Title: Comparison of oncological outcomes between low anterior resection and abdominoperineal resection for rectal cancer: a retrospective cohort study using a multicenter database in Japan

Authors: Hideki Nagano[1], Ryuji Kajitani[1], Ryo Ohno[1], Taro Munechika[1], Yoshiko Matsumoto[1], Hiroyuki Takahashi[1], Naoya Aisu[1], Daibo Kojima[1], Gumpei Yoshimatsu[1], Suguru Hasegawa[1], Hirotoshi Kobayashi[2], Kenichi Sugihara[3]

Affiliation:

[1] Department of Gastroenterological Surgery, Fukuoka University Hospital
Address: 7-45-1 Nanakuma Jonan-ku, Fukuoka, 814-0180, Japan

[2] Department of surgery, Teikyo University Mizonokuchi Hospital
Address: 5-1-1 Futago Takatsu-ku, Kawasaki, Kanagawa, 213-8504, Japan

[3] Tokyo Medical and Dental University
Address: 1-5-45 Yushima Bunkyo-ku, Tokyo, 113-8510, Japan

Corresponding author: Hideki Nagano, M.D.
Department of Gastroenterological Surgery, Fukuoka University Hospital
Address: 7-45-1 Nanakuma Jonan-ku, Fukuoka, 814-0180, Japan
Tel: +81-92-801-1011, Fax: +81-92-801-8200, email: hidekinagano@fukuoka-u.ac.jp

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Abstract

Background: It remains controversial whether the abdominoperineal resection (APR) procedure itself has a negative impact on prognosis compared with sphincter-saving surgery (SSS). The purpose of this study was to investigate whether the operation type affects the prognostic outcome in rectal cancer using a multicenter database in Japan.

Methods: The study involved 2,533 patients who underwent APR or SSS and were registered in the Japanese Society for Cancer of the Colon and Rectum database, which includes data from 74 centers, between 2003 and 2007. The primary endpoints were overall survival (OS) and relapse-free survival (RFS). The secondary endpoints were local recurrence rate (LRR) and pathological radial margin (pRM) status.

Results: Multivariate analysis identified pathological tumor depth, lymph node status, and pRM status to be associated with oncological outcomes (OS, RFS, LRR). Although the oncological outcomes were worse after APR than after SSS in univariate analysis, there was no significant difference in OS (hazard ratio 1.08; 95% confidence interval [CI] 0.85–1.37) or RFS (hazard ratio 1.06; 95% CI 0.87–1.30) between APR and SSS. There was also no significant difference in LRR (odds ratio 1.11, 95% CI 0.70–1.77). Multivariate analysis showed that operation type was associated with positive pRM (odds ratio 3.13, 95% CI 0.18–0.56).

Conclusions: There was no significant difference in oncological outcomes between APR and SSS for rectal cancer. The risk of positive pRM was higher for APR and performing radial margin-negative surgery is an important factor in improving the oncological outcomes of APR.

Keywords: Rectal cancer; Abdominoperineal resection; Low anterior resection; Circumferential radial margin; Oncological outcomes

Abbreviations

APR: abdominoperineal resection

SSS: sphincter-saving surgery

OS: overall survival

RFS: relapse-free survival

LRR: local recurrence rate

pRM: pathological radial margin

CRM: circumferential resection margin

JSCCR: Japanese Society for Cancer of the Colon and Rectum

ELAPE: extralevator abdominoperineal excision

MRI: magnetic resonance imaging

Introduction

Abdominoperineal resection (APR) for rectal cancer was first reported by Miles in 1908 [1]. Since the advent of anus-preserving surgery and mechanical anastomosis in the 1990s, anterior resection has been increasingly performed in about 70% of operations for rectal cancer [2-8]. Furthermore, total mesorectal excision, first described by Heald et al [9], dramatically improved the oncological outcomes of rectal cancer, and it has also been reported that the local recurrence rate (LRR) is higher in cases with a positive circumferential resection margin (CRM; <1 mm) than in cases with a negative CRM [10-13]. Therefore, total mesorectal excision and the negative CRM are recognized as key procedures in rectal cancer surgery.

