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ORIGINAL ARTICLE

Abdominoperineal resection and low anterior resection: comparison of long-term oncologic outcome in matched patients with lower rectal cancer

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Abstract
Purpose The current study aimed to compare the oncologic outcome and pattern of metastasis after abdominoperineal resection (APR) and low anterior resection (LAR) treating lower rectal cancer.
Methods A total of 804 patients undergoing curative resection (R0) were enrolled prospectively. The APR and LAR groups (n=402, respectively) were matched for gender, age, and stage, for a retrospectively comparative analysis.
Results In a multivariate analysis with potential variables, APR itself was not a risk factor for increased local recurrence (LR) or reduced survival (P=0.243–0.994). Circumferential resection margin (CRM) involvement as an operation-related risk was 1.6-fold more frequent in the APR group and was significantly associated with LR and systemic recurrence (OR, 2.487–4.017; P<0.01). Circumferential margin positivity (CRM+) was concurrently correlated with advanced stage, larger tumor (long diameter, >4 cm), and longer sagittal midpelvic diameter (>10 cm) in a multivariate analysis (P<0.001–0.05). The site of metastasis did not differ between the two groups, with the exception of lung metastasis which was more frequent in the APR group (APR vs. LAR: 15.9 vs. 10 %, P=0.015). In the APR group, CRM+ and the presence of an infiltrating tumor were correlated with disease-free survival (hazard ratio (HR), 1.644 and 1.654, respectively), whereas elevated serum carcinoembryonic antigen and LVI+ were correlated with overall survival (HR, 1.57 and 1.671, respectively), in a multivariate analysis with potential variables (P<0.05).
Conclusions When performed with appropriate skill to achieve R0 resection, APR can be used safely without impairing oncological outcome, although sphincter-preserving surgery should remain the preferred option.

Keywords Rectal cancer · Abdominoperineal resection · Low anterior resection · Recurrence · Survival

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Introduction

The major sphincter-saving operation (SSO) low anterior resection (LAR) is more common than abdominoperineal resection (APR) in the treatment of rectal cancer. Most studies have reported an APR to LAR ratio of 1:3 or 1:4 [1, 2]. To facilitate the performance of LAR by reducing tumor volume and ensuring a safe distal margin of <1 cm, preoperative chemoradiotherapy (CRT) is administered [3]. One comparative study, which used the treatment trade-off method, found that most rectal cancer patients preferred LAR to APR as it avoided the requirement for a permanent stoma, despite the fact that LAR was associated with a risk of fecal incontinence [4]. Another study showed that APR patients reported considerably more sexual impairment and

a more than twofold reduction in social activity compared to LAR patients [4, 5].

In a study of 608 rectal cancer patients by Marr et al., APR was associated with greater local recurrence (LR) (APR vs. LAR: 22.3 vs. 13.5 %, P=0.002) and a lower 5-year survival rate (52.3 vs. 65.8 %, P=0.003) compared with LAR [6]. However, interpretation of these results was complicated by different indications of the two operations, for example, tumor location and distal resection margin (DRM). A Dutch multicenter trial of 1,219 rectal cancer patients found a significant difference in survival rates between the two procedures in patients with circumferential resection margin (CRM) involvement (38.5 % for APR and 57.6 % for LAR; P=0.008) [7]. The authors concluded that the poor prognosis of APR was attributable to frequent CRM involvement, secondary to the complexity of the resection plane and the occurrence of intraoperative tumor perforation. Both studies reported that the incidence of CRM involvement in APR was more than threefold greater than in LAR. To avoid CRM involvement, Holm et al. recommend an extended APR, which includes en bloc excision of the levator muscles with the anus and the lower rectum [8].

APR is nevertheless accepted as a standard procedure in patients with very distal tumors (less than 4–5 cm from the anal verge), poor sphincter function, or a restricted pelvic cavity [2]. A significant number of patients undergoing LAR develop a disorder of defecation, which is termed the anterior resection syndrome [9]. Depending on the anastomosis level and other factors, urgency and fecal incontinence occur in 10–50 % of patients after LAR. One study reported that incontinent patients were less satisfied with bowel function and felt more restricted in their daily and social activities than patients with a permanent stoma [10]. Another study investigated patient preferences before and after rectal cancer resection [11]. Approximately half of the patients who underwent APR still preferred that operation at 4-year follow-up, suggesting that APR is appraised positively by patients once they have actually undergone the procedure. Unfortunately, recent trends in surgical training for rectal cancer resection appear to focus on SSO, with scant attention to APR [8].

The aim of the present study was to reevaluate the current practice of APR by comparing oncologic risk factors of APR and LAR. These results may help to determine that the selected surgical procedure, either APR or LAR, is performed safely.

