Surgery Today (2019) 49:275–285
https://doi.org/10.1007/s00595-018-1754-4

REVIEW ARTICLE

Long-term results of intersphincteric resection for low rectal cancer in Japan

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Received: 30 August 2018 / Accepted: 1 November 2018 / Published online: 2 January 2019

Abstract
Intersphincteric resection (ISR) is the ultimate sphincter-preserving procedure for low rectal cancer. A questionnaire about the standardization of ISR was given to 2125 patients who underwent curative ISR for low rectal cancer between 2005 and 2012 at 127 affiliated institutions of the Japanese Society for Cancer of the Colon and Rectum (JSCCR), and the results were compared with the results of a systematic review. The findings revealed that although mortality and morbidity were relatively low and the survival rate after ISR was good, the rates of local recurrence and postoperative fecal incontinence were relatively high. The radicality of ISR was compared with that of abdominoperineal resection and low anterior resection using the propensity score matching prognosis analysis of patients in the JSCCR nationwide registry. The local recurrence rate was significantly higher after ISR, and especially high in patients with T3 (invasion into the external anal sphincter) and T4 disease. These results provide evidence about the factors related to fecal incontinence after ISR. As measures for the standardization of ISR, it is important to reconfirm that ISR is not indicated for patients with cT3 and cT4 disease and those with poor preoperative defecatory function, based on the ISR indication criteria.

Keywords Low rectal cancer · Intersphincteric resection · Oncological outcome · Defecatory function

Introduction

Intersphincteric resection (ISR) with coloanal anastomosis has recently been adopted by many specialized institutions as the ultimate sphincter-preserving procedure for low rectal cancer, instead of abdominoperineal resection (APR) [1–6]. A systematic review of the literature indicates that the oncological outcomes after ISR for low rectal cancer are acceptable, but with diverse, often imperfect functional results [7]. However, ISR is a difficult procedure and there is insufficient evidence of its curability and postoperative defecatory function [8]. Evaluation of a standard surgical procedure for low rectal cancer should be based on satisfactory results in terms of morbidity, oncological safety, and low levels of postoperative defecatory dysfunction. ISR is widely recognized as an acceptable sphincter-preserving surgical procedure for low rectal cancer, provided that strict selection criteria are met. Thus, an evaluation has been undertaken by progressive institutions [1–7, 9–15]. This retrospective multi-institutional study was conducted by the Japanese Society for Cancer of the Colon and Rectum (JSCCR) to assess the long-term results after ISR in terms of postoperative complications, oncological safety, and defecatory function.

The surgical procedure for ISR consisted of mobilization of the rectum to the levator ani, with total mesorectal excision via the abdominal route, and resection of the internal anal sphincter via the anal route (Fig. 1). Total ISR is defined as the distal resection line of the internal anal sphincter at the intersphincteric groove; subtotal ISR is located between the dentate line and intersphincteric groove; and partial ISR is located at the dentate line (Fig. 1b) [14, 15]. After removal

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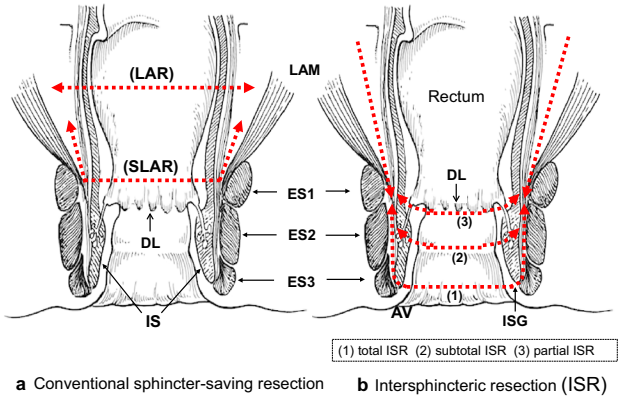

Fig. 1 Schematic representation of the transection lines for intersphincteric resection (ISR). The distal resection line of the internal anal sphincter (IS) was at the intersphincteric groove (ISG) (1) in total ISR, between the dentate line (DL) and the ISG (2) in subtotal ISR, and at the DL (3) in partial ISR. *AV* anal verge; *ES1* deep part of the external sphincter; *ES2* superficial part of the external sphincter; *ES3* subcutaneous part of the external sphincter; *LAM* levator ani muscle; *LAR* low anterior resection; *SLAR* super low anterior resection

of the specimen, the sigmoid or descending colon is pulled down and coloanal anastomosis is performed. Anastomosis is performed either with a straight colon, colonic J pouch, or coloplasty construction, using the transanal handsewn technique. A diverting ileostomy or colostomy is created in most patients, with closure planned 3–12 months later. In principle, the indication criteria for ISR were only patients with tumors that showed no evidence of extension into the external anal sphincter or the levator ani muscle, and those for whom a resection could be performed with a distal margin of at least 2 cm for T2 or T3 tumors, or 1 cm for T1 tumors. Patients with poorly differentiated adenocarcinoma diagnosed by biopsy or impaired fecal continence were excluded [14, 15]. A systematic review on ISR conducted by Martin concluded that the above indication criteria should be followed [7].

