as follows: 13 patients had recurrences or died, 15 were receiving adjuvant chemotherapy, 3 required an emergency resection because of postoperative bleeding or necrosis, 8 had severe leakages or strictures of the anastomosis, and 2 were in the planning phase for the stoma closure. Questionnaires about postoperative anal function[7] were prospectively collected from 96 of the 109 patients with closure, and these 96 patients were enrolled in the present study.

Our indications for ISR were tumor edge 5 cm above the anal verge or 3 cm above the dentate line, histologically confirmed adenocarcinoma, and age less than 76 years. Patients in whom invasion of the external sphincter muscle had occurred or distal spread of the primary cancer was suspected were excluded from this study. Digital examination, anoscopy, and fiber colonoscopy were performed preoperatively to measure the distance between the tumor edge and the anal verge, dentate line, or anal ring. Invasion of the external sphincter muscle was diagnosed by pelvic magnetic resonance imaging, and distant metastasis was diagnosed by chest, abdominal, and pelvic CT scans. We determined preoperative stage according to the UICC classification.[9]

Surgical Procedure

ISR was performed according to the method described previously.[7] The surgical procedure included both an abdominal and a perineal approach. First, dissection was performed by the abdominal approach until total mesorectal excision was complete. The puborectal muscle surrounding the lateral and posterior wall of the rectum was exposed at the pelvic diaphragm. The outside layer of the internal sphincter muscle was then exposed and circumferentially divided from the puborectal muscle and the external sphincter. Lateral lymph node dissection was generally performed for stage T3 and T4 disease.[10]

After the part of the operation performed via the abdominal approach was completed, perianal resection was performed. The mucosa and the internal sphincter muscle were incised 1 cm to 2 cm distal to the tumor. The anal orifice was closed with pursestring sutures to avoid tumor cell dissemination during the perianal operation. Once the intersphincteric space was entered, careful dissection was continued upward between the smooth and striated sphincters under constant guidance by an assistant from the abdominal side.

Total ISR involved complete excision of the internal sphincter muscle for tumors that had spread to or beyond the dentate line. The distal line of resection was at the intersphincteric groove. Total ISR was unnecessary when the tumor was located ≥2 cm from the dentate line. In such cases, subtotal ISR was performed instead. In subtotal ISR, the distal line of resection was between the dentate line and the intersphincteric groove, and the dentate line was included in the resection. Partial ISR was performed when the tumor was located 2 cm to 3 cm from the dentate line, with the distal line of resection on or above the dentate line. Partial ISR sometimes includes a conventional coloanal anastomosis procedure.[7] The definitions of each type of ISR are shown in Figure 1. If the tumor had invaded the external sphincter, ISR plus partial resection of the external sphincter was performed, but at least the subcutaneous part of the external sphincter was preserved. The distal margin was pathologically evaluated during surgery; if cancer cells were found at the distal margin, additional resection was performed. The decision whether to create a pouch—either a J-pouch or a transverse coloplasty pouch (TCP)—was left to the discretion of the surgeon.

Preoperative Therapy

Forty patients, most with T3 tumors, agreed to preoperative chemoradiotherapy (CRT). During a five-week

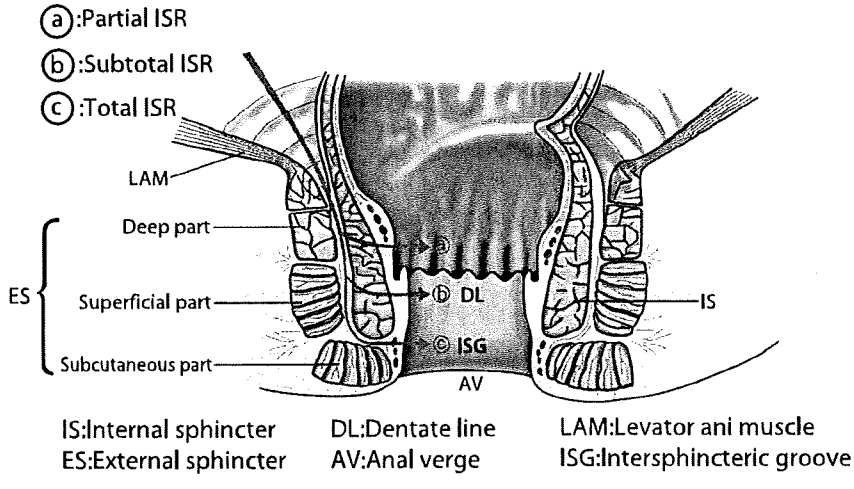

FIGURE 1. Classification of intersphincteric resection (ISR) based on extent of excision of the internal sphincter.

period, a dose of 45 Gy was administered, along with continuous intravenous infusion of 5-fluorouracil (250 mg/m^2/day) to increase the efficacy of radiotherapy. Resection was performed two weeks after the preoperative CRT was completed.[11]

Assessment of Function

Functional outcome was assessed with our function questionnaire,[7] which asked about stool frequency (number of bowel movements per 24 hours), ability to distinguish between feces and flatus, urgency (inability to defer stool evacuation for >15 minutes), fragmentation (more than two evacuations in one hour), soiling during the day or during the night, use of pads, use of medications, and alimentary restriction. Incontinence was assessed by using the continence score of Jorge and Wexner[12] (Wexner score) and the classification proposed by Kirwan *et al.*[13] Questionnaires were obtained from the patients during consultation in the doctor's office, but the patients had filled out the questionnaires by themselves at their homes. To evaluate the Wexner score, we obtained questionnaires from 88 of 96 patients at 3 months after stoma closure, 84 of 96 at 6 months, 73 of 96 at 12 months, and 60 of 96 at 24 months. In this study, evaluation of risk factors for poor anal function after ISR was performed on the basis of the Wexner score at 12 months after stoma closure. We defined poor anal function as a Wexner score of 16 points or more. Because 18 of the 19 patients with a Wexner score of 16 points or more were classified as Kirwan grade 4, this suggested that a Wexner score of 16 points or more represented frequent major soiling. The cutoff value in this study was similar to the value in Chamlou's report,[14] in which the mean Wexner score of the incontinent group was 15 points.

Statistical Analysis

Student's *t*-test and Fisher's exact test were used to evaluate changes over time in symptoms related to anal dysfunction, Wexner score and Kirwan classification after stoma closure following ISR. Clinical factors that might negatively affect anal function, i.e., sex, age, type of reconstruction, anastomotic leakage, extent of excision of the internal sphincter, partial resection of the external sphincter, lateral lymph node dissection, and preoperative CRT, were evaluated as potential confounding factors in univariate and multivariate analyses. The differences in the distribution of these factors between patients with Wexner scores <16 and those with Wexner scores ≥16 at 12 months were analyzed for significance with the chi-squared test. The effect of these variables on poor anal function was evaluated by calculating odds ratios. The patients were divided into two groups according to the extent of excision of the internal sphincter: a total ISR group and a nontotal ISR group. Nontotal ISR included partial ISR and subtotal ISR. All of the analyses were conducted with adjustment for all of the potential confounding factors by logistic regression. Next, we evaluated the effect of preoperative CRT separately in the total ISR group, subtotal ISR group, and partial ISR group.

All statistical analyses were performed with the STATISTICA data analysis software system, version 6 (StatSoft, Inc. [2003]; www.statsoft.com.). *P* values less than 0.05 were considered statistically significant.

RESULTS

Table 1 shows the clinical characteristics of the 96 patients analyzed, including mean tumor distance from the anal verge, dentate line, and anal ring; preoperative CRT; extent of excision of the internal sphincter muscle; resection of the external sphincter; type of reconstruction, and lateral lymph node dissection. Postoperative anastomotic leakage occurred in 15 (16 percent) of the 96 patients. Perioperative mortality was 0 percent.

Overall, cancer was classified as stage I in 29 (30 percent)of the 96 patients, stage II in 18 (19 percent), stage III in 37 (39 percent), and stage IV in 4 (4 percent). Of the 40 patients with preoperative CRT, 8 patients had clinical (c) T2 tumors, 31 had cT3 tumors, and 1 had a cT4 tumor. Of 56 patients without preoperative CRT, 4 had cT1 tumors, 11 had cT2 tumors, 37 had cT3 tumors,

TABLE 1. Clinical background of patients treated by intersphincteric resection (n = 96)

Characteristic	*Value*
Age (yr)	58 (27–81)
Sex	
Male	72
Female	24
Tumor distance (cm) from	
Anal verge	3.8
Dentate line	2.0
Anal ring	1.0
Preoperative CRT	
+	40
–	56
Extent of excision of the internal sphincter	
Total ISR	26
Subtotal ISR	43
Partial ISR	27
Partial resection of the external sphincter	
+	21
–	75
Reconstruction	
Straight anastomosis	84
J pouch	4
TCP	8
Lateral lymph node dissection	
+	64
–	32

CRT = chemoradiotherapy; ISR = intersphincteric resection; TCP = transverse coloplasty pouch. • Age is given as mean with range in parentheses. Other data are number of patients.