Methods

Enrollment, eligibility, and treatment

Between 1995 and 2005, a total of 804 consecutively unselected rectal cancer patients referred to the Department of Surgery at the Asan Medical Center for curative resection (R0) were enrolled prospectively for the retrospectively comparative analysis of LAR and APR (402 patients, respectively). The two groups were matched for gender, age, and cancer stage. Eligibility criteria were curatively resected adenocarcinoma of the rectum (≤stage III), a distal tumor margin located within 6 cm of the anal verge, an Eastern Cooperative Oncology Group performance status of 0 or 1, and an age of 70 years or less. Patients were excluded if they had a previous history of any cancer or hereditary colorectal cancer including hereditary nonpolyposis colorectal cancer and typical or attenuated familial adenomatous polyposis. The extent of the disease was assessed by clinical examination; colonofiberoscopy; chest radiography; computed tomography (CT) of the chest, abdomen and pelvis; and endorectal ultrasonography (EUS). Pelvic magnetic resonance imaging (MRI) was performed in all patients recruited from the year 2000. The operative method was primarily determined by tumor location (LAR for a distal tumor margin located >4 cm from the anal verge and APR for a distance of ≤4 cm), concurrently considering intraoperative findings, i.e., large tumor in a restrictive pelvis and suspicious levator–sphincter invasion. Except for a few cases, we performed preoperative CRT since 2001 in patients with advanced lower rectal cancer (lying below the peritoneal reflection with clinically T3/T4 and N+) as evaluated by pelvic MRI with EUS. Otherwise, postoperative CRT was principally indicated for lower rectal cancer patients of stage III or stage II with any one of these poor prognostic factors, namely, tumors with perforation, poorly differentiated histology, and lymphovascular or perineural invasion. Patients with CRT received a total of 45–50.4 Gy with FL (5-FU + leucovorin) or capecitabine, according to the protocol described previously [12, 13]. Preoperative and postoperative CRT was administered in 76 and 193 patients in the LAR group and 30 and 229 patients in the APR group, respectively. A scheduled dose was completed in 86 % of patients with stage III or stage II with poor prognostic factors.

Surgical procedure

Total mesorectal excision (TME) with autonomic nerve preservation (at least one side in cases with unilateral tumor invasion) was performed routinely in all patients. All operations were performed using standardized techniques by qualified colorectal surgeons (A, B, and C; >50 rectal cancer operations/year for more than 5 years). Briefly, after exploratory laparotomy, lymph node sampling around the origin of inferior mesenteric artery was performed to determine node metastasis on a frozen section prior to inferior mesenteric vessel ligation and excision. The origin of the lumbar splanchnic nerves on the aorta and the superior hypogastric plexus were carefully identified and preserved. The

mesorectum was dissected between the visceral and parietal pelvic fascia, with preservation of the superior hypogastric nerves and the pelvic plexus. Caudal mobilization up to the level of the pubococcygeus muscle was achieved primarily through the rectosacral fascia (Waldeyer's fascia) posteriorly, the iliococcygeus muscle laterally, and the posterior wall of the prostate or vagina through the avascular Denonvilliers' fascia. In cases of ultra-LAR or APR, caudal dissection was further advanced to the iliococcygeus and pubococcygeus–puborectalis muscles surrounding the lateral and posterior walls of the rectum. The lower border of dissection was determined based on the extent of tumor invasion up to the levator–sphincter muscle or intersphincteric space. For LAR, the anastomosis was mainly performed by double stapling, and the level was determined on the basis of the extent of the tumor. The lateral ends of the linear staplings and the cross points of linear and circular staplings could be safely reinforced using manual suture ligation for the purpose of preventing anastomotic leakage. For APR, the anorectal stump was excised circumferentially, including the entire levator muscles and sphincter muscle remnants, en bloc with perirectal soft tissues. The perineal resection was completed anteriorly, during which the rectal wall was identified by inserting the index finger into the rectoprostatic or rectovaginal septum. Both procedures were accompanied by lymph node sampling and the excision of metastatic nodes, as described previously, without radical pelvic lymph node dissection [12].

