Risk factor for permanent stoma and incontinence quality of life after sphincter-preserving surgery for low rectal cancer without a diverting stoma

Takuya Miura | Yoshiyuki Sakamoto | Hajime Morohashi | Tatsuya Yoshida | Kentaro Sato | Kenichi Hakamada

Department of Gastroenterological Surgery, Hirosaki University Graduate School of Medicine, Hirosaki, Japan

Correspondence
Takuya Miura, Department of Gastroenterological Surgery, Hirosaki University Graduate School of Medicine, Hirosaki, Japan.
Email: tmiura@hirosaki-u.ac.jp

Abstract
The goal of the present study was to evaluate permanent stoma formation and defecation function in long-term follow up after surgery for low rectal cancer without a diverting stoma. Subjects were 275 patients who underwent sphincter-preserving surgery for low rectal cancer between 2000 and 2012. Clinical outcomes were evaluated and defecation function was assessed based on a questionnaire survey, using Wexner and modified fecal incontinence quality of life (mFIQL) scores. Incidence of anastomotic leakage was 21.8%, and surgery-related death as a result of anastomotic leakage occurred in one male patient. Median follow-up period was 4.9 years and permanent stoma formation rate was 16.7%. Anastomotic leakage was an independent predictor of permanent stoma formation (odds ratio [OR] 5.86, P < 0.001). Age < 65 years (OR 1.99, P = 0.001) and male gender (OR 4.36, P = 0.026) were independent predictors of anastomotic leakage. A permanent stoma was formed as a result of poor healing of anastomotic leakage in 29.6% of males, but in no females. Defecation function was surveyed in 27 and 116 patients with and without anastomotic leakage, respectively. These groups had no significant differences in median follow-up period (63.5 vs 63 months), Wexner scores (quartile) (6 (2.5-9) vs 6 (3-11)), and mFIQL scores (26.1 (4.8-64.2) vs 23.8 (5.9-60.7). Defecation function associated with anastomotic leakage showed no significant dependence on gender or resection procedure. Sphincter-preserving surgery without a diverting stoma may be indicated for females with low rectal cancer. In this procedure, male gender is a risk factor for anastomotic leakage and subsequent formation of a permanent stoma in one in three patients.

Keywords
diverting stoma, low rectal cancer, sphincter-preserving surgery
INTRODUCTION

In sphincter-preserving surgery for low rectal cancer, a diverting stoma is concomitantly formed with the aim of resting the anastomosis region until it heals.\(^1\)\(^,\)\(^2\) Diverting stoma formation is recommended based on a meta-analysis showing that this procedure reduced anastomotic leakage after low anastomosis close to the anus.\(^3\) However, in a multicenter study in Japan, prevention of anastomotic leakage by a diverting stoma after low anastomosis following rectal cancer resection was not found.\(^4\) Anal function is retained without a diverting stoma in some cases, and such patients thus undergo unnecessary stoma formation.\(^5\)\(^,\)\(^6\) Our department has carried out sphincter-preserving surgery without a diverting stoma after low anterior resection (LAR) and intersphincteric resection (ISR) for low rectal cancer as a basic treatment strategy.\(^6\)\(^,\)\(^7\) The objective of this retrospective study was to investigate safety, permanent stoma formation, and defecation function in patients who underwent this procedure for low rectal cancer, and to clarify the validity and indication for this treatment.

METHODS

2.1 Patients

Of 370 consecutive patients with low rectal adenocarcinoma who underwent initial proctectomy at the Department of Gastroenterological Surgery, Hirosaki University, between 2000 and 2012, 298 received sphincter-preserving surgery. Subjects of the present study were 275 of these patients, excluding one case with concomitant ulcerative colitis and 22 patients in whom a diverting stoma was formed after preoperative radiotherapy. Rectal cancer in which the lower margin was located below the peritoneal reflection during surgery was defined as low rectal cancer. Data for anastomotic leakage and perioperative complications, permanent stoma formation, and reasons for the procedure were collected from medical records. Perioperative complications were defined using the Clavien-Dindo classification.\(^9\) Clinical leakage signs were defined as abdominal pain, abdominal distention, fever, and pus or fecal discharge from the pelvic drain. All clinically suspicious symptoms were confirmed by digital rectal examination and radiographic examination (e.g., extravasation of endoluminally given water-soluble contrast enema, pelvic abscess and fluid/air bubbles surrounding the anastomosis on computed tomography).\(^7\) Using the proposed grading system, anastomotic leakage was classified into three grades: grade A required no active therapeutic intervention; grade B required active therapeutic intervention; and grade C required reoperation.\(^9\) Anastomotic leakage with grades B and C (but not grade A) within 30 days after surgery was defined as anastomotic leakage. Age, sex, body mass index (BMI), ischemic disease, diabetes, American Society of Anesthesiologists (ASA) status, intraoperative blood transfusion, tumor diameter, tumor-anal verge distance, anastomatic height from anal verge, circumferential occupation, tumor depth, regional lymph node metastasis, distant metastasis, circumferential margin (CRM), operation time, blood loss, laparoscopy, combined resection, lateral lymph node dissection (LLND), resection procedure, and anastomosis method were examined as clinicopathological factors. When a stoma was present at final follow up, it was regarded as a permanent stoma.\(^10\) Median follow-up period was 4.9 years.