JSCCR questionnaire for the standardization of ISR

A questionnaire consisting of 35 items was given to the 397 JSCCR affiliated surgical institutions to investigate the indication criteria and long-term results of ISR. Consent to conduct questionnaire research was provided by the JSCCR ethical committee. A total of 175 JSCCR affiliated institutions responded to the questionnaire, but only 129 (73.7%) of these institutions perform ISR. However, 2 of these 129 institutions did not provide data; therefore, the analysis was based on 2125 patients who underwent curative ISR for stage I–III low rectal cancer between January 2005 and December 2012 at 127 JSCCR affiliated institutions. The Clavien–Dindo grade was used to analyze morbidity after ISR, anastomotic leakage, fistula (rectovaginal or anovaginal fistula), anastomotic stricture, and other sequela [16]. The overall survival, relapse-free survival, and local recurrence rates after surgery were calculated using the Kaplan–Meier method. Defecatory function was evaluated clinically through personal interviews to ascertain the frequency of bowel movements in a 24-h period, continence (assessed using the Wexner's continence score [17] and Kirwan's classification [18]), and evacuation disorders (constipation, dyschezia, need for enemas, and other) 12–24 months after ISR.

Total, subtotal, and partial ISR were performed on 402, 559, and 1164 patients, respectively. The selection of surgical procedures was based on the location of the tumor, its size, and the depth of invasion. Table 1 summarizes the patients' clinical characteristics. Patients who underwent partial ISR were significantly older and had a lower TNM stage than those who underwent total ISR. Subtotal ISR and partial ISR were performed on significantly more male patients and on patients with higher tumor location and shallower tumor invasion than total ISR. Moreover, total ISR was performed on significantly more patients who underwent preoperative chemoradiotherapy (CRT), open surgery, reconstruction of the rectum using a straight colon, and colostomy as a diverting stoma than subtotal ISR and partial ISR. In this study, laparoscopic ISR and robotic ISR were performed on 725 patients (34.1%) and 22 patients (1.0%), respectively. Laparoscopic and robotic ISR have been reported to be safe and efficient for selected patients and associated with less postoperative pain and disability, shorter hospitalization, and better cosmesis [19–23]. 21 patients had a pT4 tumor (8 underwent total ISR, 6 underwent subtotal ISR, and 7 underwent partial ISR), 2 had a pT4a tumor penetrating the serosa of the upper rectum, and 19 had a pT4b tumor invading into the vagina ($n=11$), prostate ($n=5$), sacral periosteum ($n=2$), and seminal vesicle ($n=1$).

Postoperative complications

Data on postoperative complications were available for 2117 of the 2125 patients. Table 2 shows the mortality, morbidity, and main postoperative complications, namely, anastomotic leakage and fistula as early complications, and anastomotic stricture as late complications. These results were compared with those of the systematic review conducted by Martin [7]. There were no differences in mortality, morbidity, and most postoperative complications among the different types of ISR. However, anastomotic stricture occurred in significantly more patients who underwent partial ISR than in those who underwent total ISR, consistent with the findings of previous studies [9, 12]. The mortality rate in this study

Table 1 Clinical characteristics of 2125 patients who underwent curative intersphincteric resection for low rectal cancer

	Total ISR ($n=402$)	Subtotal ISR ($n=559$)	Partial ISR ($n=1164$)
Age (years)[a]	59.5 (12.1)	60.6 (10.6)	61.4 (10.6)
P value[b]		0.274	0.006
Sex ratio (M:F)	239:163	380:179	822:342
P value[b]		0.006	< 0.001
Histology (well:moderately:poorly)[c]	167:221:14	234:305:20	525:603:36
P value[b]		0.456	0.991
Tumor localization (mm) [d]	5.4 (7.1)	14.4 (10.0)	20.0 (12.8)
P value[b]		< 0.001	< 0.001
pT (T1:T2:T3:T4)	64:150:180:8	140:184:229:6	321:364:472:7
P value [b]		0.006	< 0.001
pN (N0:N1:N2)	250:94:58	370:126:63	773:256:135
P value[b]		0.286	0.221
TNM stage (stage I:stage II:stage III)	157:93:152	257:113:189	543:230:391
P value[b]		0.101	0.030
Preoperative CRT (yes:no)	103:299	96:463	157:1007
P value[b]		0.001	< 0.001
Operative approach (open:laparoscopic:robotic)	295:103:4	369:182:8	714:440:10
P value[b]		0.050	< 0.001
Reconstruction of rectum (straight:J-pouch:other)	336:49:17	426:103:30	941:129:94
P value[b]		0.019	0.033
Diverting stoma (ileostomy:colostomy:no)	294:77:31	459:58:42	980:112:72
P value[b]		< 0.001	< 0.001

ISR intersphincteric resection, *TNM* tumor node metastasis, *CRT* chemoradiotherapy

[a]Values are expressed as the mean (s.d.)