Histopathological examination and patient follow-up

Preoperative CRT response of each excised specimen was evaluated using the tumor regression grade (TRG) scale from “TRG 0” defined as no regression to “TRG 4” as a complete response [14]. CRM was regarded as positive if the distance between the deepest extent of the tumor and the closest CRM was ≤1 mm on microscopic examination. All histopathological results were confirmed by two pathologists. The completeness of TME was identified primarily by the respective surgeon and confirmed by the pathologists. Patients underwent a follow-up assessment every 6 months for the first 5 years and annually thereafter until postoperative year 10. Evaluations included clinical examination, routine blood chemistry, serum carcinoembryonic antigen (s-CEA), chest radiography, and CT of the chest, abdomen, and pelvis. Colonoscopy was performed annually, and patients suspected of having recurrence or metastasis underwent specific examinations, i.e., CT, MRI, bone scan, and PET/CT. Recurrence was confirmed by radiological imaging or biopsy. LR was defined as tumor regrowth within the pelvis or perineum, whereas systemic recurrence (SR) was defined as any other recurrence. The occurrence of general postoperative complications was evaluated and documented by the respective surgeon, oncology physician, and radiation oncologist, at the three points of time including hospitalization period, 1 month post-surgery, and 6 months post-surgery. Male sexual function was assessed 2 years post-surgery in 405 patients of ≤65 years of age. The primary end points were recurrence, disease-free survival (DFS), and overall survival (OS), according to the intent-to-treat analysis. The mean follow-up periods were 76 (range, 24–164) months for the LAR group and 84 (range, 23–170) months for the APR group. All patients provided written informed consent, and the study protocol was approved by the Institutional Review Board of the Asan Medical Center (registration no: 2010-0082) in accordance with the Declaration of Helsinki.

Statistical methods

Under the assumption of an estimated survival difference between APR and LAR of 20 %, Altman's nomogram was used to determine the sample size (~800 patients) of the present study and ensure 80 % power to detect surgical outcome. The clinicopathological variables of the two groups were compared using Fisher's exact test with two-sided verification or a paired *t* test. Variables associated with recurrence were compared by cross-table analysis using Fisher's exact test with two-sided verification or Pearson's χ^2 test, depending on statistical validity. Potential variables were verified by multivariate analysis using binary logistic regression. OS and DFS were compared using the Kaplan–Meier method with the log-rank test, and potent survival factors were verified using Cox's regression model. Statistical significance was defined as a P value <0.05. All calculations were performed using SPSS software (ver.19, SPSS Inc., Chicago, IL, USA).

Results

Comparison of clinicopathological variables between the two groups

The two groups did not differ in terms of gender, age, comorbidity, or physical constitution factors such as body mass index (BMI) or pelvimetry, including interspinal distance and sagittal midpelvic diameter (Table 1). Although there were no differences in tumor stage between the two groups, tumors in the APR group were larger, more frequently low lying, anteriorly located (10 to 2 o'clock clockwise), and associated with adjacent-organ invasion ($P<0.001$). Compared to the LAR group, the APR group had longer operation times, more transfusions, and more frequent adjacent-organ excision and circumferential margin positivity (CRM+) ($P<0.001$–0.05).

Table 1 Patient characteristics

Clinicopathological parameters	LAR, n=402	APR, n=402	P value[a]
Sex, male/female	238/164	237/165	1
Age, years: mean ± SD	54±9	54±10	0.809
Comorbidity, yes	77	66	0.356
BMI, kg/m^2: mean ± SD	23.3±2.9	23.5±3	0.287
Pelvimetry, cm: mean ± SD			
Interspinal distance	10.8±1.5	10.8±1.5	0.892
Sagittal midpelvic diameter	9.8±1.3	9.8±1.2	0.963
Preop s-CEA, ng/ml: mean ± SD	8.3±29.9	8.1±26.8	0.911
Stage[b], 0/I/II/III	12/106/114/170	6/107/119/170	0.295
yStage[c], 0/I/II/III (total no. of patients)	12/19/26/20 (77)	6/7/11/6 (30)	0.878
Tumor characteristics			
Distance from AV, cm: mean ± SD	5.2±0.8	3.4±1.3	<0.001
Longest diameter, cm: mean ± SD	4.5±2	5.1±1.9	<0.001
Direction, anterior	158	217	<0.001
Growth, expanding/infiltrative	317/85	323/79	0.662
Differentiation, WD + MD/PD + Muc	361/41	355/47	0.501
Lymphovascular invasion+	74	61	0.257
Perineural invasion+	19	19	1
Adjacent-organ invasion+	7	38	<0.001
Operation procedure			
Surgeon, A/B and C	247/155	269/133	0.122
Operation time, min: mean ± SD	176±46	236±54	<0.001
Transfusion, >400 ml	8	23	0.009
DRM in LAR, cm: mean ± SD	1.4±0.9	irrelevant	
CRM+	35	56	0.026
Adjacent-organ excision, yes	1	22	<0.001
Adjuvant CRT, yes	268	259	0.54