TABLE 2. Clinical course of anal dysfunction in patients who underwent ISR followed by stoma closure

Symptoms related to anal function	*3 months*	*6 months*	*12 months*	*24 months*
Bowel movements >5 per day	53/90 (59)	41/85 (48)	27/76 (36)**	15/58 (26)**
Incontinence of gas	20/84 (24)	23/80 (29)	17/71 (24)	14/56 (25)
Incontinence of loose stools	34/88 (39)	22/84 (26)	20/74 (27)	14/60 (23)*
Incontinence of solid stools	24/88 (27)	18/84 (21)	17/74 (23)	10/60 (17)
Soiling during the day	35/90 (39)	22/85 (26)*	20/74 (27)	14/60 (23)*
Soiling during the night	21/90 (23)	13/85 (15)	13/74 (18)	11/60 (18)
Pad wearing	67/87 (77)	54/85 (64)	42/74 (57)**	37/59 (63)*
Cannot discriminate between feces or flatus	19/88 (22)	10/85 (12)	8/74 (11)	3/58 (5)**
Urgency	16/87 (18)	11/85 (13)	9/74 (12)	10/58 (17)
Stool fragmentation	45/87 (52)	35/85 (35)	34/74 (46)	30/58 (52)
Very low satisfaction	21/85 (25)	10/85 (12)*	10/72 (14)	10/58 (17)

ISR = intersphincteric resection. • Data are proportion of patients reporting daily problems via questionnaire, with percentages in parentheses. Percentages with each anal dysfunctions in 6, 12 and 24 months were statistically compared with those in 3 months using Fisher's exact test.
*: $P < 0.05$ **: $P < 0.01$.

and 4 had cT4 tumors. There were no significant differences in clinical stage between patients with and those without preoperative CRT. In the group with preoperative CRT, 8 patients (20 percent) had histologically complete remission after CRT, according to the UICC TNM classification; 4 patients (10 percent) had a pT1 tumor; 10 (25 percent) had a pT2 tumor; 17 (43 percent) had a pT3 tumor; and 1 (3 percent) had a pT4 tumor. In the group without preoperative CRT, 6 patients (11 percent) had a pT1 tumor, 17 (30 percent) had a pT2 tumor, 31 (55 percent) had a pT3 tumor, and 2 (4 percent) had a pT4 tumor.

Pathologic examination showed that the mean distal margin of all patients was 1.5 cm (range, 0.2–5.5 cm). We routinely performed pathologic examination of the distal margin during the operation, and positive margins were diagnosed in three patients. In such cases, additional resections of distal margins were performed during the operation, and we made sure that the distal margins in all patients were free from cancer cells. Of all 96 patients who underwent ISR, 3 patients were found to be positive for circumferential margins, and an R0 operation was achieved in 93 patients (97 percent).

Median follow-up was 37 months (range, 1–90 months). The three-year disease-free survival rate was 67 percent and three-year overall survival rate was 81 percent. The three-year local disease-free survival rate was 87 percent. Three patients underwent abdominoperineal resection or Hartman's operation and were converted to permanent stomas within one month after ISR because of early complications, which included two episodes of postoperative bleeding and one necrosis of the anastomosis.

Table 2 shows the clinical course of anal dysfunction based on the patients' answers to the questionnaires 3, 6, 12, and 24 months after the diverting stoma was closed. At 24 months after the stoma was closed, 26 percent of patients reported more than five bowel movements a day; 25 percent reported daily incontinence of gas; 23 percent reported incontinence of loose stools; 17 percent reported incontinence of solid stools; and 52 percent reported stool fragmentation. The percentage of patients who could not discriminate between feces and flatus decreased gradually from 22 percent at 3 months to 5 percent at 24 months. A very low level of satisfaction with anal function was reported by 25 percent of patients at 3 months, but by only 14 percent at 12 months, and 17 percent at 24 months.

Table 3 shows the Wexner scores and Kirwan classification over time for all patients for whom data were available. Gradual improvement in the Wexner score was seen from 3 to 6 months, and slight further improvement was observed between 6 and 24 months. In the Kirwan classification, the percentage of patients with frequent major soiling decreased over 24 months (particularly

TABLE 3. Incontinence scores after stoma closure in patients who underwent ISR

	3 months (n=88)	*6 months (n=84)*	*12 months (n=73)*	*24 months (n=60)*
Wexner score	11.7 (5.3)	10.3 (5.8)	10.0 (6.0)	9.6 (5.3)*
Kirwan classification				
Perfect	8 (9)	15 (18)	18 (25)**	13 (22)*
Incontinence of flatus	9 (10)	8 (10)	8 (11)	11 (18)
Occasional minor soiling	36 (41)	39 (46)	27 (37)	22 (37)
Frequent major soiling	35 (40)	22 (26)*	20 (27)	14 (23)*
Incontinent (required colostomy)	0 (0)	0 (0)	0 (0)	0 (0)

Data are means with standard deviation in parentheses for Wexner score and numbers of patients with percentages in parentheses for Kirwan classification. Wexner score and Kirwan classification in 6, 12 and 24 months were statistically compared with those in 3 months.
*: $P < 0.05$ **: $P < 0.01$.

TABLE 4. Analysis of variables associated with poor Wexner scores after ISR

Variable	Wexner score <16	Wexner score ≥16	Univariate analysis Odds ratio (95% CI)	Univariate analysis P value	Multivariate analysis Odds ratio (95% CI)	Multivariate analysis P value
Sex						
F	15	2 (12)				
M	39	17 (30)	3.3 (0.7–16.3)	0.1	2.1 (0.4–12.9)	0.4
Age (yr)						
<70	49	18 (27)				
≥70	5	1 (17)	0.5 (0.06–5.2)	0.5		
Reconstruction						
Straight	46	17 (27)				
Pouch	8	2 (20)	0.7 (0.1–3.6)	0.6		
Anastomotic leakage						
–	44	16 (27)				
+	10	3 (23)	0.8 (0.2–3.5)	0.7		
Extent of excision of the internal sphincter						
Subtotal ISR or partial ISR	42	10 (19)				
Total ISR	12	9 (43)	3.2 (1.0–9.7)	0.04	1.2 (0.3–4.5)	0.8
Partial resection of the external sphincter						
–	43	13 (23)				
+	11	6 (35)	1.8 (0.5–5.9)	0.3		
Lateral lymph node dissection						
–	22	3 (12)				
+	32	16 (33)	3.7 (0.9–14.4)	0.06	3.8 (0.8–18.8)	0.1
Preoperative CRT						
–	35	3 (9)				
+	19	16 (46)	9.8 (2.5–38.9)	<0.01	10.3 (2.3–46.3)	<0.01

CRT = chemoradiotherapy; 95% CI = 95 percent confidence interval. • Data for Wexner score are number of patients, with percentage in parentheses for the category ≥16 points. Data for odds ratios are relative likelihood of having a Wexner score ≥16 (poor anal function), with 95% CI in parentheses.

from 40 percent at 3 months to 26 percent at 6 months), and the percentage with perfect function increased during the first year (from 9 percent at 3 months to 18 percent at 6 months, and to 25 percent at 12 months).

As shown in Table 4, in the univariate analysis, poor anal function assessed by the Wexner score at 12 months was significantly associated with greater extent of excision of the internal sphincter (total ISR) ($P = 0.04$) and with preoperative CRT ($P < 0.01$). Sex, age, type of reconstruction, presence of anastomotic leakage, partial resection of the external sphincter, and lateral lymph node dissection were not associated with poor anal function after ISR. In the multivariate analysis, preoperative CRT was the only independent factor associated with poor anal function after ISR ($P < 0.01$).

As shown in Table 5, mean Wexner scores in each type of ISR were higher in patients who received preoperative CRT than in those who did not. This difference was significant in the group with subtotal ISR ($P < 0.01$).

TABLE 5. Effect of preoperative CRT on anal function (Wexner score) in patients who underwent partial ISR, subtotal ISR, or total ISR

	Partial ISR (n=17)	Subtotal ISR (n=36)	Total ISR (n=20)
Preoperative CRT			
–	6.1 (14)	6.9 (19)*	8.6 (5)
+	13.3 (3)	13.6 (17)*	13.1 (15)

CRT = chemoradiotherapy; 95 percent CI = 95 percent confidence interval; ISR = intersphincteric resection. • *$P < 0.01$. • Data are mean Wexner score with number of patients in parentheses.