[b]Versus total ISR, Tukey–Kramer's test or Pearson's Chi square test

[c]Differentiation of adenocarcinoma

[d]Mean (s.d.) distance between the distal margin of the tumor and the dentate line

was 0.1%, which is lower than that in the systematic review, but the incidence of postoperative complications tended to be a little higher. The postoperative complications of ISR in this questionnaire study indicated a relatively safe outcome.

Oncological results

The median follow-up period was 58 (range 1–129) months. The 5-year overall survival rate according to the TNM stage was 92.8% for stage I, 89.3% for stage II, and 73.6% for stage III (Fig. 2a). The 5-year relapse-free survival rate was 87.5% for stage I, 73.0% for stage II, and 56.4% for stage III. Pelvic local recurrence was found in 223 patients (11.5%), lung metastasis in 203 patients (10.3%), liver metastasis in 105 patients (5.2%), and other in 97 patients (5.0%) (Fig. 2b). On the other hand, the 5-year overall survival rate according to the TNM stage of 2449 patients with low rectal cancer between January 2000 and December 2004 in the JSCCR nationwide registry was 88.3% for stage I, 81.7% for stage II, 70.0% for stage IIIa, and 51.4% for stage IIIb [8]. The 5-year cumulative local recurrence rate after ISR was 11.5% (Fig. 3a): 5.7% for stage I, 14.0% for stage II, and 17.9% for stage III (Fig. 3b). Moreover, the 5-year cumulative local recurrence rate according to the pT category was 4.2% for pT1, 8.5% for pT2, 18.1% for pT3, and 36.0% for pT4. The 5-year cumulative local recurrence rate of 1647 patients with rectal cancer (Ra, Rb, P) between 1991 and 1996 in the JSCCR project research was 8.8% [8]. From those observations, the survival rate after ISR was relatively good, but the local recurrence rate was high in this questionnaire study.

Functional results

Diverting stoma closure was not performed in 239 patients because of recurrence or other diseases. Data on postoperative defecatory function was not available for 896 patients. Table 3 shows the results of defecatory function 12 to 24 months after ISR in 990 patients who underwent stoma closure and these results were compared with those of the systematic review conducted by Martin [7]. However, of the 14 papers selected for the systematic review, only 8 reported on postoperative defecatory function. There was no significant

Table 2 Postoperative complications in 2117 patients who underwent intersphincteric resection

	Total ISR [n = 399]	Subtotal ISR [n = 559]	Partial ISR [n = 1159]	[n= 2117]	Systematic review [d] [n=1289]
Mortality	2 (0.5 %)	0	0	2 (0.1 %)	0.8 % (0-6 %)
Morbidity	141 (35.3 %)	208 (37.2 %)	427 (36.8 %)	776 (36.7 %)	25.8 % (8-65 %)
Anastomotic leak [Grade Ⅱ:ⅢaⅢb:Ⅳa, b] [a]	32 (8.0 %) [8 : 18 : 6 : 0]	55 (9.8 %) [28 : 13 : 14 : 0]	115 (9.9 %) [50 : 44 : 21 : 0]	202 (9.5 %)	9.1 % (0.9-48 %)
Fistula [b] [Grade Ⅱ:ⅢaⅢb:Ⅳa, b] [a]	9 (1.4 %) [3 : 2 : 4 : 0]	8 (1.4 %) [1 : 3 : 3 : 1]	20 (1.7 %) [6 : 5 : 9 : 0]	37 (1.7 %)	2.2 % (0-19 %)
Anastomotic stricture [Grade Ⅱ:ⅢaⅢb:Ⅳa, b] [a] *P* value [c]	14 (3.5 %) [7 : 6 : 1 : 0]	26 (4.7 %) [9 : 14 : 3 : 0] 0.384	71 (6.1 %) [32 : 31 : 7 : 0] 0.047	111 (5.2 %)	2.7 % (0-16 %)
Other [Grade Ⅱ:ⅢaⅢb:Ⅳa, b] [a]	95 (23.8 %) [58 : 26 : 8 : 3]	137 (24.5 %) [100 : 30 : 5 : 2]	269 (23.2 %) [158 : 76 : 29 : 6]		

Values in parentheses are percentages

ISR intersphincteric resection

[a]Clavien–Dindo grade

[b]Rectovaginal and anovaginal fistula

[c]Versus total ISR, Tukey–Kramer's test

[d]Systematic review [7]