A number of studies have compared oncological outcomes between APR and low anterior resection (LAR) for rectal cancer. Several reports based on large datasets, mainly from the US and Europe, have shown that the oncological outcomes are worse after APR than after LAR in terms of overall survival (OS) and LRR [14-18]. However, whether APR itself adversely affect prognosis of rectal cancer is still controversial because of potential bias in treatment selection. APR are likely to be selectively performed to elderly patients, lower rectal cancer, or locally advanced cancer, which may affect the oncological outcome [19, 20]. Moreover, APR might also be associated with poor surgical outcomes, such as intraoperative perforation and positive CRM, due to the surgical difficulties resulting from complex anatomy around the perineum and anus [16, 21, 22]. Therefore, it is necessary to examine whether the procedure itself affects oncological outcomes after full statistical adjustment of patient factors and oncological factors. Previous studies have not sufficiently adjusted for these factors and may not reflect the true treatment-related outcome of APR. The purpose of this study was to investigate whether the APR or LAR procedures themselves affect oncological outcome in rectal cancer after adjusting for patient and oncological factors. The primary endpoints were OS and relapse-free survival (RFS), which were compared between APR and sphincter-saving surgery (SSS), namely high and low anterior resection (HAR and LAR). The secondary endpoints were LRR and pathological radial margin (pRM) status.

Patients and Methods

This retrospective study analyzed data from the Japanese Society for Cancer of the Colon and Rectum (JSCCR) database between 2003 and 2007. The database holds information on patients from 74 institutions which are major high-volume centers in Japan.

Eligibility criteria were as follows: 1) pathologically diagnosed adenocarcinoma with localization of the main tumor in the middle or lower rectum (Ra and Rb, respectively, according to the Japanese Classification of Colorectal Carcinoma [23]), and 2) undergoing macroscopic curative surgery by APR or SSS. The following exclusion criteria were applied: 1) main tumor located in the rectosigmoid region or anal canal, 2) distant metastasis, 3) surgery that included a Hartmann procedure or intersphincteric resection, 4) preoperative treatment, such as chemoradiation or chemotherapy, and 5) intramucosal cancer or cancer invading other organs.

Statistical covariates included both patient factors, such as age and sex, and tumor factors, such as tumor location, size, and circumference, pT, pN, histopathological type, vascular invasion, lymphatic invasion, and pRM status. Oncological factors were mainly determined based on findings in fresh or pathological specimens. Tumor location and pRM status were defined according to the Japanese Classification of Colorectal Carcinoma [23]. Positive pRM was diagnosed when tumor cells were exposed at the dissection margin [11] [24, 25].

Statistical Analysis

Data of patients without missing outcomes or covariates were analyzed. In descriptive statistics, categorical variables were described as the frequency and proportion. Continuous variables were described as the median and interquartile range. Cumulative survival was analyzed using the Kaplan-Meier method and compared between groups using the log-rank test. The cut-off was defined as patient death or termination of follow-up. All covariates, namely, age, sex, tumor location, tumor wall location, pT, pN, histopathological type, lymphatic invasion, vascular invasion, pRM status, and operation type were included in the final analysis. The reference date was the day of surgery. For comparisons between groups, a p-value <0.05 was considered to be statistically significant. pT, pN, lymphatic invasion, vascular invasion, and other pathological examinations were assessed in accordance with the Japanese Classification of Colorectal Carcinoma [23]. Multivariate analysis was performed by Cox proportional hazards regression or logistic regression analysis, and variables with a p-value of <0.05 in univariate analysis were included in multivariate analysis. All statistical analyses were performed using JMP software (version 15; SAS Institute, Tokyo, Japan).

The study was approved by the Ethics Committee of Fukuoka University Hospital and the

Japanese Society for Cancer of the Colon and Rectum (JSCCR). The need for informed consent was waived in view of the retrospective observational nature of the research and the anonymity of the data in the database. There is no conflict of interest in this study.