DISCUSSION

Of the factors investigated in our study, preoperative CRT had the greatest negative impact on anal function after ISR. Total ISR was more strongly associated with anal dysfunction than either subtotal or partial ISR. Moreover, a negative effect of preoperative CRT on anal function was found regardless of the extent of preservation of the internal sphincter muscle. This study confirmed the recent report by Chamlou *et al.*[14] that functional results after ISR are altered by preoperative CRT.

We evaluated postoperative anal function after ISR on the basis of prospective data obtained from questionnaires on function that were filled out by the patients themselves. Self-report data are important in obtaining an accurate picture regarding anal function.[15]

Previous reports have mentioned postoperative dysfunction after ISR, mostly regarding incontinence of gas or stools.[5–7] Rullier *et al.*[16] found that 10 percent (2/21) of patients with major soiling after ISR had received preoperative radiotherapy. A long-term study by Shiessel *et al.*[17] showed incontinence of gas or liquid stools in 13.7 percent of patients. The rate of incontinence in our study was similar to that found by Chamlou *et al.*,[14] but worse than that found by others. Comparison is difficult

because most reports did not clearly state the time after stoma closure at which results for function were assessed or what methods were used for assessment. Moreover, the effects of preoperative CRT or extent of excision of the internal sphincter were not investigated. At 12 months after stoma closure, 25 percent of the patients in our study were continent ("perfect" according to the Kirwan classification), and this rate was similar to the 29.6 percent reported by Kohler *et al.*[5] and the 20 percent reported by Teramoto *et al.*[18] The long-term study by Bretagnol *et al.*,[8] in which anal function was evaluated by means of a questionnaire similar to the one used in our own study, yielded a mean Wexner score of 10.8, comparable to our 2-year mean score of 9.6.

The cause of the negative effects of conventionally fractionated chemoradiotherapy on anorectal function is still unclear. Lim *et al.*[19] attributed poor anorectal function after a conventionally fractionated 45-Gy dose of preoperative CRT to damage to the pudendal nerve. Other reports[20,21] showed that, after radiotherapy, rectal function was worsened by radiation proctitis and reduced rectal compliance from fibrosis of the rectal wall. Moreover, anal sphincter dysfunction after radiation may be a result of direct radiation injury to the internal anal sphincter muscle.[22] Incontinence after ISR with preoperative CRT might be at least partially explained by these findings. Our results also showed that conventional CRT was associated with anal dysfunction 12 months after stoma closure, and the adverse effects had occurred at only 3 months. We cannot clearly explain why this adverse effect of preoperative CRT occurred so early after irradiation. Moreover, we do not know whether this anal dysfunction caused by preoperative CRT will continue permanently or improve in the future. It will be important to determine whether the anal dysfunction caused by CRT improves in a long-term follow-up. The mechanism responsible for the anal dysfunction caused by preoperative CRT should also be further investigated.

Despite its potential negative effects on anal function, preoperative CRT has been shown to increase the sphincter-saving rate, thus avoiding permanent colostomy.[23] Guillem *et al.*[24] reported that after preoperative combined-modality therapy, a 1-cm margin of distal clearance beyond the mucosal edge should assure a negative distal margin in the majority of rectal cancer patients. We agree that some patients could avoid permanent stoma by ISR if a 1-cm distal clearance is achieved after preoperative CRT.

Consistent with results reported by Gamagami *et al.*,[25] our study indicated that total resection of the internal sphincter also had an impact on anal function. One year after stoma closure, the mean Wexner score in our patients who underwent total ISR without preoperative CRT was 8.6, which was higher than the mean of 6.9 found in patients with subtotal ISR group or the 6.1 in patients with partial ISR. However, these scores were lower than those in patients who received preoperative CRT, who had mean Wexner scores above 13 points whether they had undergone partial ISR, subtotal ISR, or total ISR. These results suggested that, in the absence of irradiation, anus preservation with tolerable function can be expected even after total ISR.

Our results did not clearly show superiority of a J-pouch or a TCP after low anterior resection[26,27] or ISR.[28,29] In our early experience of ISR, anastomosis of a colonic J-pouch down to the level of the dentate line was often not technically feasible because of the bulk of mesocolic fat or inadequate length of preserved colon. Thus, we had only 12 patients with a J-pouch or TCP. Fazio *et al.*[30] also commented that some patients were ineligible for a J-pouch because of a bulky mesocolon. However, we agree that creation of a pouch is widely accepted as a better means of preserving of anal function and reducing postoperative morbidity,[26,31,32] and this issue should be addressed by other studies of ISR for very low rectal cancer.

It is also important to decide on the indications for ISR in elderly patients. We generally excluded patients who had anal dysfunction before surgery. Old age itself affects anal function[33] and should be considered in the decision to perform ISR. However, before surgery, most patients with rectal cancer have poor anal function because of irritation from a tumor near the anus. Thus, it is difficult to clearly identify an indication for ISR based on preoperative anal symptoms in either elderly or younger patients. In our series, the postoperative anal function of patients 70 years and older was comparable to that of patients under 70 years of age, and our results were similar to those of Dehni *et al.*[34] These findings suggest that ISR may be acceptable in elderly patients who do not require preoperative CRT or total ISR.

The local recurrence rate of 13 percent in our patients was higher than the 8.8 percent reported by Chamlou *et al.*[14] The difference may be due to a higher proportion of patients with stage III cancer in our study than in that of Chamlou *et al.* (39 percent *vs.* 28 percent). Moreover, 15 of our 37 patients with stage III had more than 3 lymph nodes involved and were potentially in a high risk group for recurrences.

In conclusion, preoperative CRT was found to be the factor most strongly associated with poor anal function after ISR, suggesting that patients with rectal cancer who undergo ISR after preoperative CRT are very likely to experience incontinence. This information should be given to patients when they are offered a choice of treatment. Since postoperative anal function after ISR with reconstruction by a straight anastomosis can be predicted based on our results, additional treatment to rescue poor anal function will be needed for patients who

are expected to have poor postoperative anal function. Prospective trials of ISR with preoperative CRT for very low rectal cancer should be performed to clarify both its survival benefit and adverse effects on anal function.

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Evaluation of Postoperative Damage to Anal Sphincter/Levator Ani Muscles with Three-Dimensional Vector Manometry after Sphincter-Preserving Operation for Rectal Cancer

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BACKGROUND: The aim of this study was to examine correlations between pressure profile of the anal canal and postoperative defecatory disorder after sphincter-preserving operation (SPO) for rectal cancer.

STUDY DESIGN: Using three-dimensional vector manometry, pressure profile and length of the anal canal were evaluated more than 1 year after SPO according to operation method and degree of postoperative defecatory function in 53 patients with rectal cancer.

RESULTS: Compared with high anterior resection as a control, the anal canal was shorter in operations with a pelvic floor maneuver, namely, low anterior resection, ultra-low anterior resection, and intersphincteric resection. Patients with postoperative defecatory disorder showed significantly shorter anal canal length than patients with fair function. Length of the circular high-pressure zone ($\geq$ 20 mmHg) $<$ 20 mm in the resting state was a strong predictor of severe postoperative defecatory malfunction, with Wexner score $\geq$ 10.

CONCLUSIONS: Operative maneuvers at the pelvic floor during SPO for rectal cancer may damage anal sphincter or levator ani muscles. The circular high-pressure zone can be measured only by three-dimensional manometry and may offer a useful indicator of sphincter damage after SPO for rectal cancer. (J Am Coll Surg 2009;208:362–367. © 2009 by the American College of Surgeons)

Sphincter-preserving operation (SPO) has been the surgical treatment of choice for the majority of rectal cancer patients. But causes of the postoperative defecatory disorder after SPO that is seen in approximately half of patients[1] have not been well delineated. Studies using anal manometry have revealed that resting pressure and maximum squeeze pressure are both degraded after surgery.[2] Postoperative anal sensation[3] or the physiologic rectoanal inhibitory reflex[4] may be reduced simultaneously. Such sphincter malfunctions may be caused by direct injury during operation,[5] or may result from denervation of the anal sphincter muscles during surgical maneuvers.[6]

Three-dimensional vector manometry (3D manometry) has recently been used to evaluate patients with anal incontinence[7] or postoperative anal damage, as seen in Hirschsprung's disease.[8] This study examined the postoperative pressure profile of the anal sphincter using 3D manometry in patients who underwent SPO for rectal cancer. Characteristic findings commonly seen in patients with postoperative defecatory disorder were investigated. In addition, whether the pressure profile in 3D manometry can predict severe postoperative defecatory disorder was examined.