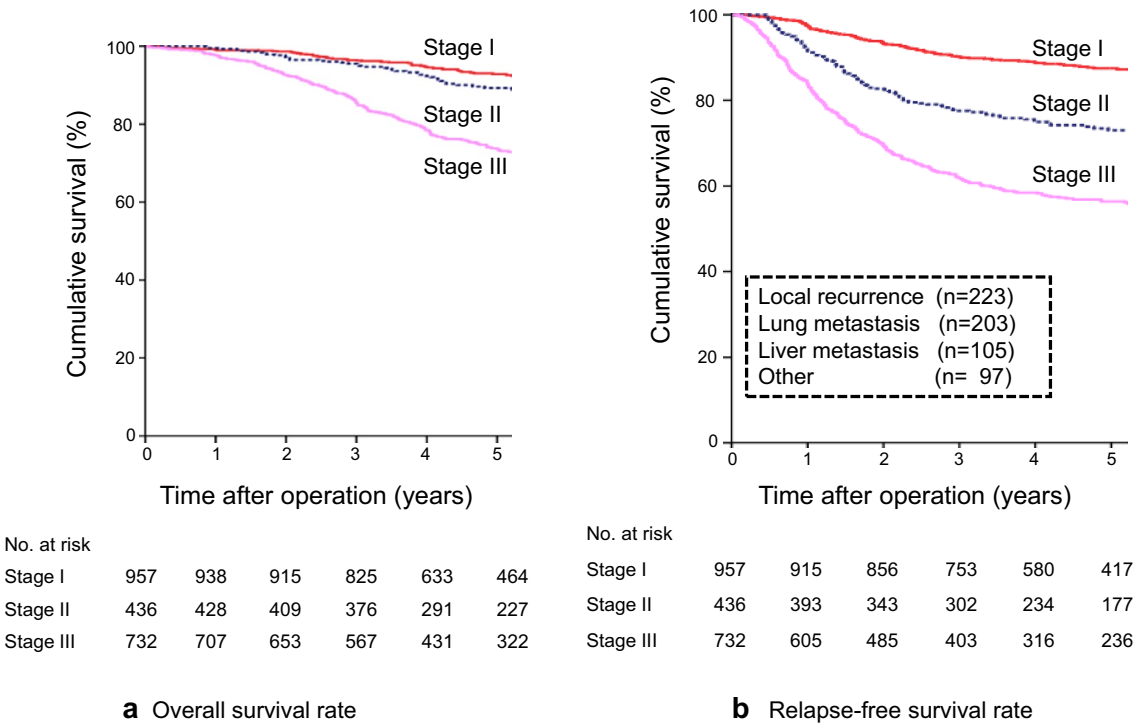

Fig. 2 Overall survival rates and relapse-free survival rates according to TNM stage for 2125 patients who underwent ISR

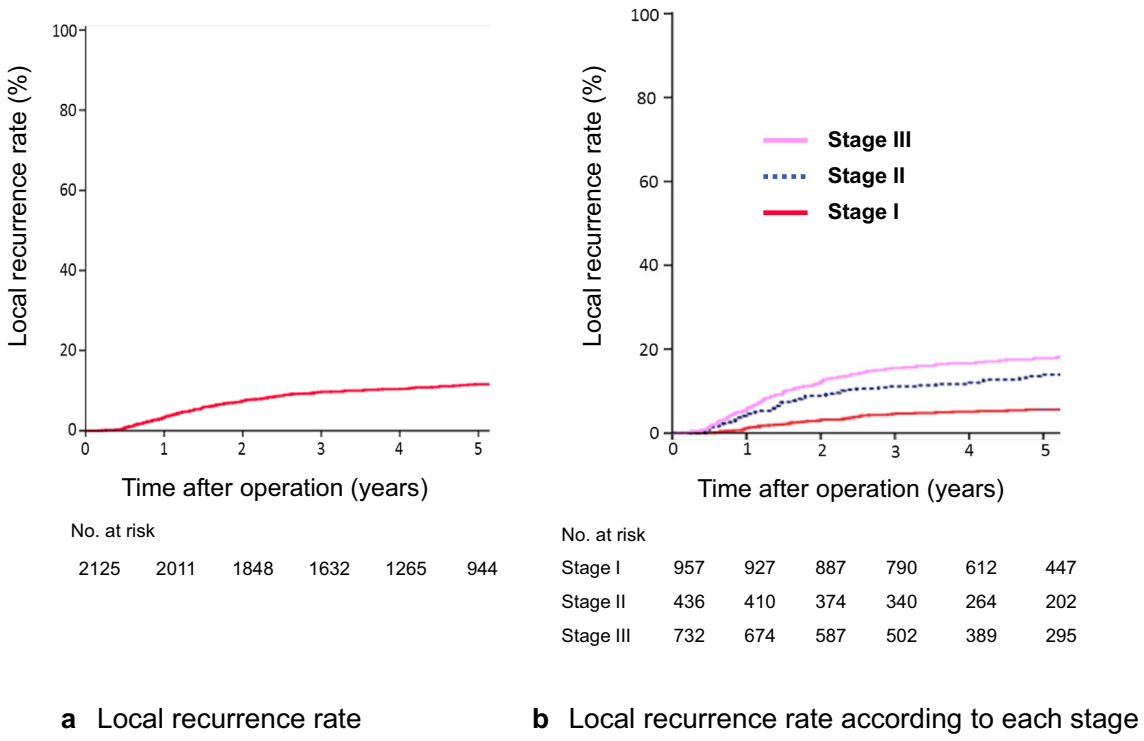

Fig. 3 Cumulative local recurrence rate according to TNM stage for 2125 patients who underwent ISR