LAR lower anterior resection, *APR* abdominoperineal resection, *BMI* body mass index, *s-CEA* serum carcinoembryonic antigen, *yStage* AJCC stage after preoperative CRT, *AV* anal verge, *WD + MD/PD + Muc* well + moderately/poorly differentiated + mucinous, *DRM* distal resection margin, *CRM* circumferential resection margin, *CRT* chemoradiotherapy

[a]All parameters were compared by Fisher's exact test with two-sided verification or a paired *t* test

[b]Cancer staging according to the American Joint Committee on Cancer (7th ed., 2010). The mucosal cancer (Tis) and complete response (TRG4) after preoperative CRT were included in stage 0

[c]In patients who underwent preoperative CRT

Local recurrence

Less than 10 % of LR was identified in the two groups (Fig. 1), and APR was not associated with LR in a multivariate analysis with potential variables (OR, 1.51; 95 % CI, 0.756–3.016; P=0.243). In the APR group, LR was significantly associated with adjacent-organ or perineural invasion, CRM+, and advanced stage (stage III) on a multivariate analysis (P=0.003–0.04) (Table 2). Of these risk factors, CRM+ was concurrently correlated with advanced stage, larger tumor (long diameter, >4 cm), and longer sagittal midpelvic diameter (>10 cm) in a multivariate analysis (P<0.001–0.05). Among patients with stage 0–II disease, LR was associated with BMI (≤25 vs. >25, 2/171 vs. 4/61, P=0.043) and anteriorly located tumors (anterior vs. others, 5/84 vs. 1/148, P=0.025) in the LAR group, and with CRM+ (− vs. +, 7/213 vs. 4/19, P=0.007) in the APR group. In the LAR group, LR was not associated with DRM (either 5 or 10 mm), irrespective of stage (P=0.222 and 0.813, respectively).

Systemic recurrence

Of the 151 patients with SR, the lung (12.9 %) was the most frequent site of metastasis followed by the liver (5.3 %), the systemic lymph nodes, bone, and the brain in descending order (Fig. 1). The site of metastasis did not differ between the two groups, with the exception of lung metastasis which was more frequent in the APR group (APR vs. LAR, 15.9 vs. 10 %, P=0.015). Multivariate analysis showed that SR was significantly associated with advanced stage, CRM+, elevated preoperative s-CEA, and perineural invasion in the APR group, whereas advanced stage, CRM+, and lymphovascular invasion in the LAR group (P<0.001–0.05) (Table 3). In APR group patients with stage III disease, SR occurred more frequently in male patients than in female patients (44.8 vs. 28.4 %, P=0.038). In LAR group patients with stage 0–II disease, SR was approximately threefold more frequent in patients with lower-located tumors compared to patients with higher-located tumors (≤4 vs. >4 cm of the anal verge: 15.2 vs. 5 %, P=0.045). In the LAR

Table 2 Local recurrence in association with clinicopathological parameters in the two study groups

Parameters	Operation type	No. of patients with LR (%)	*P* value[a]	OR	95 % CI	*P* value[b]
Preop s-CEA, ≤ vs. >6 ng/ml	LAR	15/307 (4.9) vs. 3/95 (3.2)	0.582			
	APR	24/309 (7.8) vs. 14/83 (15.1)	0.043	1.428	0.668–3.052	0.357
Stage[c], 0–II vs. III	LAR	6/232 (2.6) vs. 12/170 (7.1)	0.048			
	APR	11/232 (4.7) vs. 27/170 (15.9)	<0.001	2.788	1.29–6.023	0.009
Perineural invasion, − vs. +	LAR	17/383 (4.4) vs. 1/19 (5.3)	0.59			
	APR	33/383 (8.6) vs. 5/19 (26.3)	0.025	3.385	1.055–10.868	0.04
Adjacent-organ invasion, − vs. +	LAR	18/395 (4.6) vs. 0/7 (0)	1			
	APR	29/364 (8) vs. 9/38 (23.7)	0.006	3.856	1.566–9.494	0.003
Operating time, ≤ vs. >180 min	LAR	13/303(4.3) vs. 5/99 (5.1)	0.781			
	APR	5/111 (4.5) vs. 33/291 (11.3)	0.037	2.103	0.766–5.771	0.149
CRM, − vs. +	LAR	14/367 (3.8) vs. 4/35 (11.4)	0.061			
	APR	25/346 (7.2) vs. 13/56 (23.2)	0.001	3.006	1.355–6.669	0.007

OR Odds ratio, *CI* confidence interval, *LAR* lower anterior resection, *APR* abdominoperineal resection, *s-CEA* serum carcinoembryonic antigen, *CRM* circumferential resection margin

[a] All parameters were compared by Fisher's exact test with two-sided verification

[b] Multivariate analysis using potential parameters by binary logistic regression

[c] Cancer staging according to the American Joint Committee on Cancer (7th ed., 2010)

group, systemic lymph node metastasis was significantly associated with CRM+ and lymphovascular invasion ($P<0.001$ and 0.041, respectively).