METHODS

Patients

The study comprised 53 patients (35 men, 18 women; median age, 63 years; range, 52 to 71 years) who underwent anal SPO for rectal cancer. Among these, 13 patients

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Abbreviations and Acronyms

C = length of circular pressure
CHPZ = circular high-pressure zone
HAR = high anterior resection
ISR = intersphincteric resection
LAR = low anterior resection
SPO = sphincter-preserving operation
T = total length of anal canal
3D = three dimensional

received high anterior resections (HAR), in which the anastomotic line was above the peritoneal reflection; 21 patients received low anterior resections (LAR), in which the anastomotic line was below the peritoneal reflection; 12 patients had ultra-low anterior resections (ultra-LAR), in which the anastomotic line was inside the anal canal, and 7 patients had either partial or total intersphincteric resection (ISR) with transanal coloanal anastomosis as the reconstruction. In this series, seven patients received preoperative radiotherapy. The interval between the initial operation and the time the physiologic study was performed was 1 year in 36 patients (68%), 2 years in 6 patients (11%), and 3 years or more in 11 patients (21%).

Procedure for three-dimensional manometry

A 5-mm thick perfusion catheter comprising eight independent thin lumens was specifically manufactured (Asahi BioMed). Drainage holes of the lumens were situated radially at 45-degree intervals, 2 cm from the tip of the catheter. At the entry, all lumens were connected to pressure transducers, then to a capillary water perfusion system with a pressure of 150 mmHg. The transducers were connected to an amplifier, from which data were transferred to a personal computer for storage and analysis using Polygram software (Japan Medtronic).

Measurements were taken with the patient in the left lateral position. Before taking measurements, water pressure at the height of the anus was set to zero, then 68 cm above this zero point was adjusted to 50 mmHg. Just before examination, patients were asked to defecate completely by applying 110 mL of glycerin enema.

Resting pressure was taken using the pull-through method, where the catheter inserted inside the neorectum was manually pulled from 6 cm above the anal verge at 1 cm/ in conjunction with a signal sound from a personal computer. Using the same method, squeeze pressure was measured by asking the patient to maximally squeeze for approximately 10 seconds. All measurements were repeated five or more times until stable data were obtained.

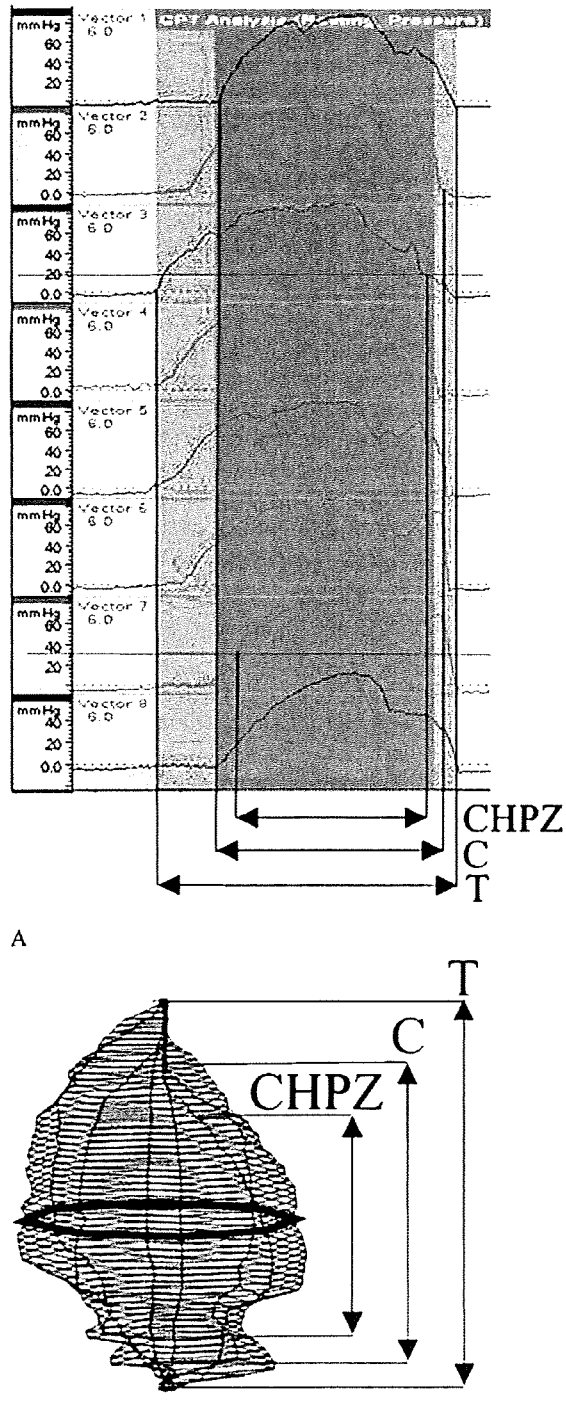

Figure 1. Definition of anal canal lengths according to pressure profiles in each channel. (A) Pressure distributions in channels 1 to 8 and definitions of anal canal length. (B) Three-dimensional construction of an 8-channel pressure profile. C, length of anal canal with circular pressure; CHPZ, length of anal canal with circular high pressure ≥ 20 mmHg above baseline, T, total length.

Table 1. Length of Anal Canal in Resting State Categorized by Different Criteria in Accordance with Operation Methods

Measurement	HAR (n = 13)	LAR (n = 21)	Ultra-LAR (n = 12)	ISR (n = 7)
T, cm	51.2 ± 5.6	44.0 ± 8.8*	45.6 ± 5.2*	36.3 ± 5.1†
C, cm	40.2 ± 6.6	30.2 ± 9.0†	30.5 ± 6.5†	12.0 ± 9.5†
CHPZ, cm	31.1 ± 7.4	22.5 ± 9.0†	23.0 ± 8.2*	7.6 ± 5.9†

Values are reported as mean ± standard deviation. Reported p values are for pairwise comparisons of LAR, Ultra-LAR, or ISR versus HAR.
*$p < 0.05$ versus HAR.
†$p < 0.01$ versus HAR.
C, length of circular pressure; CHPZ, circular high-pressure zone; HAR, high anterior resection; ISR, intersphincteric resection; LAR, low anterior resection; T, total length of anal canal.

Evaluation of data

Figure 1 summarizes the definition of anal canal length as measured by 3D manometry. Under the pull-through method, total length of the anal canal (T) was defined as the length from the point at which any one channel is higher than the baseline to the point at which all channels drop to baseline. T presumably represents the longest length of the anal canal measurable by manometry, and may well reflect the conventional functional anal canal length measured by a single-channel manometer. Length of circular pressure (C) was defined as the length from the point at which all eight channels are higher than baseline to the point at which any one channel drops to baseline. This may reflect the length of the anal canal that shows pressure from 360 degrees. In addition, we defined the length of the circular high-pressure zone (CHPZ) as the distance from the point at which all eight channels are ≥ 20 mmHg above rectal baseline pressure to the point at which any one channel drops to < 20 mmHg. The reason we set 20 mmHg as the cut-off value was that pressure inside the neorectum has not fluctuated ≥ 20 mmHg at rest in most of the patients tested to date.

Evaluation of defecatory dysfunction

Patients were interviewed using a self-administered questionnaire about recent defecatory status within 1 month before or after each examination. Fecal soiling was categorized based on previously reported criteria proposed by Jorge and Wexner,[9] taking into account the degree and frequency of incontinence. The Wexner incontinence scale (Wexner score) measures five types of incontinence: solid, liquid, gas, wearing a pad, and lifestyle alteration. Each category was scored from 0 (never) to 4 (>1 episode/d). So perfect continence is scored as 0; complete incontinence is scored as 20.

RESULTS

Operation method and pressure profile

Lengths of the anal canal categorized by different definitions compared with operation methods are summarized in Tables 1 and 2. Compared with HAR, length of the anal canal in resting state, which may reflect length of the internal sphincter muscle, was significantly decreased in LAR, ultra-LAR, and ISR (Table 1). For length of the anal canal in a squeezing state, which may be determined by external sphincter and levator ani muscles, significant differences were seen in patients who received ISR compared with patients who received HAR. In patients having LAR or ultra-LAR, significant differences in squeezing state were seen only in length of the CHPZ in LAR, although all categories in LAR and ultra-LAR tended to be reduced compared with HAR (Table 2).

Defecatory disorder and pressure profile

Table 3 summarizes comparisons of length of the anal canal between patients with good defecatory function (Wexner score ≤ 5) and those with poor function (Wexner score > 5). In all the defined parameters, patients with fair postoperative defecatory function showed significantly longer anal canals when compared with those with poor function. 3D reconstruction of luminal pressure from

Table 2. Length of Anal Canal in Squeeze State Categorized by Different Criteria in Accordance with Operation Methods

Measurement	HAR (n = 13)	LAR (n = 21)	Ultra-LAR (n = 12)	ISR (n = 7)
T, cm	52.6 ± 5.0	48.8 ± 8.7	48.6 ± 5.7	41.3 ± 4.5†
C, cm	43.1 ± 5.6	38.7 ± 9.9	40.4 ± 7.3	25.7 ± 3.7†
CHPZ, cm	39.0 ± 8.3	31.7 ± 9.2*	33.6 ± 8.2	17.0 ± 7.0†

Values represent mean ± standard deviation. Reported p values are for pairwise comparisons of LAR, Ultra-LAR, or ISR versus HAR.
*$p < 0.05$ versus HAR.
†$p < 0.01$ versus HAR.
C, length of circular pressure; CHPZ, circular high-pressure zone; HAR, high anterior resection; ISR, intersphincteric resection; LAR, low anterior resection; T, total length of anal canal.