Table 3 Defecatory function evaluated 12–24 months after intersphincteric resection in 990 patients who underwent stoma closure

		Total ISR [n = 170]	Subtotal ISR [n = 254]	Partial ISR [n = 566]	[n= 990]		Systematic review [d] [n= 727]
Bowel frequency (per day) [a]		5.4 ± 4.3	4.9 ± 3.8	5.0 ± 3.9	5.0 ± 4.0		2.7 ± 0.6
Continence							
Kirwan's [b]	Grade 1	66	80	234	380		
	Grade 2	39	55	143	237		
	Grade 3	45	88	144	277		
	Grade 4	16	19	41	76	37.7 %	29.1 %
	Grade 5	4	12	4	20		(11-63 %)
Wexner's score [a]							
Continent (Kirwan's Grade 1, 2)		4.2 (3.7)	4.5 (4.3)	4.6 (4.1)			
Incontinent (Kirwan's Grade 3, 4, 5)		11.6 (4.6)	12.1 (3.9)	11.2 (4.2)			
Evacuation disorder [c]							
Constipation		14 (8.2 %)	20 (7.9 %)	56 (9.9 %)			
Dyschezia		5 (2.9 %)	16 (6.3 %)	28 (4.9 %)			
Used enemas		0 (0 %)	1 (0.4 %)	1 (0.2 %)			
Other		18 (10.6 %)	24 (9.4 %)	30 (5.3 %)			

ISR intersphincteric resection

[a]Values are expressed as means with s.d.

[b]Kirwan's classification [18]

[c]Values in parentheses are percentages

[d]Systematic review [7]

difference in bowel frequency among the groups (5.0 ± 4.0). Defecatory incontinence, classified as Kirwan's grades 3, 4, and 5, was identified in 373 patients (37.7%). Evacuation disorders such as constipation, dyschezia, need for enemas, and other symptoms were reported by some patients in each group, but with no significant difference among the groups. Based on these findings, bowel frequency and the incidence of fecal incontinence were higher than those in the systematic review. The high defecatory dysfunction rate after ISR is a problem needing resolution.

Problems and measures for radicality in ISR

The JSCCR questionnaire responses identified a high local recurrence rate, which indicates a problem with the radicality of ISR. Therefore, we compared radicality among ISR, APR and low anterior resection (LAR), and examined the appropriate indication criteria for ISR based on the results of the comparison. A propensity score matching analysis of 2125 patients who underwent ISR, as indicated in the JSCCR questionnaire, was conducted to compare the 1462 patients who underwent APR and the 3917 patients who underwent LAR (including super low anterior resection) for stage I–III low rectal or anal canal adenocarcinoma, between January 2000 and December 2006 (data taken from the JSCCR nationwide registry).

Age, sex, histology, pT, and pN were used as the background factors. The propensity score was calculated using the logistic regression model and the caliper was 0.03. Propensity score one-to-one matching was done by identifying matched pairs of ISR and APR or LAR groups using calipers set at a standard deviation of 0.2 from the propensity score. Patients with an unknown prognosis were excluded from the groups after matching and not included in Tables 4 and 5. Permission to use the data in the JSCCR nationwide registry was granted by the JSCCR.

Prognostic score matching analysis was based on the background factors of 2125 patients with ISR and 1462 patients with APR, and an analysis of their prognoses (Table 4). Although the cumulative survival rate was significantly better after ISR than after APR, the postoperative

Table 4 Propensity score matching prognosis analysis of patients who underwent intersphincteric resection vs. those who underwent abdominoperineal resection

	Before propensity score matching					After propensity score matching				
	ISR		APR		Log rank	ISR		APR		Log rank
	n	%	*n*	%	*P* value	*n*	%	*n*	%	*P* value
Survival rate	2125	85.4	1462	74.8	< 0.001	1174	82.0	1174	75.7	< 0.001
Relapse-free survival rate	2125	70.5	1414	60.6	< 0.001	1174	63.3	1137	61.5	0.237
Recurrence rate	2125	26.3	1414	29.1	0.074	1174	33.3	1137	28.4	0.017
Local recurrence rate	2125	11.5	1462	7.5	< 0.001	1174	15.0	1174	7.9	< 0.001
Liver recurrence rate	2125	5.2	1445	8.7	< 0.001	1174	6.5	1161	8.2	0.148
Lung recurrence rate	2125	10.3	1455	8.6	0.116	1174	13.0	1168	8.3	0.001
Hematogenous recurrence rate	2125	14.4	1438	16.1	0.152	1174	18.1	1155	15.4	0.097
Other recurrence rate	2125	5.0	1456	7.5	0.013	1174	6.3	1170	7.3	0.324