2.2 Operative and perioperative management

In standard perioperative management, the patient fasted from the day before surgery, and received mechanical pretreatment and perioperative antibiotics before surgery and for 3 days after surgery. After pressure reduction by transanal drainage for about 1 week after surgery, food ingestion was started. After transection of the inferior mesenteric artery and vein, total mesorectal excision (TME) was carried out as a standard surgical procedure, and bilateral LLND was done when the depth was T3 or deeper, as a rule.\(^11\) To secure a 2-cm resection margin, ISR was selected for tumors located within 2 cm from the upper margin of the levator ani muscle attachment region.\(^7\)\(^,\)\(^8\)\(^,\)\(^12\) For anastomosis in LAR and ISR, double-stapled and hand-sewn coloanal anastomosis were carried out, respectively. Side-to-end anastomosis was applied as a rule, and end-to-end anastomosis was used when the pelvis was narrow or the reconstructed intestine was short. When anastomotic leakage was clinically suspected after surgery, its presence or absence was confirmed by fluoroscopy or computed tomography (CT). If anastomotic leakage was observed, it was treated with antibiotics, a drainage tube, or stoma formation, depending on the details in each case. In approximately 6 months after stoma formation as a result of leakage, integrity of the anastomosis was checked by digital rectal examination and a water-soluble contrast enema examination. Patients without any findings of anastomotic leakage underwent stoma closure. When findings of anastomotic leakage were sustained and the anastomosis was not expected to heal, stoma was not closed or permanent colostomy was formed. When patients had poor general condition such as unreseactable distant metastases or dementia, stoma was not closed permanently even if integrity of the anastomosis was recovered.

2.3 Evaluation of function

Defecation function and quality of life (QOL) were surveyed using a questionnaire in patients who did and did not develop anastomotic leakage, and evaluated based on the frequency of defecation per day and the Wexner Score\(^13\) and modified fecal incontinence quality of life (mFIQL) score.\(^14\)

2.4 Statistical analyses

Risk factors for permanent stoma formation and for anastomotic leakage were analyzed by Fisher exact test. Factors with a significant difference were subjected to multivariate logistic regression analysis. Defecation function was compared between groups by Mann-Whitney U-test. Two-sided P<0.05 was regarded as significant. Statistical analysis was carried out using EZR.\(^15\)
3 RESULTS

3.1 Background of patients and complications

Median age was 64 years old (interquartile range, IQR: 55-71.5), 199 patients (72.4%) were male, and median BMI was 22.7 (IQR: 20.8-24.5). Fourteen patients (5.1%) had concomitant cerebral and cardiovascular lesions, 40 (14.5%) had diabetes, 30 (10.9%) had severe complications of ASA grade 3 or 4 or higher, and nine (3.3%) received blood transfusion during surgery. Median tumor diameter was 4.5 cm (IQR: 3.0-6.1), median tumor-anal verge distance was 4.5 cm (IQR: 3.0-6.0), and the tumor was circumferential in 46 cases (16.7%). Disease stage was 0 in 10 cases (3.6%), I in 72 (26.2%), II in 60 (21.8%), III in 101 (36.7%), and IV in 32 (11.6%). LAR was carried out in 157 patients (57%) and ISR was carried out in 118 (43%). Laparoscopic surgery was carried out in eight patients (2.9%), combined resection of other organs in 18 (6.5%), LLND in 167 (60.7%), and side-to-end anastomosis in 222 (80.7%). Median operative time was 169 (138-238) minutes, and median blood loss was 360 mL (180-628). CRM was positive in seven patients (2.5%). Surgery-related death occurred in one male patient as a result of anastomotic leakage after LAR. Clavien-Dindo classification was III or higher in 72 cases (26.2%), and respiratory or dialysis management in an intensive care unit was necessary in six (2.2%). Anastomotic leakage of grades B and C occurred in 30 patients each (rates of 10.9% each) and the overall incidence was 21.8% (60/275) (Table 1).