Table 3. Postoperative Defecatory Function and Length of Anal Canal

Measurement	Wexner score ≤ 5 (n = 36)	Wexner score > 5 (n = 17)	p Value
T, cm			
At rest	46.6 ± 6.9	40.1 ± 8.6	< 0.05
Squeezing	50.6 ± 6.9	44.5 ± 7.2	< 0.01
C, cm			
At rest	34.3 ± 7.3	21.1 ± 12.7	< 0.01
Squeezing	41.2 ± 7.3	31.8 ± 10.2	< 0.01
CHPZ, cm			
At rest	27.5 ± 6.7	15.1 ± 10.0	< 0.01
Squeezing	35.1 ± 8.6	24.9 ± 11.3	< 0.01

Values represent mean ± standard deviation.
C, length of circular pressure; CHPZ, circular high-pressure zone; T, total length of anal canal.

Table 4. Cut-Off Value of Each Parameter as a Predictor of Patients Showing Major Soiling

Parameter (cut-off)	Scored less than cut-off, n	With major soiling* scoring less than cut-off, n	Predictive value, %
T			
At rest (40)	13	8	62
Squeezing (44)	10	5	50
C			
At rest (37)	14	10	71
Squeezing (34)	15	9	60
CHPZ			
At rest (20)	10	10	100
Squeezing (24)	13	9	69

*Wexner score ≥10.
C, length of circular pressure; CHPZ, circular high-pressure zone; T, total length of anal canal.

sphincter muscles, as seen in Figure 2, indicated that patients with good defecatory function who underwent HAR showed uniform pressure from 360 degrees, with minimal differences among lengths of T, C, and CHPZ (Fig. 2A). Some deformities were detected in the majority of patients with LAR or ultra-LAR, resulting in discrepancies among T, C, and CHPZ (Fig. 2B). In patients who underwent ISR, severe deformity, with decreased pressure and shortening of the anal canal, was observed to various degrees (Fig. 2C–1). But squeeze pressure was often stored when external sphincter or levator ani muscles were preserved undamaged (Fig. 2C–2).

Next, we defined cut-off values for each parameter as the mean value minus 1 SD to examine whether severe defecatory malfunction with major soiling (Wexner score ≥ 10) can be predicted. Cut-off values in all six categories significantly discriminated patients with severe defecatory malfunction in the chi-square test (data not shown), but as shown in Table 4, some patients with scores below cut-off levels did not show severe dysfunction in most of the categories except CHPZ at rest. In CHPZ at rest, all patients with a score below the cut-off value showed severe defecatory malfunction, with Wexner score ≥ 10. The positive predictive value for cut-off of CHPZ at rest was 100%. Two patients suffering from severe defecatory dysfunction with Wexner score ≥ 10 were included among patients with CHPZ at rest above the cut-off value, so the true positive rate was 83% (10 of 12) for the cut-off of CHPZ at rest.

DISCUSSION

3D manometry is a useful tool for evaluating gastrointestinal luminal pressure, as seen from this study. Unlike single-channel manometry, circular pressure can be evaluated using this approach. In addition, whether circular pressure is uniformly applied from 360 degrees can also be determined. These merits have been used for evaluation of the luminal pressure disorder seen postoperatively in esophageal atresia[10] or Hirschsprung's disease[8] to clarify whether pressure disequilibrium is present inside the lumen.

This study evaluated pressure profiles in patients after SPO for rectal cancer. Based on the 3D pressure profile, we defined three different anal canal lengths: T, C, and CHPZ. T is regarded as the longest length of the anal canal measured by manometry, and may well be measured by a single-lumen catheter. C is an anal length with pressure from 360 degrees. C is considered a unique length that only 3D manometry can evaluate, not single-channel manometry. In addition, we defined CHPZ as the length showing a circular pressure ≥ 20 mmHg above baseline. CHPZ can also be measured only by 3D manometry.

By comparing pressure profiles among operation methods, length of the anal canal in a resting state was seen to be shorter with LAR, ultra-LAR, and ISR than with HAR. In HAR, surgical maneuvers do not extend to the pelvic floor; in LAR and other operations with anastomosis lying distally, the internal anal sphincter muscles seem to be damaged. In ultra-LAR or ISR, at least part of the internal sphincter muscles is mechanically transected during the operative procedure, which may be one of the major reasons for postoperative deteriorations in anal resting pressure. Luminal squeezing pressure was preserved in the majority of patients who underwent ultra-LAR (Table 2). In patients who underwent ISR, luminal squeezing pressure was preserved in some patients (Fig. 2C) despite significant overall damage, suggesting that the external anal sphincter or levator ani muscles can be preserved undamaged even in ISR.

In LAR, the internal sphincter muscles and part of the rectal wall are supposed to be preserved, but postoperative

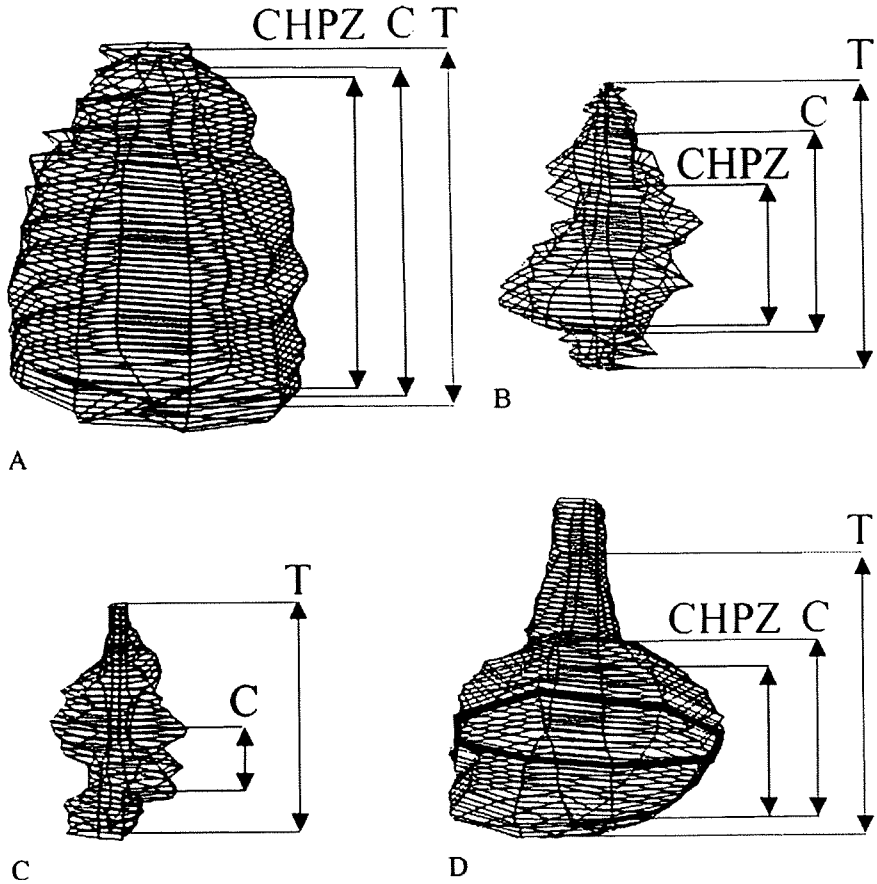

Figure 2. Three-dimensional reconstruction of luminal pressure from sphincter muscles. (A) A patient with good defecatory function with Wexner score 0 who underwent HAR. Minimal differences are seen among lengths of T, C, and CHPZ in a resting state. (B) A patient with moderate defecatory function with Wexner score 5 who underwent LAR. Some deformities are apparent in shape and thee are also discrepancies among T, C, and CHPZ in a resting state. (C) A patient with severe defecatory malfunction with Wexner score 16 who underwent ISR, showing severe deformity with decreased pressure and shortening of the anal canal in a resting state. No CHPZ was determined. (D) Squeeze pressure in the same patient from C. Despite severe defecatory disorder, luminal squeezing pressure was preserved. C, length of circular pressure; CHPZ, circular high-pressure zone; HAR, high anterior resection; ISR, intersphincteric resection; LAR, low anterior resection; T, total length of anal canal.

resting pressure was still adversely affected in some patients. This suggests that surgical maneuvers at the bottom of the pelvic floor may, at least in some patients, be a causative factor for damage to the internal sphincter muscles, either mechanically or through injury to the nerve supply. This issue warrants additional investigation. Scarring near the sphincter muscle may be an alternative cause of postoperative sphincter damage. Careful surgical maneuvers at the pelvic floor are warranted when SPO with total mesorectal excision is applied for treatment of rectal cancer.