Results

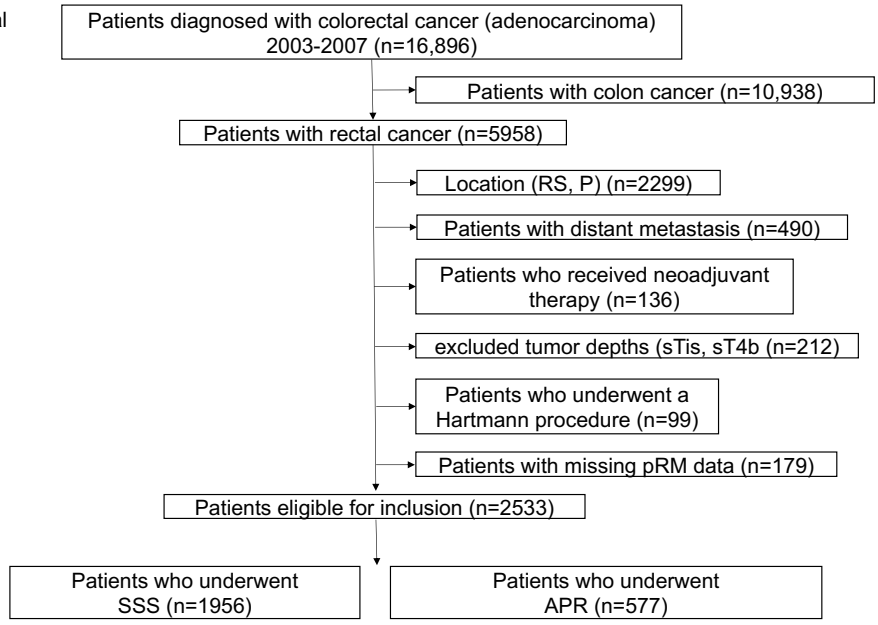
Patient and tumor characteristics

In total, 2,533 patients were enrolled into the study (Supplemental Figure). The median observation period for surviving patients was 2223 days. Background patient characteristics were shown according to operation type in Table 1. A total of 1956 patients (77.2%) underwent SSS and 577 (22.8%), underwent APR. Although there was no significant difference in mean age between the APR group (66.4 [24–94] years) and the SSS group (66.3 years [23–92] years), the proportion of patients over 60 years of age was significantly higher in the APR group (73.8% [n=426] vs 64.2% [n=1257]; p<0.001, chi-square test).

There was no significant difference in wall location between the two groups. In terms of tumor depth, the proportion of patients with advanced cancer was higher in the APR group than in the SSS group. There was no significant difference in pN, histopathological type, or lymphovascular invasion between the groups.

The pRM-positive rate was 2.6% (66/2533) overall, 1.64% (32/1956) in the SSS group, and 5.89% (34/577) in the APR group, and was significantly higher in the APR group (p<0.001).

Supplemental Figure .



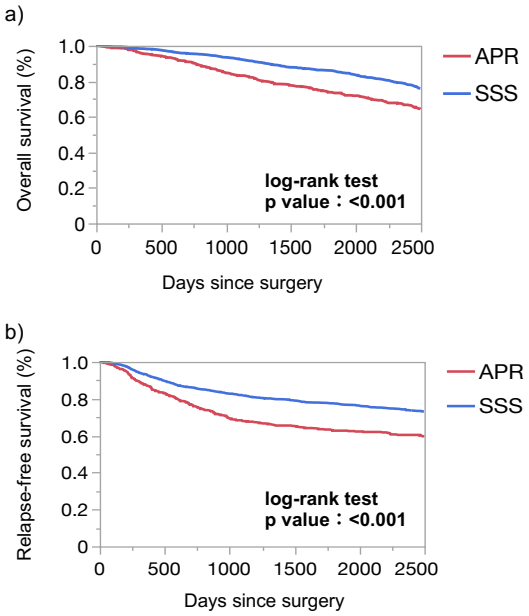
Survival outcomes

The Kaplan-Meier curves for OS after APR and SSS are shown in Figure 1a. OS was significantly worse after APR than after SSS (p<0.001, log-rank test). The results of univariate and multivariate Cox regression analysis for OS are shown in Table 2. In univariate analysis, OS was significantly worse after APR than after SSS (hazard ratio [HR] 1.67, 95% confidence

interval [CI] 1.38–2.03). In multivariate analysis, there was no significant difference in OS between SSS and APR (HR 1.12, 95% CI 0.88–1.42; p=0.3425). However, older age (80–100 years), sex (male), tumor location (Rb), pT (≥T3), pN (≥N1), and lymphatic invasion (ly3) status were identified as independent risk factors for shorter OS.

The Kaplan-Meier curves for RFS after APR and SSS are shown in Figure 1b. RFS was worse after APR than after SSS (p<0.001, log-rank test). The results of univariate and multivariate Cox regression analysis for RFS are shown in Table 3. In univariate analysis, RFS was significantly worse after APR than after SSS (HR 1.52, 95% CI 1.29–1.78). In multivariate analysis, older age (80–100 years), sex (male), tumor location (Rb), wall location (Left), pT (≥T3), pN (≥N1), and lymphatic invasion (ly3) status were identified as independent risk factors for shorter RFS. On the other hand, there was no significant difference in RFS between the SSS and APR procedures (HR 1.10, 95% CI 0.91–1.34; p=0.3359).

Figure 1.



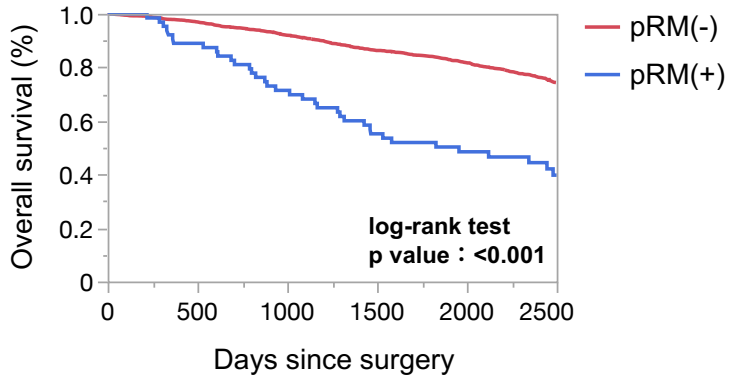
Local recurrence and pathological radial margin status