3.2 Risk factors for permanent stoma formation

Five-year cumulative permanent stoma formation rate was 16.7% in a median follow-up period of 4.9 years (Figure 1). Reason for permanent stoma was poor healing of anastomotic leakage in 16 patients (35.5%), metastatic disease after anastomotic leakage in three (6.7%), delayed onset of anastomotic leakage in four (8.9%), local recurrence in 19 (42.2%), poor defecation function in two (4.4%), and perforation of sigmoid colon resulting from radiation therapy for bone metastasis in one (2.2%). Delayed onset of anastomotic leakage occurred between 2 months and 8 years after surgery. All resulted in the status of permanent stoma because of dementia in one male and one female, metastatic disease in one man, and poor healing of anastomotic leakage in one male. In univariate analysis, tumor-anal verge distance <5 cm, ISR, end-to-end anastomosis, and anastomotic leakage were identified as significant risk factors, and anastomotic leakage was an independent risk factor for permanent stoma formation in multivariate analysis (odds ratio (OR): 5.86, P<0.001) (Table 2).

3.3 Risk factors for anastomotic leakage

Age <65 years old and male gender were significant risk factors for anastomotic leakage in univariate analysis, and were also independent risk factors in multivariate analysis (age <65 years old: OR=1.99, P=0.001; male: OR=4.36, P=0.026) (Table 3). After development of anastomotic leakage, a permanent stoma was formed as a result of poor healing of anastomotic leakage in 29.6% of males (about one in three patients), regardless of age. In contrast, no

| Variable | Value |
|----------|-------|
| Age (y)  | 64 (55-71.5) |
| Gender, n (%) | 199 (72.4) |
| Male | 199 (72.4) |
| Female | 76 (27.6) |
| Body mass index (kg/m²) | 22.7 (20.8-24.5) |
| Ischemic disease, n (%) | 14 (5.1) |
| Diabetes, n (%) | 40 (14.5) |
| ASA 3-4, n (%) | 30 (10.9) |
| Blood transfusion, n (%) | 9 (3.3) |
| Tumor size (cm) | 4.5 (3.0-6.1) |
| Distance from anal verge to tumor (cm) | 4.5 (3.0-6.0) |
| Anastomotic height from anal verge (cm) | 3.0 (1.5-4.0) |
| CRM positive, n (%) | 7 (2.5) |
| Type of resection, n (%) | 0 10 (3.6) |
| Low anterior resection | 157 (57.1) |
| Intersphincteric resection | 118 (42.9) |
| Combined resection, n (%) | 8 (2.9) |
| Lateral lymph node dissection, n (%) | 18 (6.5) |
| Side to end anastomosis, n (%) | 167 (60.7) |
| Operation time (min) | 222 (80.7) |
| Blood loss (mL) | 169 (138-238) |
| CRM positive, n (%) | 360 (180-628) |

| Complications (Clavien-Dindo), n (%) | 7 (2.5) |
| All (I-V) | 135 (49.1) |
| III | 66 (24.0) |
| IV | 6 (2.2) |
| V | 1 (0.45) |
| Anastomotic leakage, n (%) | 30 (10.9) |
| Grade B | 30 (10.9) |
| Grade C | 30 (10.9) |

aMedian (interquartile range). 
ASA, American Society of Anesthesiologists; CRM, circumferential margin.
permanent stoma as a result of poor healing of anastomotic leakage formed in females, regardless of age (Table 4).

3.4 Defecation function and QOL

Defecation function was surveyed by mailing a questionnaire to 27 patients who developed anastomotic leakage (response rate: 45.0%) and 116 patients who did not develop anastomotic leakage (response rate: 53.9%). Frequency of defecation per day and Wexner and mFIQL scores were compared for these groups. Comparing the backgrounds of the two groups, the anastomotic leakage group had a significantly higher rate of BMI $\geq 25$ kg/m$^2$ (44.4% vs 23.3%), but the median follow-up periods of 63.5 and 63 months, respectively, and all other clinicopathological factors did not differ significantly between the groups. Median (quartile) frequency of defecation per day and Wexner and mFIQL scores were 4 (1.5-4), 6 (2.5-9), and 26.1 (4.8-64.2), respectively, in patients with anastomotic leakage, and 4 (1.5-4), 6 (3-11), and 23.8 (5.9-60.7), respectively, in those without anastomotic leakage, with no significant differences between the groups (Table 5). Gender and resection procedure had no significant effect on anastomotic leakage-associated defecation function or QOL (Table 5).