ISR intersphincteric resection, *APR* abdominoperineal resection

Table 5 Propensity score matching prognosis analysis of patients who underwent intersphincteric resection vs. those who underwent low anterior resection

	Before propensity score matching					After propensity score matching				
	ISR		LAR		Log rank	ISR		LAR		Log rank
	n	%	*n*	%	*P* value	*n*	%	*n*	%	*P* value
Survival rate	2125	85.4	3910	86.1	0.975	2091	85.3	2088	87.8	0.059
Relapse-free survival rate	2125	70.5	3846	74.4	0.015	2091	70.4	2063	76.1	0.001
Recurrence rate	2125	26.3	3846	19.9	< 0.001	2091	26.5	2063	19.0	< 0.001
Local recurrence rate	2125	11.5	3917	4.1	< 0.001	2091	11.7	2091	3.5	< 0.001
Liver recurrence rate	2125	5.2	3879	6.1	0.202	2091	5.2	2073	5.5	0.662
Lung recurrence rate	2125	10.3	3888	6.7	< 0.001	2091	10.4	2076	6.2	< 0.001
Hematogenous recurrence rate	2125	14.4	3865	12.1	0.015	2091	14.5	2066	11.0	0.002
Other recurrence rate	2125	5.0	3898	3.1	< 0.001	2091	5.1	2084	3.5	0.006

ISR intersphincteric resection, *LAR* low anterior resection

recurrence rate, especially the local recurrence rate, was significantly higher in ISR. A prognostic score matching analysis was also performed on the background factors of 2125 patients who underwent ISR and 3917 patients who underwent LAR (Table 5). Although there was no significant difference in the cumulative survival rate between ISR and LAR, the cumulative relapse-free survival rate was significantly better for LAR than for ISR, but the postoperative recurrence rate, especially the local recurrence rate, was significantly higher after ISR.

The high rate of local recurrence taken from the ISR questionnaire results is an important problem of the radicality of ISR. Table 6 shows the results of the multivariate analysis on the factors influencing the local recurrence rate. The pT factor, pN factor, and the level of ISR were significant factors, and the local recurrence rate was particularly high in patients with pT3 (invasion into the external anal sphincter) and pT4 disease. These results reinforce the importance of reconfirming that patients with cT3 and cT4 disease are outside the indications for ISR based on the ISR indication criteria.

Problems and evaluation of defecatory function after ISR

We investigated the defecatory function after ISR, by evaluating and comparing the results of postoperative defecatory function of ISR at Takano Hospital.

Postoperative defecatory function of ISR at Takano Hospital

Regarding the radicality of ISR at Takano Hospital, the cumulative survival rate and relapse-free survival rate according to the TNM stage (JSCCR) were 93.0% and 92.1% for stage I, 100% and 84.2% for stage II, 86.7% and 87.7% for stage IIIa, and 66.5% and 66.3% for stage IIIb, and the cumulative 5-year local recurrence rate for all patients was 4.4% [24]. Moreover, at Takano Hospital, partial external sphincter resection (ESR), categorized as combined resection of the external sphincter muscle and puborectalis muscle partially surrounding the tumor, is performed as intersphincteric resection with ESR [24, 25]. We studied the postoperative defecatory function of 178 patients who underwent curative resection with ISR or partial ESR for lower rectal cancer at Takano Hospital between April 2001 and December 2013 [25]. Diverting stoma closure could not be performed in ten patients because of cancer recurrence in four patients, other diseases in four patients, and postoperative defecatory dysfunction in two patients. Daily bowel frequency and continence as defecatory function was evaluated 12 months after ISR in 168 patients who underwent diverting stoma closure (Table 7). There was no significant difference in bowel frequency according to the type of ISR performed. Although there were no patients with postoperative fecal incontinence of Kirwan's grade 5, the rate of fecal incontinence of Kirwan's grades 3 and 4 was relatively high for both ISR (33.8%) and partial ESR (52.9%). At Takano

Table 6 Factors influencing local recurrence rate after intersphincteric resection (JSCCR questionnaire)

	Univariate analysis	Multivariate analysis	Hazard ratio
	P value	*P* value	
Age	0.051		
Sex ratio (M:F)	0.808		
Histology (well:moderately:poorly)	< 0.001	0.154	
pT (T1:T2:T3:T4)	< 0.001	< 0.001	1.873
T1 vs. T2		0.078	
T1 vs. T3		< 0.001	3.107
T1 vs. T4		< 0.001	7.323
pN (N0:N1:N2)	< 0.001	< 0.001	1.515
N0 vs. N1		0.016	1.557
N0 vs. N2		< 0.001	2.229
Preoperative CRT (yes:no)	0.823		
Level of ISR (partial ISR: subtotal ISR, total ISR)	0.010	0.038	1.317
Operative approach (open:laparoscopic, robotic)	0.005	0.589	
Postoperative chemotherapy (yes:no)	< 0.001	0.232	
Postoperative complication (yes:no)	0.414		
Anastomotic leakage (yes:no)	0.934		