The results of univariate and multivariate logistic regression analyses for local recurrence were shown in Table 4. In univariate analysis, tumor location (Rb), wall location (full circumference), pT (≥T3), pN (≥N1), histopathological type (por, muc), lymphatic invasion (≥ly1), vascular invasion (≥v1), pRM status (positive), and operation type (APR) were identified as significant risk factors for local recurrence. Multivariate analysis of these variables showed no significant difference in LRR between the type of operation (OR 1.11, 95% CI 0.70–1.77; p=0.6530). On the other hand, pathological T3/T4, positive lymph nodes,

positive pRM were significantly associated with higher LRR.

Comparison of the Kaplan-Meier curves for OS according to pRM status were shown in Figure 2. OS was significantly worse for positive pRM than for negative pRM (p<0.001, log-rank test). The results of the univariate and multivariate logistic regression analyses for positive pRM status were shown in Supplemental Table. We found that APR (OR 3.13, 95% CI 0.18–0.56; p<0.0001) was independent predictor of positive pRM, as well as pathological T3/T4 and positive lymph nodes.

Figure 2.



Discussion

APR has a long history in the treatment of rectal cancer and is widely performed worldwide as an essential surgical procedure. There have been many reports on the impact of surgical procedure (APR or SSS) on oncological outcomes [14-18, 26-28]. Analysis of the Spanish Rectal Cancer Project dataset (n=3355) found that the OS and RFS were significantly worse after APR than after SSS, although there was no significant difference in LRR [18]. Pooled analysis of data from five randomized clinical trials, the Swedish Rectal Cancer Trial, Dutch TME trial, CAO/ARO/AIO-94 trial, EORTC 22921 trial and Polish Rectal Cancer Trial, on rectal cancer in Europe (n=3633) showed that APR was associated with increased risk of CRM involvement, increased LRR, and decreased cancer-specific survival, compared to LAR [14]. In the ACOSOG Z6051 trial, comparison of the secondary outcomes of laparoscopic and open surgery in patients with rectal cancer revealed that APR had significantly worse outcomes than LAR in terms of DFS (HR 2.21 95% CI 1.30–3.77) and LRR (HR 1.59; 95% CI 0.92–2.74) [15]. Thus, although some reports resulted in no difference in prognosis between APR and SSS [18, 27, 28], most of the papers described that APR had a worse prognosis than SSS.

There are several possible reasons for why the prognosis is worse after APR than after SSS. These include the potential selection bias arising from the fact that APR is more likely to be performed in patients who are elderly, at higher risk, and have more advanced disease. Previous studies may not have adjusted sufficiently for background factors, such as tumor location and T/N stage, and not been able to completely exclude bias in procedure selection. In this study, we used a large multicenter Japanese database to examine differences in treatment outcomes between SSS and APR after adjusting as far as possible for factors that may affect outcomes. Univariate analyses showed that APR had significantly poorer outcomes, whereas after adjustment for patient and oncological factors in multivariate analysis, there was no significant difference in OS, RFS or LRR between APR and SSS. Our study findings suggest that the oncological outcomes of APR are not inferior to those of SSS and answer the question of whether there is a difference in outcomes associated with these surgical procedures themselves in the treatment of rectal cancer.

Positive CRM and intraoperative perforation are known to be poor prognostic factors in terms of recurrence and survival [11, 25, 29]. CRM is not often included in pathological evaluation in Japan; however, in this study, positive pRM was defined as presence of cancer tissue at the surgical margin and was associated with significantly worse OS, RFS, and local recurrence. Furthermore, APR was associated with a higher rate of positive pRM than SSS, even when adjusting for other background factors. This finding is consistent with that of Wilkins et al [30], who reported a positive CRM rate of 3.7–49.6% for APR, and other recent

studies [14-18, 26] that have found positive CRM rates of 7.0–14.3% for APR and 2.0–7.0% for LAR. Examination of pathological specimens obtained during APR showed that the CRM on the anterior wall was more likely to be positive [21, 29]. Moreover, although not examined in this study, the intraoperative perforation rate has been shown to be higher in APR than in SSS (13.7% vs 2.5%) [15, 19], possibly because it is anatomically difficult to identify the dissection layer on the anterior wall side. Especially, in a male patient, the anterior anorectum has no anatomical landmarks at the level of the puborectalis muscle [31]. The smooth muscles that make up the longitudinal muscle are complexed within the puborectalis muscle bilaterally and continue to the rectourethralis muscle on the anterior wall. The anatomical complexity of the anterior wall is thought to increase the risk of positive pCRM or pRM and intraoperative perforation [20, 32].

