of the influences of postoperative mental factors and surgery-associated reduction of function. From a QOL perspective, the significance of preservation of sexual function is low if the patient's satisfaction with this function is low. The IIEF [12–15] is a questionnaire on sexual function that is completed by patients without intervention by a third party and provides a comprehensive evaluation of sexual function. Therefore, our hospital uses the IIEF as a postoperative functional questionnaire. In this study, two items concerning erection and ejaculation were selected from the IIEF items to identify patients with active sexual function before surgery.

Patient satisfaction with sexual function is of most importance and some patients are satisfied even though they are unable to become erected or to ejaculate. However, from the viewpoint of function-preserving surgery, the ability to obtain an erection and to ejaculate is important with regard to surgical accuracy. Therefore, both functional and psychological approaches are necessary to assess sexual function after surgery, but accurate evaluation of these issues is difficult and has not previously been described in detail. Thus, we selected patients with active preoperative sexual function and investigated their postoperative function. Satisfaction was evaluated by questionnaire and functional preservation was investigated by examining impotence. It is difficult to obtain information on sexual function from all patients because the survey may markedly intrude on patient privacy. Therefore, we performed a prospective postoperative functional survey after surgery for rectal cancer, extracted cases in which sexual function could be evaluated from the results and selected cases with active preoperative sexual function. There have been very few reports in which the status of sexual function has been examined after surgery for rectal cancer.

The incidence of sexual dysfunction was slightly higher than those in previous reports [3–5], which may have been due to inclusion of only TME cases, a preoperative T factor of T3 in many cases, and treatment with lateral lymph node dissection as the standard treatment in Japan. ISR was also applied in many cases. Since preoperative chemoradiotherapy has been shown to have a negative influence on anal function after ISR [16, 17], our hospital generally does not perform preoperative chemoradiotherapy (CRT). This is one reason for the high frequency of T3 cases. Preoperative CRT was performed in only one case, and therefore the influence of CRT on sexual function could not be evaluated.

Reportedly, the presence of a stoma after surgery is associated with postoperative sexual dysfunction. This effect may also be dependent on mental issues. We found no significant difference in postoperative sexual function between patients with or without a stoma, but this may have been due to the investigation being limited to erection and ejaculation, since we attached greater importance to function. An association between postoperative complications and sexual dysfunction has been suggested. Anastomotic leakage and intrapelvic abscess occurred in three patients (incidence, 6%) and sexual dysfunction occurred after surgery in one of these patients. However, it was difficult to investigate the correlation between complications and dysfunction because of the small number of complications.

Table 3 Male sexual function after TME (n=49)

Item		Erection Disorder (%)		Ejaculation Disorder (%)	
	After surgery	3 months	12 months	3 months	12 months
Age (years)	□60 (n=28)	82	73	89	82
	□60 (n=21)	76	71	71	82
Tumour size (cm)	□5 cm (n=21)	76	76	81	67
	□5 cm (n=28)	82	75	82	71
Type of resection	LAR (n=12)	75	67	83	75
	vLAR (n=19)	84	89	74	63
	ISR (n=17)	76	65	88	75
	APR (n=1)	100	100	100	0
Tumour stage	T1 (n=1)	100	100	100	100
	T2 (n=8)	87	62	75	75
	T3 (n=40)	77	77	82	67
Stoma	Yes(n=21)	81	75	81	62
	No(n=28)	79	76	82	71
Lateral lymph node dissection	Yes (n=35)	83	86 *]	86	80 *]
	No (n=14)	71	50	71	43
Hypogastric nerve damage	Total preservation (n=45)	80	76	80	67
	Unilateral resection (n=4)	75	75	100	100
Pelvic plexus damage	Total preservation (n=43)	80	74	80	65
	Partial resection (n=6)	83	83	100	100

*$p \leq 0.01$

Lateral lymph node dissection is an important factor involved in sexual and urinary dysfunctions [8, 18, 19] and was the only surgical factor that influenced postoperative sexual function in our patients. This shows the high