ISR intersphincteric resection, *JSCCR* Japanese Society for Cancer of the Colon and Rectum, *CRT* chemoradiotherapy

Table 7 Defecatory function evaluated 12 months after intersphincteric resection in 168 patients who underwent diverting stoma closure

	Total ISR (n=18)	Subtotal ISR (n=43)	Partial ISR (n=90)	ISR (n=151)	Partial ESR (n=17)
Bowel frequency (per day)	4.0 ± 2.3	3.7 ± 1.9	3.9 ± 2.2	3.9 ± 2.1	4.0 ± 1.9
P value [a]	*0.129*	*0.163*			*0.129*
Continence					
Kirwan's [b] Grade 1	2	5	20	27	3
Grade 2	8	22	43	73	5
Grade 3	5	14	23	42	8
Grade 4	3 (44.4 %)	2 (37.2 %)	4 (30.0 %)	9 (33.8 %)	1 (52.9 %)
Grade 5	0	0	0	0	0
Wexner's score					
Continent patients (Kirwan's Grade 1, 2)	3.5 ± 1.5	4.8 ± 3.1	4.2 ± 3.2		3.6 ± 2.8
Incontinent patients (Kirwan's Grade 3, 4)	12.4 ± 2.7	12.1 ± 2.0	12.1 ± 2.8		14.3 ± 2.4

ISR intersphincteric resection, *ESR* external sphincter resection

[a]Versus partial ISR, Tukey–Kramer's test

[b]Kirwan's classification [18]

Hospital, anorectal manometry and anorectal sensation inspection were done for all patients undergoing ISR and partial ESR, before surgery and then 3, 6, and 12 months postoperatively, and defecatory function was evaluated 1 year after surgery. As preoperative CRT involving irradiation of the anal sphincter for patients with very low rectal cancers was reported to have a deleterious effect on anorectal function [26–28], preoperative CRT is no longer used for low rectal cancer. Instead, lateral lymph node dissection is performed for patients with cT2–3 or stage III tumors at Takano Hospital.

Prospects of fecal incontinence after ISR

The prospects of defecatory dysfunction after ISR, especially fecal incontinence, are very important. Table 8 shows the results of multivariate analysis of the factors related to postoperative fecal incontinence after ISR, as indicated in the JSCCR questionnaire responses, and the study of ISR at Takano Hospital. According to the JSCCR questionnaire, age, sex, preoperative CRT, and operative approach were significant factors. On the other hand, in the series at Takano Hospital, the level of ISR and reconstruction of the rectum were significant factors. In fact, the fecal incontinence rates of patients who underwent total ISR or partial ESR were significantly higher than those of patients who underwent partial ISR or subtotal ISR, and the incontinence rate of patients with straight reconstruction was significantly higher than that of those with a colonic J-pouch or coloplasty reconstruction. These results serve as a reference for the indication criteria of ISR and should be treated as an important consideration when selecting the most appropriate reconstruction type.

Treatment for fecal incontinence after ISR at Takano Hospital

The treatment strategy for fecal incontinence after ISR at Takano Hospital is shown in Fig. 4a. Fecal incontinence was assessed as follows:

The Wexner's score [17] and LARS score [29] are used to represent the symptom scores, Kirwan's classification [18] is used to represent the symptomatic grade, and FIQL [30] is used to represent the fecal incontinence specific quality of life. Anorectal manometry, anorectal sensation inspection, and electromyography are also performed, and a treatment policy is decided [14, 25]. First, pharmacotherapy or biofeedback therapy [31] is performed as conservative therapy, and percutaneous tibial nerve stimulation (PTNS) or transanal electrical stimulation (TaES), as electrical stimulation therapy, is performed according to the individual patient [32, 33]. If these treatments are ineffective or insufficient, sacral neuromodulation (SNM) as a surgical treatment is considered [34].

We treated 16 patients with fecal incontinence after ISR at Takano Hospital between December 2016 and December 2017 (Fig. 4b). Biofeedback therapy was initiated and continued for all patients after ISR. Pharmacotherapy resulted in significant improvements in fecal incontinence frequency and in the Wexner's score. PTNS and TaES also showed significant improvements in the Wexner's score. Significant improvements in the FIQL and LARS scores were confirmed using multimodality treatment. SNM as surgical treatment

Table 8 Factors influencing postoperative incontinence (Kirwan's grades 3, 4, or 5)