On the other hand, CRM or RM is a factor that can be controlled by the surgeon, in that it is important to perform CRM-negative surgery. In APR, dissection of the mesorectum along the levator ani muscle increases the risk of “waisting”, resulting in a positive CRM due to proximity to the tumor. Therefore, Holm et al [33] devised extralevator abdominoperineal excision (ELAPE) to gain a margin by dissecting the levator muscle at its origin. In this way, CRM negativity can be secured for the lateral margin. However, at the anterior side, it is difficult to obtain an adequate margin because of the proximity to the anterior organs and the difficulty of finding a clear anatomical dissection line due to the complex three-dimensional intertwining of striated and smooth muscles. We believe that the following are mandatory in order to obtain optimal oncological outcomes from APR for advanced rectal cancer: understanding of the complex anatomy around the anorectum, accurate preoperative diagnosis of tumor spread using high-resolution magnetic resonance imaging (MRI), selection of appropriate preoperative treatment, appropriate surgical technique enabling good access in the deep anorectum, including robotic-assisted surgery, a transanal endoscopic approach [34], and the prone jack-knife position [35] ,and not to hesitate to carry out combined resection of adjacent organs if invasion is suspected. On the other hand, unnecessary expansion of the resection area can lead to serious complications such as dead space infection, so it is important to determine a tailor-made resection area based on accurate preoperative diagnosis in APR[36].

This study has several limitations. First, it had a retrospective design and analyzed data from a multi-institutional database in which there is no information on some of known prognostic factors (e.g. postoperative anastomotic leakage) and preoperative anal function or performance status affecting the choice of surgical procedure. Therefore, selection bias of surgical procedures could not be completely excluded. Second, preoperative treatment is standard in Europe and the US but not in Japan historically. In the present cohort, only 5.3%

of patients (136/2533) received preoperative treatment and were excluded from the study to simplify the interpretation of the data. Despite these limitations, we believe that this study is significant because it shows the actual outcomes of APR in patients with advanced rectal cancer in Japan.

Conclusion

There were no significant differences in oncological outcomes between APR and SSS for rectal cancer. The risk of positive pRM was higher after APR than after SSS and performing RM-negative surgery should improve oncological outcomes in the future.

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Figure Legends

Supplemental Figure. Flow diagram of patient selection. APR, abdominoperineal resection; SSS, sphincter-saving surgery

Figure 1a. Overall survival in patients with rectal cancer according to type of operation. APR, abdominoperineal resection; SSS, sphincter-saving surgery

Figure 1b. Relapse-free survival in patients with rectal cancer according to type of operation. APR, abdominoperineal resection; SSS, sphincter-saving surgery

Figure 2. Overall survival for patients with rectal cancer according to pRM status. pRM, pathological radial margin

Tables

Table 1. Patient and tumor characteristics in the two groups (N=2533)

Variable	SSS (n=1956, 77.2%) N(%)	APR (n=577, 22.8%) N(%)	p value
Age, years			<0.001
20-40	58 (2.97)	14 (2.43)	
40-60	641 (32.77)	137 (23.74)	
60-80	1157 (59.15)	364 (63.08)	
80-100	100 (5.11)	62 (10.75)	
Sex			<0.001
Female	759 (38.80)	168 (29.12)	
male	1197 (61.20)	409 (70.88)	
Location			<0.001
Ra	1268 (64.83)	119 (20.62)	
Rb	688 (35.17)	458 (79.38)	
Wall location			0.3555
Anterior	420 (27.04)	119 (24.84)	
Posterior	443 (28.53)	137 (28.60)	
Right	183 (11.78)	56 (11.69)	
Left	215 (13.84)	58 (12.11)	
Circumference	292 (18.80)	109 (22.76)	
pT			<0.001
T0/1	363 (18.56)	36 (6.24)	
T2	476 (18.79)	140 (24.26)	
T3	800 (40.90)	241 (41.77)	
T4a	311 (15.90)	156 (27.04)	
T4b	6 (0.31)	4 (0.69)	
pN			<0.001
N0	1223 (62.53)	345 (59.79)	
N1	490 (25.05)	118 (20.45)	