Next, we evaluated correlations between length of the anal canal as defined by several parameters and degree of postoperative defecatory dysfunction. Data clearly indicated that patients with defecatory disorder had significantly shorter anal canal lengths than patients with fair function. These findings are consistent with previous evaluations using single-channel manometry.[11,12] In addition, we examined whether any length of anal canal defined by the various pressure profiles could predict severe postoperative defecatory dysfunction with Wexner score $\geq$ 10. All defined lengths correlated with manifestations of severe defecatory dysfunction when analyzed using a chi-square test. But in most of the lengths defined, some patients displayed anal canal length below the cut-off, but had fair function, indicating that these parameters do not represent a precise predictor of severe postoperative defecatory mal-

function, despite displaying a correlation with poor function statistically. Among the parameters, CHPZ at rest seemed to be the best predictor of poor function; all 10 patients who scored below the cut-off (20 mm) also suffered from severe defecatory dysfunction. The positive predictive value for severe postoperative defecatory malfunction was 100%, with a true positive rate of 83% (10 of 12). For the two patients in whom CHPZ was above the cut-off, but who still showed severe postoperative defecatory malfunction, other factors such as motility disorder of the neorectum[13] may have contributed to the disorder.

In conclusion, this study suggests that 3D manometry is a useful tool for evaluating postoperative defecatory malfunction. In particular, CHPZ, which can only be evaluated by 3D manometry, appears to offer a good prediction of severe postoperative defecatory malfunction. Operative maneuvers at the pelvic floor, including the approach to the anal sphincter, seem to exert significant influences on circular sphincter tonus, so may represent a causative factor for severe postoperative defecatory malfunction. In SPO, preservation of a certain length of anal canal with circular high pressure is essential to avoid severe postoperative defecatory disorder.

Author Contributions

Study conception and design: Koda, Yasuda, Kosugi, Saito
Acquisition of data: Koda, Hirano, Kosugi, Suzuki, Yamazaki, Tezuka, Higuchi, Tsuchiya
Analysis and interpretation of data: Koda, Hirano, Kosugi
Drafting of manuscript: Koda, Yasuda
Critical revision: Koda, Yasuda, Saito

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World Journal of Surgery

Oncologic Outcome of Intersphincteric Resection for Very Low Rectal Cancer

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Abstract
Background In 2000 we launched a prospective program of intersphincteric resection (ISR) for very low rectal cancer. In this study we compared the oncologic outcome of patients who underwent ISR with the outcome of patients who underwent abdominoperineal resection (APR).
Methods The data of 202 patients with very low rectal cancer who underwent curative ISR ($n = 132$) or curative APR ($n = 70$) between 1995 and 2006 were analyzed. Patients were divided into ISR and APR groups. Survival and local recurrence were investigated in both groups.
Results The median follow-up was 40 months in the ISR group and 57 months in the APR group. The 5-year local relapse-free survival rate was 83% in the ISR group and 80% in the APR group ($p = 0.364$), and the 5-year disease-free survival rate was 69% in the ISR group and 63% in the APR group ($p = 0.714$).
Conclusions For very low rectal cancers, ISR appears to be oncologically acceptable and can reduce the number of APRs.

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Introduction

The main goal of rectal cancer surgery is to cure the carcinoma and achieve local control. An additional goal is to preserve anal sphincter function for a better quality of life. The development of surgical techniques and combined adjuvant therapy has led to improved local control and patient survival [1]. The technique of total mesorectal excision, developed by Heald et al. [2], is now the gold standard in the operative management of rectal cancer in the middle and lower thirds. The advent of mechanical low-stapling and double-stapling techniques, as well as sutured coloanal anastomosis, has facilitated anastomosis at the distal rectum. These methods have increased the incidence of sphincter salvage. Further understanding of the safe distal resection margin has increased the incidence of successful sphincter-saving surgery. Distal intramural spread rarely extends more than 1 cm beyond the edge of the tumor [3, 4]. Nevertheless, lower rectal cancers located less than 5 cm from the anal verge or less than 2 cm from the dentate line are traditionally treated by abdominoperineal resection (APR) [5–7].

In recent years additional efforts have been made to increase the rate of sphincter preservation. The most extreme form of rectal resection is abdominoperineal intersphincteric resection with coloanal anastomosis (ISR) [7–21]. It is an alternative to APR for tumors in the suprasphincteric part of the rectum and tumors extending into the anal canal. Since 2000 this procedure has often been performed at our institute as an alternative to APR for consenting patients, although APR is still the standard surgical procedure for patients with very low rectal cancer in Japan.

The aims of this study were to determine the oncologic outcome following ISR of very low rectal cancer and to

compare these results with the outcome following standard APR.

Patients and methods

Patients

Between 1995 and 2006, a total of 202 consecutive patients who underwent curative ISR with coloanal anastomosis or curative APR for low-lying primary rectal cancer located between 1.0 and 5.0 cm from the anal verge were identified from the hospital databases, and these patients' medical charts were retrospectively reviewed. The inclusion criteria for this study were histologically proven rectal adenocarcinoma without synchronous metastasis, patients with cancer-free distal and circumferential margins by ISR or APR, and patients with clinical T1, T2, T3, or part of T4 rectal tumors involving the prostate or the vagina. The tumor staging was done by digital examination, computed tomography (CT), magnetic resonance imaging (MRI), barium enema, or colonoscopic examination. Endorectal ultrasonography was occasionally performed to rule out local excision. The exclusion criteria in this study were tumorous invasion of the intersphincteric groove, definitive massive invasion into the levator ani muscle and/or the external anal sphincter by T4 tumors, and synchronous distant metastasis. Patients with diffusely infiltrating carcinoma such as macroscopic type 4 gastric cancer were also excluded. Thus, patients with tumorous invasion into the intersphincteric groove, the levator ani muscle, and the external anal sphincter muscle were candidates for only APR. Therefore, those patients undergoing APR were excluded from the APR group in this study. However, patients with T3 tumors undergoing ISR combined with partial external anal sphincter resection (PESR) for obtaining safe surgical margins were included in the ISR group in this study.

In the present study, 132 patients underwent curative ISR and 70 patients underwent curative APR for very low rectal cancer. All patients had cancer-free surgical margins. Intersphincteric resection including PESR was performed between 2000 and 2006 as an alternative to APR. Of the 132 patients in the ISR group, 27 also underwent PESR for portions of T3 or T4 tumors. Abdominoperineal resection was performed mainly between 1995 and 2002. In fact, only 11 patients underwent APR between 2000 and 2006. In 1999, we started to evaluate the indications for ISR in patients with advanced lower rectal cancer, and the basis of a new therapeutic algorithm for very low rectal cancer was established in 2000 at our institute. Postoperative mortality and mobility, local control, and survival were investigated. Detailed documentation of the histopathological findings permitted classification of the patients in accordance with the 6th (2002) edition of the UICC TNM classification [22]. Postoperative complications were defined as all events necessitating diagnostic or therapeutic measures and those prolonging hospital stay. Postoperative mortality included all patients who died postoperatively in the hospital, irrespective of the time interval from the operation.

Follow-up examinations were performed every 3 months for 2 years postoperatively and every 6 months there after using clinical examination, laboratory tests (including tumor markers CEA and CA19-9), and radiologic examination (liver and pelvic CT, and pulmonary CT or chest radiography). Local recurrence was defined as the presence of any anastomotic, pelvic, or perineal tumor and regional lymph node metastases documented by clinical, radiologic, and/or pathological examination, even if distant metastases were present.

The analyzed parameters were compared between the ISR group and the APR group.

Intersphincteric resection technique

Intersphincteric resection was performed following the methods previously reported by Schiessel et al. [8] and others [11–15]. The surgical technique included both abdominal and peranal approaches. In the abdominal approach, ligature of inferior mesenteric blood vessels close to the origin, total mesorectal excision, and pelvic lateral node dissection with autonomic nerve preservation were performed, although lateral node dissection is not the standard of care outside of Japan [23–25]. The rectum was mobilized carefully, as low as possible to the pelvic floor, to facilitate the peranal approach. The surgical anal canal that commences at the anorectal angle and ends at the anal verge was then divided circumferentially from the puborectalis muscle and the external sphincter.