Survival outcome

APR did not affect OS or DFS (OS: HR, 0.994; 95 % CI, 0.724–1.364; $P=0.969$; DFS: HR, 0.875; 95 % CI, 0.588–1.304; $P=0.513$) in a multivariate analysis with potential variables (Fig. 2). Both LR and SR significantly reduced OS and DFS, irrespective of operation type ($P<0.001$–0.05) (Supplementary Table 1). In the APR group, CRM+ and the presence of an infiltrating tumor were correlated with DFS (HR, 1.644 and 1.654, $P=0.026$ and 0.035, respectively), whereas elevated s-CEA and LVI+ were correlated with OS (HR, 1.57 and 1.671, $P=0.029$ and 0.047, respectively), in a multivariate analysis with potential variables. A tendency towards different 5-year OS rates in the APR group was observed between the three different surgeons (surgeon A vs. B and C; mean ± SEM, 84.9±2.2 vs. 78.4±3.6 %, $P=0.076$).

Postoperative complications including genitourinary dysfunctions

Postoperative complications other than genitourinary dysfunction occurred as 41 events in 41 patients (10.2 %) in the APR group and as 49 events in 40 patients (10 %) in the LAR group, and no differences were observed between the two groups (Table 4). Postoperative ileus was the most frequent postoperative complication in both groups. Diverting ileostomy was performed in 26 patients (6.5 %) of the LAR group. Anastomotic leakage and pelvic abscess occurred in 20

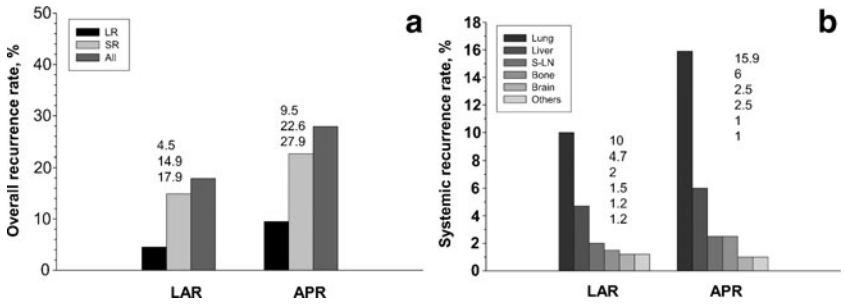

Fig. 1 Local and systemic recurrence rates (*LR* and *SR*) (**a**) and organs affected by SR (**b**) in the lower anterior resection (*LAR*) group and abdominoperineal resection (*APR*) group. Figures (*top→down*) indicate percent rates of LR, SR, and LR + SR (**a**), and the lung, liver, systemic lymph node (*S-LN*), bone, brain, and others (**b**), in order

Table 3 Systemic recurrence in association with clinicopathological parameters in the two study groups

Parameters	Operation type	No. of patients with LR (%)	*P* value[a]	HR	95 % CI	*P* value[b]
Preop s-CEA, ≤ vs. >6 ng/ml	LAR	38/307 (12.4) vs. 22/95 (23.2)	0.013	1.625	0.844–3.129	0.146
	APR	56/309 (18.1) vs. 35/93 (37.6)	<0.001	2.041	1.174–3.546	0.011
Stage[c], 0–II vs. III	LAR	15/232 (6.5) vs. 45/170 (26.5)	<0.001	3.648	1.874–7.102	<0.001
	APR	27/232 (11.6) vs. 64/170 (37.6)	<0.001	3.361	1.961–5.76	<0.001
Lymphovascular invasion, − vs. +	LAR	38/327 (11.6) vs. 22/74 (29.7)	<0.001	2.052	1.044–4.032	0.037
	APR	65/341 (19.1) vs. 22/61 (42.6)	<0.001	1.818	0.938–3.522	0.077
Perineural invasion, − vs. +	LAR	55/383 (14.4) vs. 5/19 (26.3)	0.18			
	APR	80/383 (20.9) vs. 11/19 (57.9)	0.001	3.592	1.249–10.324	0.018
CRM, − vs. +	LAR	44/367(12) vs. 16/35 (45.4)	<0.001	4.017	1.819–8.873	0.001
	APR	66/346 (19.1) vs. 25/56 (44.6)	<0.001	2.487	1.31–4.722	0.005