N2	193 (9.87)	58 (10.05)	
N3	50 (1.97)	56 (2.21)	
pRM			<0.001
(-)	1924 (98.36)	543 (94.11)	
(+)	32 (1.64)	34 (5.89)	
Histological type			0.01
tub1/2	1902 (97.24)	547 (94.80)	
por	24 (1.23)	16 (2.77)	
muc	30 (1.53)	14 (2.43)	
Lymphatic invasion			0.0289
ly0	768 (39.26)	194 (33.62)	
ly1	837 (42.79)	264 (45.75)	
ly2	299 (15.29)	94 (16.29)	
ly3	52 (2.66)	25 (4.33)	
Venous invasion			0.002
v0	669 (34.20)	150 (26.00)	
v1	744 (38.04)	235 (40.73)	
v2	402 (20.55)	142 (24.61)	
v3	141 (7.21)	50 (8.67)	
Adjuvant chemotherapy			0.235
(-)	1283 (65.59)	363 (62.91)	
(+)	673 (34.41)	214 (37.09)	
Operative approach			<0.001
Open	1652 (84.46)	512 (88.73)	
Laparoscopic	232 (11.86)	23 (3.99)	
Unknown	72 (3.68)	42 (7.28)	

Table 2. Univariate and multivariate Cox regression analyses for overall survival

Variable (n=2533)	N	Univariate analysis			Multivariate analysis		
		HR	95% CI	p-value	HR	95% CI	p-value
Age, years							
20-40	72	1	—	—	1	—	—
40-60	778	1.20	0.59-2.47	0.6152	1.04	0.50-2.15	0.9175
60-80	1521	1.93	0.95-3.89	0.0673	1.73	0.85-3.53	0.1319
80-100	162	4.80	2.28-10.1	<0.0001	5.26	2.46-11.26	<0.001
Sex							
Female	927	1	—	—	1	—	—
male	1606	1.39	1.14-1.70	0.001	1.33	1.07-1.67	0.0098
Location							
Ra	1387	1	—	—	1	—	—
Rb	1146	1.30	1.12-1.50	0.0005	1.51	1.20-1.90	0.0004
Wall location							
Anterior	539	1	—	—	1	—	—
Posterior	580	1.21	0.92-1.60	0.1636	1.09	0.83-1.44	0.5379
Right	239	1.09	0.76-1.56	0.6398	1.06	0.74-1.53	0.7384
Left	273	0.93	0.65-1.34	0.701	0.79	0.85-1.44	0.5379
Circumference	401	1.70	1.28-2.25	0.0002	1.14	0.83-1.44	0.5379
pT							
T0-2	1015	1	—	—	1	—	—
T3	1041	2.03	1.60-2.57	<0.0001	1.34	1.01-1.77	0.0430
T4a	467	4.02	3.14-5.15	<0.0001	1.96	1.44-2.67	<0.0010
T4b	10	6.42	2.36-17.44	<0.0001	4.66	1.67-13.01	0.0033
pN							
N0	1568	1	—	—	1	—	—
N1	608	2.03	1.63-2.52	<0.0001	1.62	1.26-2.10	0.0002
N2	251	3.69	2.87-4.76	<0.0001	3.18	2.31-4.36	<0.0010
N3	106	4.06	3.03-5.44	<0.0001	4.35	2.96-6.40	<0.0010
Histological type							

tub1/2	2449	1	—	—	1	—	—
por	40	1.80	0.99-3.28	0.054	0.97	0.47-1.97	0.9263
muc	44	1.86	1.04-3.31	0.035	1.12	0.60-2.10	0.7183
Lymphatic invasion							
ly0	962	1	—	—	1	—	—
ly1	1101	1.40	1.12-1.74	0.0026	0.91	0.71-1.17	0.4846
ly2	393	1.99	1.53-2.58	<0.0001	0.90	0.65-1.25	0.5304
ly3	77	5.37	3.70-7.81	<0.0001	2.18	1.36-3.48	0.0011
Vascular invasion							
v0	819	1	—	—	1	—	—
v1	979	1.86	1.46-2.37	<0.0001	1.25	0.95-1.66	0.1087
v2	544	2.14	1.64-2.80	<0.0001	1.18	0.85-1.63	0.3175
v3	191	2.45	1.74-3.45	<0.0001	1.03	0.68-1.55	0.9000
Type of operation							
SSS	1956	1	—	—	1	—	—
APR	578	1.67	1.38-2.03	<0.0001	1.12	0.88-1.42	0.3425

Abbreviations: APR, abdominoperineal resection; SSS, sphincter-saving surgery

Table 3. Univariate and multivariate Cox regression analyses for relapse-free survival

Variable (n=2533)	**N**	**Univariate analysis**			**Multivariate analysis**		
		HR	95% CI	p-value	HR	95% CI	p-value
Age, years							
20-40	72	1	—	—	1	—	—
40-60	778	0.81	0.52-1.26	0.3500	0.88	0.54-1.44	0.6173
60-80	1521	1.03	0.67-1.58	0.8970	1.20	0.74-1.94	0.4671
80-100	162	2.20	1.35-3.59	0.0015	3.03	1.75-5.22	0.0001
Sex							
Female	927	1	—	—	1	—	—
male	1606	1.30	1.11-1.52	0.0014	1.20	1.01-1.43	0.0449