If a patient had a clinical T3 tumor in the anal canal area, the puborectal muscle and/or the external sphincter were partially resected to obtain sufficient safety margins. As a result, the fatty tissue of the ischiorectal fossa was sometimes visualized. This procedure is called ISR plus PESR and has been reported in our previous studies [15, 18]. In the present study, patients who had PESR were included in the ISR group. After the abdominal approach, peranal ISR was performed. Circumferential incision of the mucosa and ISR was initiated 1-2 cm distal from the lower edge of the tumor. The anal orifice of the rectum was immediately closed with purse string suture to avoid the spread of tumor cells during the peranal procedure. Once the intersphincteric plane [26] was entered, careful dissection continued upward. A frozen-section examination of the resected specimen was carried out to ensure the

oncologic safety margins after material removal. Following that, the sigmoid colon was pulled down and a coloanal anastomosis with or without colonic pouch was made using peranal manual suturing. Finally, a diverting stoma using the ileum or transverse colon was established. This stoma was closed 3 months or more postoperatively.

Adjuvant therapy

Most patients with a stage III tumor (pTNM pathologic classification) received postoperative chemotherapy with 5-fluorouracil and folic acid, tegafur uracil, or other drugs for 6 months or more. Preoperative radiochemotherapy (45 Gy delivered over a 5-week period with continuous infusion of 5-fluorouracil) was performed in 48 patients in the ISR group with T3 clinical tumors who agreed to preoperative adjuvant therapy, although preoperative radiochemotherapy for resectable rectal cancer was not standard at that time in Japan.

Statistical analysis

Patients were divided into two groups: the ISR group and the APR group. Overall survival (OS) and disease-free survival (DFS) were calculated using the Kaplan-Meier method. Time to final follow-up evaluation, treatment failure, or death was measured from the date of proctectomy. Local recurrence was evaluated using a cumulative local relapse-free survival curve (LFS). Assessment of recurrence and survival was performed in patients with microscopically curative surgery. Differences between curves were evaluated with the log-rank test. All statistical analyses were performed using SPSS software for Windows, version 13.0 J (SPSS-Japan Inc., Tokyo, Japan). A value of $p < 0.05$ was considered statistically significant.

Results

Of the 202 patients with very low rectal cancer treated radically during the study period, 70 underwent APR and 132 underwent ISR intended to be curative. The characteristics of the patients in each group are given in Table 1. Age, sex, tumor distance from the anal verge, distribution of T stage and node involvement, rate of perioperative complications, and morbidity rate were comparable in the two groups. The median distance between the lower edge of the tumor and the anal verge was 3.5 cm (range = 1.5-5.0 cm) in the ISR group and 3.0 cm (range = 1.0-5.0 cm) in the APR group. With respect to T-stage distribution, 92 patients (69.7%) had clinical T3 tumors in the ISR group and 47 patients (67.1%) had clinical T3 tumors in the APR group. The ISR group included 27 patients who underwent ISR plus PESR for T3 or T4 tumors. There were no significant differences in the tumor characteristics between these two groups. The median follow-up period was 58 months (range = 5-160 months) in the APR group and 40 months (range = 6-89 months) in the ISR group. No patient was lost to follow-up.

Local recurrences

During follow-up, 48 of 202 patients developed recurrence: 24 patients in the ISR group and 24 patients in the APR group (Table 2). A total of 29 local recurrences, including regional lymph node metastasis, were observed: 14 patients (10.6%) in the ISR group and 11 patients (15.7%) in the APR group. Four patients (3.0%) developed margin recurrence in the ISR group and 8 patients (11.4%) developed margin recurrence in the APR group. There was a significant difference in margin recurrence rate between the two groups ($p = 0.017$). The 5-year local relapse-free survival (LFS) rates were not significantly different as shown in Fig. 1 ($p = 0.364$).

In the 14 patients with local recurrence in the ISR group, 12 (85.7%) had recurrence that was pathologic T3 and 2 had recurrence that was pathologic T2. With respect to the local recurrence site, lateral nodal recurrence occurred in eight patients and surgical marginal recurrence occurred in only four patients. Ten of these 14 patients also had distant metastases.

Survival

The disease-free 5-year survival rate (DFS) was 69.1% in the ISR group and 63.3% in the APR group. The 5-year overall survival rate (OS) was 80.0% in the ISR group, regardless of tumor stage, and 61.5% in the APR group, as shown in Figs. 2 and 3. Although a significant difference in OS was observed ($p = 0.033$), there was no significant difference in DFS between the two groups. ($p = 0.714$).

Discussion

The general consensus is that most rectal cancers less than 5 cm from the anal verge or less than 2 cm from the dentate line are to be treated using APR. In recent years, progress in rectal cancer surgery, including conventional coloanal anastomosis (CAA), has led to the preservation of anal sphincter function. Use of CAA for treating benign disease without eversion of the rectal stump was first described by Parks in 1972 [27]; he also performed the first ISR with CAA for rectal cancer in 1982 [26]. In 1981,

Table 1 Patients' characteristics before treatment

	Curative ISR ± PESR (n = 132)[a]	Curative APR (n = 70)	p value
Age, median (range) (years)	57 (27–80)	59 (34–82)	0.662
Male/female	97/35	45/25	0.187
Tumor			
Distance from anal verge, median (range) (cm)	3.5 (1.5–5.0)	3.0 (1.0–5.0)	0.465
Clinical T stage[b]			
Depth of invasion			
T1	4	3	0.798
T2	28	11	
T3	92 (69.7%)	47 (67.1%)	
T4	8	9	
Node involvement			
N−	76 (57.6%)	37 (52.9%)	0.521
N+	56 (42.4%)	33 (47.1%)	
Morbidity rate	30.3% (40/132)	28.6% (20/70)	0.307
Mortality rate	0%	0%	1.000
Follow-up, median (months)	40	57	

[a] Forty-eight patients received preoperative chemoradiotherapy (CRT: 45 Gy 5-Fu)

[b] Determined by CT or MRI or endorectal ultrasound

Table 2 Patterns of recurrence

Recurrence[a]	ISR ± PESR (n = 132)[b]	APR (n = 70)[b]	p value
No. of patients	24	24	0.011
Local recurrence	14 (10.6)	11 (15.7)	0.295
Margin	4 (3.0)	8 (11.4)	0.017
Regional lymph node	10 (7.6)	4 (5.7)	0.621
Lung	18 (13.6)	6 (8.6)	0.291
Liver	8 (6.1)	8 (11.4)	0.180
Inguinal lymph node	5 (3.8)	3 (4.3)	0.863
Ovary	1	0	0.466

[a] Including duplicate organs

[b] Follow-up term (median): ISR ± PESR = 40 months, APR = 57 months

Shafik et al. [28] reported the anatomy and physiology of defecation in this new concept for lower rectal tumors.

Since the beginning of the 1990s, the indication for ISR has been progressively evaluated and rigorously applied. A distal margin of 1-2 cm is now considered sufficient in most instances. However, APR has remained the standard surgical procedure for lower rectal cancers. The risk of local recurrence is due more to circumferential margin involvement than to distal margin involvement because the mesorectal fat surrounding the tumor is thinner in the lowest part of the rectum [20]. For this reason, the ISR plus PESR procedure is sometimes needed. Unless the external anal sphincter is involved, a safe circumferential margin can be achieved using our ISR procedure. The present study was designed to retrospectively compare the oncologic results of ISR with or without PESR to those of APR.

From an oncological point of view, local control is the most important objective in surgery for lower rectal cancer. The local recurrence rate for lower-third rectal cancer has been reported to range between 9 and 35% [12, 19, 29, 30]. In the Schiessel series of ISR [17], a 5.3% local recurrence rate was reported in 113 patients who underwent ISR, including 31% of patients with T3 tumors and 37% of those with stage III lesions who had no radiotherapy. Rullier et al. [7] reported that 1 (2%) of 58 patients with mostly T3 tumors developed local recurrence during a median follow-up of 40 months. Hohenberger et al. [19] reported a 25.1% local recurrence rate following ISR and 14.2% of ISR patients treated with radiochemotherapy developed local recurrence. According to the long-term results from a median follow-up of 56.2 months by Chamlou et al. [21], an 8.8% local recurrence rate was reported in 90 patients

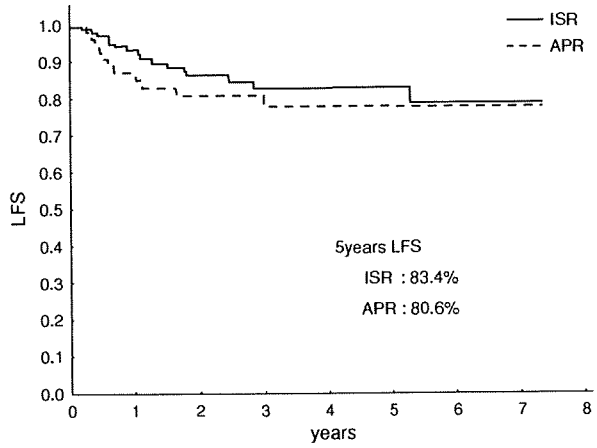

Fig. 1 Local relapse-free survival according to the type of operation; (—) ISR; (- - -) APR