HR hazard ratio, *CI* confidence interval, *LAR* lower anterior resection, *APR* abdominoperineal resection, *s-CEA* serum carcinoembryonic antigen, *CRM* circumferential resection margin

[a] All parameters were compared by Fisher's exact test with two-sided verification

[b] Multivariate analysis using potential parameters by binary logistic regression

[c] Cancer staging according to the American Joint Committee on Cancer (7th ed., 2010)

patients (5 %) in the LAR group. Permanent stoma was positively appraised in approximately 85 % of patients in the APR group, i.e., satisfied in 20.9 %, tolerable in 63.9 %, and unsatisfied in 15.2 %. The rate of substantial voiding dysfunction (greater than two-thirds functional impairment) was twofold higher in the APR group than in the LAR group (12.9 vs. 5 %, $P<0.001$), although none of the patients experienced permanent dysfunction. Similarly, moderate to severe dysfunction of erectile potency (greater than one-third functional impairment) was more frequent in the APR group than in the LAR group (21.5 vs. 12.7 %, $P=0.024$).

Discussion

As the operation type of lower rectal cancer is mainly determined by tumor location maintaining R0 resection and adequate DRM (generally accepted as 2 cm) [3], the

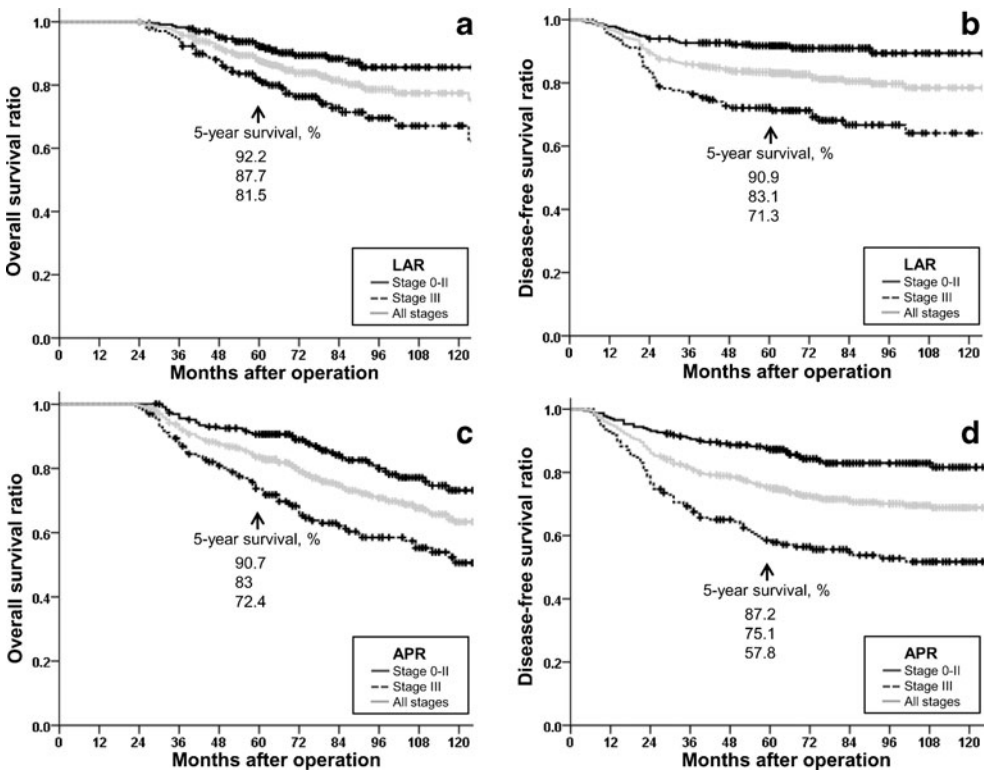

Fig. 2 Overall survival and disease-free survival in the LAR group (**a** and **b**, respectively) and APR group (**c** and **d**, respectively). $P<0.001$, between the patients with stage 0–II and stage III in the lower anterior resection (*LAR*) group and abdominoperineal resection (*APR*) group

Table 4 Postoperative complications in the two study groups

Complication types	LAR, n=402 (%)	APR, n=402 (%)	P value[a]
General			
Ileus	17 (4.2)	25 (6.2)	0.267
Anastomotic leakage	17 (4.2)	Irrelevant	Irrelevant
Pelvic abscess	3 (0.7)	4 (1)	0.726
Wound infection	6 (1.5)	7 (1.7)	0.789
Enteric fistula	3 (0.7)	3 (0.7)	1
Others[b]	3 (0.7)	2 (0.5)	0.687
Genitourinary[c]			
Voiding difficulty	20 (5)	52 (12.9)	<0.001
Sexual dysfunction	38/205 (18.5)	56/200 (28)	0.026
Erectile dysfunction	26/205 (12.7)	43/200 (21.5)	0.024
Ejaculatory dysfunction	31/205 (15.1)	42/200 (21)	0.155