Location							
Ra	1387	1	—	—	1	—	—
Rb	1146	1.3	1.12-1.50	0.0005	1.3	1.08-1.57	0.0056
Wall location							
Anterior	539	1	—	—	1	—	—
Posterior	580	1.14	0.91-1.42	0.2532	1.03	0.82-1.29	0.8020
Right	239	0.99	0.74-1.33	0.9446	0.98	0.73-1.32	0.8931
Left	273	0.73	0.54-0.99	0.0457	0.62	0.45-0.85	0.0028
Circumference	401	1.68	1.34-2.10	<0.0001	1.10	0.87-1.38	0.4434
pT							
T0-2	1015	1	—	—	1	—	—
T3	1041	2.37	1.95-2.87	<0.0001	1.57	1.25-1.98	0.0001
T4a	467	4.34	3.53-5.34	<0.0001	2.10	1.62-2.71	<0.0001
T4b	10	7.27	2.98-17.75	<0.0001	5.61	2.25-14.02	0.0002
pN							
N0	1568	1	—	—	1	—	—
N1	608	2.16	1.81-2.56	<0.0001	1.75	1.42-2.15	<0.0001
N2	251	3.78	3.07-4.66	<0.0001	3.31	2.56-4.29	<0.0001
N3	106	5.43	4.16-7.11	<0.0001	4.39	3.17-6.07	<0.0001
Histological type							
tub1/2	2449	1	—	—	1	—	—
por	40	1.79	1.09-2.94	0.0217	1.04	0.60-1.81	0.9038
muc	44	1.92	1.20-3.07	0.0066	1.43	0.85-2.40	0.1736
Lymphatic invasion							
ly0	962	1	—	—	1	—	—
ly1	1101	1.45	1.22-1.74	0.0026	0.97	0.79-1.19	0.7603
ly2	393	1.99	1.60-2.46	<0.0001	0.16	0.63-1.08	0.1618
ly3	77	4.96	3.57-6.88	<0.0001	1.73	1.15-2.64	0.0094
Vascular invasion							
v0	819	1	—	—	1	—	—

v1	979	1.79	1.47-2.17	<0.0001	1.20	0.95-1.50	0.1195
v2	544	2.21	1.78-2.73	<0.0001	1.26	0.97-1.64	0.0786
v3	191	2.47	1.88-3.25	<0.0001	1.08	0.77-1.50	0.6573
Type of operation							
SSS	1956	1	—	—	1	—	—
APR	577	1.52	1.29-1.78	<0.0001	1.10	0.91-1.34	0.3359

Abbreviations: APR, abdominoperineal resection; SSS, sphincter-saving surgery

Table 4. Univariate and multivariate logistic regression analyses for local recurrence

Variable (n=2533)	N	Univariate analysis			Multivariate analysis		
		OR	95% CI	p-value	OR	95% CI	p-value
Age, years							
20-40	72	1	—	—	1	—	—
40-60	778	1.08	0.42-2.78	0.8743	1.31	0.43-3.94	0.6330
60-80	1521	0.87	0.34-2.21	0.7747	1.02	0.34-3.06	0.9604
80-100	162	0.25	0.06-1.01	0.0648	0.24	0.04-1.40	0.1126
Sex							
Female	927	1	—	—	1	—	—
male	1606	1.27	0.90-1.80	0.1646	1.36	0.89-2.07	0.1448
Location							
Ra	1387	1	—	—	1	—	—
Rb	1146	1.42	1.03-1.96	0.0323	1.41	0.91-2.17	0.1159
Wall location							
Anterior	539	1	—	—	1	—	—
Posterior	580	0.89	0.52-1.53	0.6767	0.87	0.49-1.54	0.6312
Right	239	1.14	0.59-2.20	0.706	1.10	0.55-2.20	0.7922
Left	273	0.91	0.46-1.79	0.7902	0.88	0.44-1.79	0.7316
Circumference	401	2.54	1.57-4.12	0.0002	1.60	0.95-2.68	0.0755
pT							