	Univariate analysis *P* value	Multivariate analysis *P* value	Odds ratio
Analysis of ISR patients in the JSCCR questionnaire			
Age	0.004	0.004	1.019
Sex ratio (M:F)	0.033	0.047	1.337
Tumor localization (mm) [a]	0.263		
Histology (well:moderately:poorly)	0.922		
TNM stage (I:II:III)	0.843		
Preoperative CRT (yes:no)	0.022	0.030	0.655
Level of ISR (partial ISR:subtotal ISR, total ISR)	0.042	0.107	
Operative approach (open:laparoscopic, robotic)	0.002	0.012	0.693
Reconstruction of rectum (J-pouch:coloplasty:straight)	0.680		
Anastomotic leakage (yes:no)	0.532		
Analysis of ISR patients at Takano Hospital			
Age	0.354		
Sex ratio (M:F)	0.431		
Histology (well:moderately:poorly)	0.279		
TNM stage (I:II: III)	0.545		
Level of ISR (partial ISR, subtotal ISR:total ISR, partial ESR)	0.080	0.025	2.603
Reconstruction of rectum (J-pouch:coloplasty:straight)	0.187	0.022	1.548

ISR intersphincteric resection, *JSCCR* Japanese Society for Cancer of the Colon and Rectum

[a]Distance between the distal margin of the tumor and the dentate line

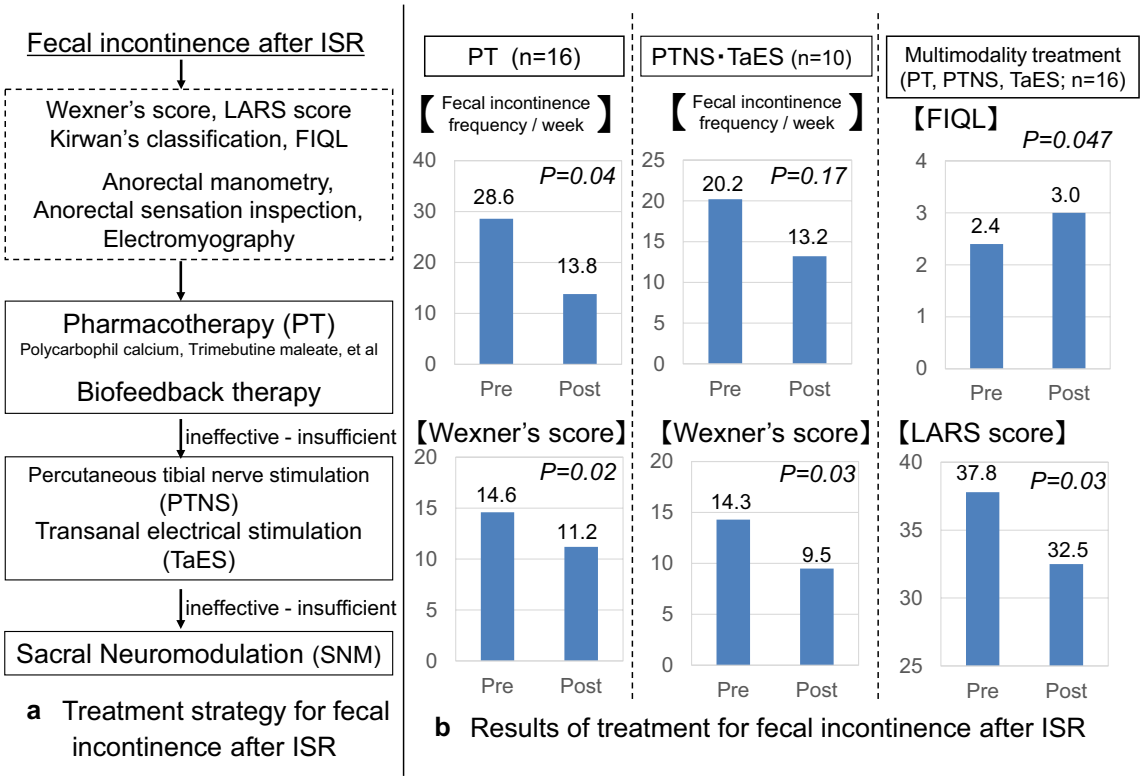

Fig. 4 Treatment for fecal incontinence after ISR at Takano Hospital. *LARS* low anterior resection syndrome; *FIQL* fecal incontinence quality of life scale

for fecal incontinence after ISR was also introduced and will become a policy.

Conclusion

An analysis of responses to the JSCCR questionnaire, designed to evaluate ISR as an acceptable treatment for low rectal cancer in terms of postoperative complications, oncological safety, and postoperative defecatory function, revealed that local recurrence and postoperative defecatory dysfunction were problems to be resolved in the standardization of ISR as a treatment for low rectal cancer. To standardize ISR for low rectal cancer, it is important first to adhere strictly to the indication criteria, and second, to confirm the indication by conducting a preoperative evaluation of defecatory function and then deciding on concrete treatment methods, such as the selection of the best type of reconstruction. Through these strategies, ISR for low rectal cancer will be standardized. It is also expected that advanced surgical procedures such as partial ESR will be standardized as the ultimate sphincter-preserving procedure for low rectal cancer in the future.

Compliance with ethical standards

Conflict of interest Kazutaka Yamada and his co-authors have no conflicts of interest to declare.

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