LAR low anterior resection, *APR* abdominoperineal resection

[a] All parameters were compared by Fisher's exact test with two-sided verification

[b] Including two cases of anastomotic bleeding and one case of pneumonia in the LAR group, and one case of pneumonia and one case of deep vein thrombosis in the APR group

[c] Moderate to severe dysfunction, such as greater than one-third functional impairment compared with the preoperative state. Erectile or ejaculatory potency was assessed in 405 male patients of ≤65 years

LAR and APR groups cannot be compared in terms of recurrence rate and survival outcome. The LR rates of the two groups in the current study are within the lower ranges of those reported by previous studies [2, 6, 15, 16]. Some studies have reported no association between operation type (either APR or LAR) and LR or survival, whereas others have shown that APR is associated with a 1.5–2.3-fold increase in LR rate and reduced cancer-specific survival compared to LAR [2, 6, 16]. In the present study, APR itself was associated with neither increased LR nor reduced survival. The lower LR and better survival rates in the present study compared with those in a previous study by our group is probably attributable to improved TME [12]. There is convincing evidence that TME reduces LR rates by 1–6 % and that it improves survival regardless of operation type [6].

CRM+, advanced stage, adjacent-organ invasion, and lymphovascular or perineural invasion are established risk factors for LR, SR, and survival outcome following rectal cancer surgery, as demonstrated in previous studies [7, 17–19]. CRM+ was found to be a powerful predictor of recurrence and survival in a meta-analysis involving 17,568 patients [20]. In the present cohort, CRM+ was found in 13.9 % of the APR group and 8.7 % of the LAR group (P= 0.026), and CRM+ has been reported more frequently in APR patients compared to LAR patients by previous studies (12–41 vs. 5–12 %, respectively) [6, 7, 18]. The present study also found that CRM+ and lymphovascular invasion were associated with systemic lymph node metastasis in the LAR group. These associations probably occur because tumor-replaced nodes or intravascular tumor aggregates, which frequently incur CRM+, are connected to systemic lymph nodes via lymphovascular channels [20, 21]. A previous study reported that severe tumor budding was associated with pelvic lymph node metastasis in early rectal cancers [22]. Lateral and downward lymphatic channels remain after LAR and provide pathways to systemic lymph nodes. CRM+, which was significantly associated with LR in the present APR cohort, could be considered as an operation-related error to some extent. Increased CRM+ in association with LR is frequently caused by rectal perforation and an insufficient resection plane during APR [6–8]. Although we did not evaluate these technical errors in individual cases, these events mostly arise secondary to difficulties in dissection within the restrictive bony pelvis in lower rectal cancers. We confirmed that CRM+ was closely correlated with advanced stage, large tumor size, and a narrow elliptical pelvis. This may also explain the close correlation between increased LR and high BMI score or anteriorly located tumors in our LAR group. Therefore, these obstacles must be eliminated, or at least reduced, by improved surgical technique. Otherwise, the surgical treatment of advanced tumors can be supported by preoperative CRT, which is administered for the purposes of downsizing and downstaging [2, 13, 15, 23].

According to one quality assessment study of APR, the plane of resection lies within the sphincter muscle, submucosa, and lumen in more than one third of all cases and in the sphincter muscles in all remaining cases [7]. Consequently, there is an urgent need to improve the surgical approach to APR, and several authors have reported changes in approach [6, 8, 24]. APR and LAR do not differ until the end of the TME procedure, at which point the mesorectum tapers to the levator–sphincter junctions and intersphincteric plane. Herein, some surgeons have suggested an extralevator APR, in which the mesorectum is not dissected off the levator muscles and the perineal procedure includes en bloc resection of the levator and sphincter muscles with the anorectum in a prone jackknife position [8]. This procedure was usually accompanied by the removal of the coccyx and a flap procedure for the perineal wound closure. A recent European study reported a greater incidence of CRM+ in conventional APR patients compared to extralevator APR patients (49.6 vs. 20.3 %, P<0.001), although the former group included patients with more advanced tumors (T3 and 4) [24]. The aims of all revised APR procedures are to enable wide perineal excision and the creation of a cylindrical specimen, as originally advocated by Miles [25]. In the present study, the rectum was

dissected up to the level of the levator–sphincter junction during the abdominal procedure, and the perineal procedure was then performed with the patient in a lithotomy position without removal of the coccyx. During the perineal procedure, it is possible to achieve sufficient exposure and excision of the levator muscles by pushing the rectum in the opposite direction to the excision site. As accidental perforation frequently occurs in the rectoprostatic and rectovaginal septum, the rectourethralis or bulbocavernous muscle exposed on the index finger was cautiously divided from the prostate or vagina, having been preceded by complete division of the levator and sphincter muscles at their posterior and lateral directions in turn.