T0-2	1015	1	—	—	1	—	—
T3	1041	3.15	1.93-5.14	<0.0001	2.41	1.31-4.41	0.0046
T4a	467	7.69	4.69-12.61	<0.0001	3.92	2.04-7.55	<0.0001
T4b	10	5.02	0.60-41.31	<0.0001	2.20	0.22-21.50	0.4989
pN							
N0	1568	1	—	—	1	—	—
N1	608	2.49	1.69-3.65	<0.0001	1.87	1.18-2.96	0.0073
N2	251	3.27	2.03-5.24	<0.0001	1.95	1.07-3.54	0.0287
N3	106	6.05	3.48-10.52	<0.0001	3.73	1.89-7.34	0.0001
Histological type							
tub1/2	2449	1	—	—	1	—	—
por	40	3.97	1.80-8.77	0.0006	1.99	0.73-5.43	0.1809
muc	44	2.50	1.04-6.03	0.0399	1.10	0.35-3.40	0.8598
Lymphatic invasion							
ly0	962	1	—	—	1	—	—
ly1	1101	2.60	1.70-4.00	<0.0001	1.80	0.58-1.71	09861
ly2	393	3.13	1.90-5.16	<0.0001	1.20	0.67-2.15	0.5369
ly3	77	3.60	1.59-8.16	0.0021	0.78	0.36-1.74	0.5569
Vascular invasion							
v0	819	1	—	—	1	—	—
v1	979	2.09	1.32-3.30	0.0017	0.88	0.50-1.53	0.6454
v2	544	2.90	1.79-4.70	<0.0001	1.12	0.62-2.03	0.6954
v3	191	3.05	1.64-5.67	0.0004	0.83	0.37-1.86	0.6561
pRM							
(—)	2463	1	—	—	1	—	—
(+)	66	4.31	2.33-7.96	<0.0001	2.49	1.22-5.09	0.0119
Type of operation							
SSS	1956	1	—	—	1	—	—
APR	577	1.56	1.10-2.21	0.0132	1.11	0.70-1.77	0.6530

Abbreviations: APR, abdominoperineal resection; SSS, sphincter-saving surgery

Supplemental Table.

Univariate and multivariate logistic regression analyses for positive pRM

Variable (n=2533)	N	Univariate analysis			Multivariate analysis		
		OR	95% CI	p-value	OR	95% CI	p-value
Age, years							
20-40	72	1	—	—			
40-60	778	1.49	0.19-11.40	0.7005			
60-80	1521	2.12	0.29-15.57	0.4621			
80-100	162	0.25	2.26-19.71	0.4602			
Sex							
Female	927	1	—	—			
male	1606	0.77	0.47-1.28	0.3205			
Location							
Ra	1387	1	—	—			
Rb	1146	1.38	0.84-2.25	0.1995			
Wall location							
Anterior	539	1	—	—	1	—	—
Posterior	580	0.72	0.33-1.61	0.4299	0.75	0.32-1.74	0.5009
Right	239	1.13	0.45-2.84	0.7925	1.40	0.52-3.76	0.5007
Left	273	0.99	0.39-2.47	0.9775	1.19	0.45-3.17	0.7254
Circumference	401	1.97	0.98-3.95	0.0563	0.93	0.44-1.95	0.8378
pT							
T0-2	1015	1	—	—	1	—	—
T3	1041	19.9	2.66-148.3	0.0036	12.7	1.67-97.31	0.0141
T4a	467	102.8	13.11-749.2	<0.0001	48.5	6.38-369.5	0.0002
T4b	10	253.5	20.82-3085.9	<0.0001	114.5	7.39-1775.7	0.0007
pN							
N0	1568	1	—	—	1	—	—
N1	608	2.10	1.16-3.81	0.0147	1.89	0.96-3.73	0.0669

N2	251	3.92	2.04-7.55	<0.0001	1.78	0.77-4.09	0.1760
N3	106	3.70	1.49-9.23	0.0050	1.30	0.44-3.81	0.6325
Histological type							
tub1/2	2449	1	—	—	1	—	—
por	40	5.69	2.15-15.02	0.0005	2.95	0.90-9.70	0.0745
muc	44	0.93	0.13-6.84	0.9399	0.33	0.04-2.74	0.3097
Lymphatic invasion							
ly0	962	1	—	—	1	—	—
ly1	1101	1.45	0.79-2.67	0.2312	0.90	0.44-1.86	0.7812
ly2	393	1.90	0.91-3.95	0.0852	0.83	0.33-2.06	0.6816
ly3	77	6.45	2.68-15.46	<0.0001	2.47	0.80-7.65	0.1167
Vascular invasion							
v0	819	1	—	—	1	—	—
v1	979	5.68	2.20-14.61	0.0003	2.19	0.80-5.96	0.1257
v2	544	4.61	1.67-12.77	0.0032	1.36	0.46-4.04	0.5763
v3	191	11.89	4.19-33.78	<0.0001	2.39	0.73-7.84	0.1498
Type of operation							
SSS	1956	1	—	—	1	—	—
APR	577	3.76	2.30-6.16	<0.0001	3.13	0.18-0.56	<0.0001

Abbreviations: APR, abdominoperineal resection; SSS, sphincter-saving surgery