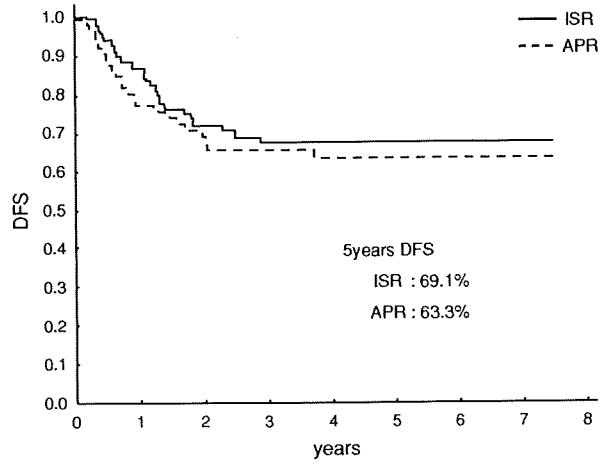

Fig. 2 Disease-free survival according to the type of operation; (—) ISR; (- - -) APR

who underwent ISR, including 41% of patients who had preoperative radiotherapy. Portier et al. [20] reported that the 5-year pelvic recurrence rate, regardless of tumor stage, was 10.6% in 173 patients who underwent ISR with a mean follow-up of 66.8 months.

In the present study with a median follow-up of 40 months, the overall local recurrence rate, including regional lymph node metastasis, was 10.6%, which was higher than the 6.7% rate that we reported in our previous series [18]. About 70% of the patients in the present series had a T3 tumor, and the rate of T1-T2 tumors was only 24%. The percentage of tumors limited to the rectal wall (T1-T2) ranges between 50 and 68% in most reported ISR series, with the exception of the series of Rullier et al. [7]. In the present study, the decrease in local control was caused mainly by the high rate of T3 tumors; in fact, 85.7% (12 of 14) of the patients with local recurrence had a pathologic T3

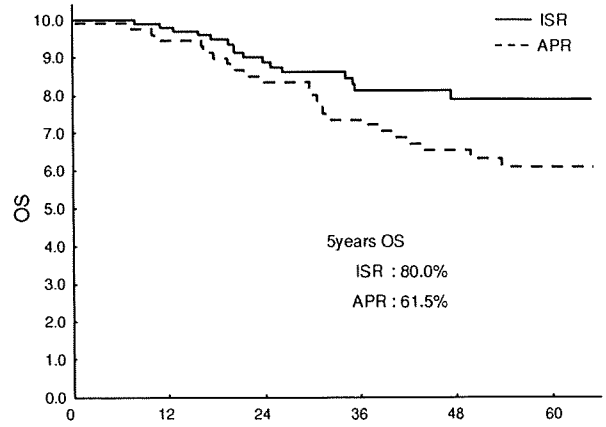

Fig. 3 Overall survival according to the type of operation; (—) ISR; (- - -) APR

tumor. With respect to the local recurrence site, margin recurrence rate was lower in the ISR group than in the APR group. This might have been caused by short-term follow-up in the ISR group, preoperative chemoradiotherapy in ISR group (48 patients), and incomplete total mesorectal excision in patients who underwent APR between 1995 and 1996. Akasu et al. [31] also reported that both invasion through the muscularis propria (T3) and a positive microscopic resection margin were significantly associated with local recurrence after ISR.

Paty et al. [32] analyzed the data of 134 patients with rectal cancer located 2-11 cm (median = 6.5 cm) from the anal verge who underwent not only ISR but also low anterior resection or CAA; they found that mesenteric implants, a positive microscopic resection margin, T3 tumor, perineural invasion, blood vessel invasion, and poorly differentiated histology were significantly associated with pelvic recurrence on univariate analysis. On the other hand, the local recurrence rate at a mean follow-up of 40 months was 2% in the Rullier series of 92 patients with mostly T3 tumors (72 patients) [7]. Eighty-one (88%) of their patients received preoperative radiotherapy (median dose = 44 Gy to the pelvis and 54 Gy to the tumor bed). Bonadeo et al. [33] observed a higher recurrence rate for very low T3 rectal tumors in the absence of radiotherapy. The results of the Hohenberger study [19] suggested that preoperative radiochemotherapy might increase local control. Therefore, preoperative radiochemotherapy or radiotherapy may be necessary for patients with T3 tumors to increase local control with ISR.

While locoregional recurrence rates following APR were as high as 21% in the reports by Enker et al. [30] and Hohenberger et al. [19], the overall 5-year local recurrence rate in our own patient population was 15.7% after APR. The local recurrence rate was similar in the ISR group and the control APR group, although there was no difference in

the distribution of clinical and pathologic T stage between these two groups. On the basis of these data, ISR does not increase local recurrence in patients with very low rectal cancer, especially in patients with T1 and T2 tumors.

In the present series involving mostly T3 tumors, the 5-year disease-free survival rate was 69.1% in the ISR group and 63.3% in the APR group. The 5-year overall rate was 80% in the ISR group and 64% in the APR group. We previously reported a local recurrence rate of 10% and a 5-year disease-free survival rate of 65.1% after APR. There were no differences in survival between the two groups. Although no randomized study has compared these two surgical procedures, Gamagami et al. [34] compared the local recurrence rate and the survival rate in patients with distal-third rectal cancer treated by either CAA or APR in a prospective study. According to their report, the local recurrence rate was 7.9% after sphincter-saving resection and 12.9% after APR, and the 5-year actuarial survival rate was 78% after sphincter-saving resection and 74% after APR. These results suggest that the oncological benefits of ISR are the same as those of APR in patients with lower rectal cancer. It can be concluded that when ISR is feasible, the oncologic prognosis is not compromised.

There are some fears about the long-term functional outcomes after ISR when ISR is technically feasible and oncologically safe, because loss of the rectum and internal anal sphincter may induce anal dysfunction such as changes in stool frequency, urgency, fragmentation, soiling, and fecal incontinence. However, most patients who underwent ISR had acceptable anal function according to the Schissel series [17], our previous report [18], the other series of Yamada et al. [35], and other studies [13, 14, 16], although there are few reports on long-term anal function outcomes after ISR.

In conclusion, acceptable oncologic results were obtained with ISR in patients with very low rectal cancer located within 5 cm of the anal verge. The use of ISR can reduce the number of APRs. Compared with APR, local recurrence and survival are not compromised with ISR.

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特集　下部直腸癌の診断と治療—最近の進歩

I. 総論

下部直腸癌——大腸癌治療ガイドラインの解説*

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〔要旨〕下部直腸癌に対する治療は，術後患者のQOLに直結する．そのため，病巣に対する正確な診断，適切な治療法の選択が必要不可欠である．また，下部直腸癌に対する手術手技は大腸外科としてもっとも技量を要するものである．本稿では下部直腸癌の治療につき，大腸癌治療ガイドラインにおける指針を概説する．

はじめに

病変の主座が下部直腸の場合，その治療法は多岐にわたる．それは下部直腸の解剖学的特性による．すなわち，ほかの大腸癌と違い，下部直腸では病変の位置や進行度によって，患者は術後永久人工肛門による生活を余儀なくされる．ゆえに，病変の的確な診断の後，最善の治療法を選択する必要がある．下部直腸癌に対する治療は内視鏡治療に始まり，直腸局所切除，低位前方切除術，内肛門括約筋切除術，腹会陰式直腸切断術，骨盤内臓器全摘術までさまざまである．また，現在ではこれら治療の一部は，腹腔鏡補助下にも行われている．

キーワード：下部直腸癌，大腸癌治療ガイドライン

* Low rectal cancer ; interpretation of guideline for treatment of colorectal cancer

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本稿では，下部直腸癌の治療について，2005年に出版された大腸癌治療ガイドラインにおける記述を概説する．

I. 下部直腸癌に対する治療の変遷

直腸癌に対する系統的な切除術は，1908年にMilesが腹会陰式直腸切断術を発表したことに始まり[1]，その後の長きにわたり腹会陰式直腸切断術が直腸癌に対する標準的手術となった．一方で，肛門管や歯状線での吻合を目的として種々のpull-through術式が考案されたが[2,3]，これらは合併症の多さや排便機能のわるさより，治療としては不十分なものであった．1980年にKnightとGriffen[4]によってdouble stapling techniqueが紹介され，以降，現在につながる括約筋温存手術が確立された．一方，直腸癌術後の局所再発を抑える目的で，全直腸間膜切除(total mesorectal excision：TME)という概念が，1982年Healdら[5]によって提唱された．これは直腸と直腸間膜を直腸固有筋膜に包まれた状態で切除することを提唱したものであり，直腸間膜は肛門挙筋まで全切除するというものである．また，欧米では直腸