In the present study, elevated s-CEA was a significant risk factor for SR and reduced OS in the APR group. CEA, which is implicated in intercellular adhesion and acts as a chemoattractant, facilitates tumor cell aggregation by homotypic or heterotypic binding and thus increases metastatic capability [26, 27]. CEA has been reported to contribute to liver metastasis by upregulating the adhesion of colorectal carcinoma cells to the endothelium, in a process mediated by cytokines from CEA-stimulated Kupffer cells [28]. According to one population-based study, male rectal cancer patients showed a significantly increased risk of metachronous liver metastasis [29], and male sex was associated with SR in the present APR cohort. Although the present study excluded inoperable cases and could not measure synchronous SR rates according to the respective organ, lung metastasis was found to be more frequent than liver metastasis in lower rectal cancer patients undergoing R0 resection. The lung is the most common site of extra-abdominal metastasis in patients with colorectal cancer, and this occurs more frequently for rectal cancers than for colon cancers [30]. Lower rectal cancers have dual venous drainage channels with portal and systemic communications via the superior rectal vein and internal iliac vein, respectively [31]. A dual venous drainage of the lower rectum may explain the present findings that APR rather than LAR (mean length above the anal verge, 3.1 vs. 5.2 cm) and a lower-located tumor (≤4 cm above the anal verge) in LAR patients with less advanced cancers were associated with more frequent SR and with lung metastasis or SR, respectively.

Relatively lower morbidities of the current study compared to the other studies are more or less based on our limited evaluation periods until 6 months post-surgery [2, 5, 32]. Anastomotic leakage or pelvic abscess has been regarded as one of the major complications of LAR and occurred in 5 % of our LAR patients. These leakage rates were relatively low compared with other studies, and one meta-analysis showed a leakage rate of 11–12 % following rectal cancer surgery [33]. We reinforce possibly weak points of staplings using manual suture ligation during LAR which appears to diminish leakage rates. In the current cohorts of LAR patients, we did not assess Wexner's incontinence scoring (IS) which has been validated as an efficient method of assessing various components of incontinence [33]. The other study of LAR in which the subjects had a mean tumor site of 9.4 cm from the anal verge presented mean IS of 6.9 at 24 months postoperatively [34]. A permanent stoma appears to be mostly tolerated in the APR group, as 85 % of our patients live an ordinary life without a significant problem. Postoperative voiding difficulty and sexual dysfunction occur more frequently in APR patients than in LAR patients, as found in the present study [4]. We confined the assessment of moderate to severe sexual dysfunction (greater than one-third functional impairment) to male patients (≤65 years) 2 years postoperatively; the incidence was ranked in the lower ranges of previous studies (28 vs. 15–72 % for APR and 18.5 vs. 0–67 % for LAR, respectively) [4, 5, 35]. However, autonomic nerve preservation was performed at least unilaterally in all patients, which may have reduced the incidence of postoperative voiding and male sexual dysfunction in the present cohort. Ejaculatory dysfunction occurs more frequently than erectile dysfunction, and neurogenic impotence following rectal excision may be only temporary in a significant proportion of men [5]. The rate of moderate to severe incontinence was 15.7 % at 24 months postoperatively.

Unfortunately, in the current study, we do not reliably assess the oncologic and functional outcomes of preoperative vs. postoperative CRT, due to limited number of patients with preoperative CRT. Another of our recent studies showed that low-lying-rectal-cancer patients (tumor distal margin, <5 cm from the anal verge) in the preoperative CRT arm had significantly better sphincter preservation than did patients in the postoperative CRT arm (68 vs. 42 %, P=0.008) without increment of complication rate and recurrence [13].

Although the present study involved inevitable selection bias in the determination of operation type mainly according to tumor location, it investigated unselectively matched patients undergoing surgery for lower rectal cancer. Most of the significant risk factors for LR and SR, which were associated with CRM+, can be reduced by improvements in surgical technique and preoperative or postoperative CRT. Although sphincter-preserving surgery must be considered the procedure of choice, APR can be safely used in patients with proper technique without impairing oncological outcome. Additionally, the potent risk factors identified in the present study may help to determine the most appropriate treatment option, and to achieve R0 resection, in patients with lower rectal cancer.

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