4 DISCUSSION

A diverting stoma may contribute to prevention of anastomotic leakage in cases with low anastomosis near the anus, and is generally formed in anus-preserving surgery for low rectal cancer.\(^1\)\(^-\)\(^3\) However, in a recent multicenter study in Japan, a diverting stoma did not reduce the incidence of anastomotic leakage after low anastomosis, but did significantly reduce the rate of reoperation after anastomotic leakage.\(^4\) There was no difference in mortality between patients with and without diverting stoma formation,\(^4\) suggesting that a diverting stoma is unnecessary if anastomotic leakage is treated appropriately, including with reoperation.

As complications associated with diverting stoma formation and stoma closure may develop, this procedure is not necessarily a safe intervention.\(^16\) Therefore, if a diverting stoma does not reduce anastomotic leakage- and surgery-related deaths, patients who are unlikely to develop anastomotic leakage undergo an unnecessary and risky procedure. Therefore, the significance of a diverting stoma requires investigation, including the rate of permanent stoma formation and defecation function. The significance of the present study is that the indication for diverting stoma was investigated based on long-term anal conditions, defecation function, and QOL as outcomes.

One of the main goals was to identify the perioperative risk factors for permanent stoma in all aspects in consecutive patients with low rectal cancer at a tertiary hospital. We considered that this analysis could offer valuable overview of the consequences after sphincter-preserving surgery for low rectal cancer without a diverting stoma to patients and physicians. We first identified anastomotic leakage as a risk factor for permanent stoma formation, as previously found.\(^17\)\(^-\)\(^21\) Age $<65$ years and male gender were then identified as independent risk factors for anastomotic leakage. A permanent stoma was formed as a result of poor healing of anastomotic leakage in one in three males, regardless of age and resection procedure. In contrast, in females, the incidence of anastomotic leakage was low and there was no permanent stoma formation as a result of poor healing of anastomotic leakage.

Reduction of defecation function is of concern when anastomotic leakage occurs, but findings have varied among previous studies.\(^22\)\(^-\)\(^24\) In our patients, anastomotic leakage did not contribute to reduction of long-term defecation function and QOL, and there was no influence of sex or resection procedure. Thus, in female patients, sphincter-preserving surgery for low rectal cancer without diverting stoma formation is unlikely to have a negative influence on permanent stoma formation as a result of poor healing of anastomotic leakage and reduced long-term defecation function and QOL. In a study of short-term anastomotic leakage following diverting stoma formation after low anastomosis, a diverting stoma was found to be useful in males, but not in females.\(^25\) The long-term anal function in our study supports the validity of low anastomosis without diverting stoma formation after rectal resection in female patients. As there is no clear basis for expecting long-term improvement of defecation function and QOL by accepting reduction of QOL as a result of diverting stoma formation, a diverting stoma should be formed only in cases in which it is likely to be beneficial.

The incidence of anastomotic leakage was high in our patients, but mortality was low, suggesting that appropriate treatment was carried out. However, strategies to prevent anastomotic leakage are necessary.\(^26\) Many factors influence anastomotic leakage, but male gender is a common risk factor in many reports, but no specific countermeasures for males have been developed.\(^2\)^\(^-\)\(^4\),\(^25\),\(^27\)\(^-\)\(^29\) Diverting
Stoma formation has been proposed, but it is uncertain if this approach reduces the incidence of anastomotic leakage.4,25 A low incidence of anastomotic leakage has been reported in laparoscopic surgery, and we have introduced laparoscopic rectal resection and attempted to improve the quality of the operation by pursuing the Japan Society for Endoscopic Surgery (JSES) technical qualifications. Reduction of the incidence of anastomotic leakage is expected with improvement of the surgical technique,30 but male gender is still a risk factor for anastomotic leakage after laparoscopic surgery.29,31 In addition to the improvement of surgical quality, a new strategy such as transanal approach with intraoperative blood perfusion assessment might offer safe sphincter-preserving surgery to patients at high risk of anastomotic leakage.32,33 Given the high incidence of anastomotic leakage and high rate of permanent stoma formation as

| Variables                  | Univariate analysis | Multivariate analysis |
|----------------------------|---------------------|-----------------------|
| Age (y)                    |                     |                       |
| ≥65                        | 132                 | 16 (12.1) 0.074       |
| <65                        | 143                 | 29 (20.3)             |
| Gender                     |                     |                       |
| Female                     | 76                  | 10 (13.2) 0.467       |
| Male                       | 199                 | 35 (17.6)             |
| Body mass index (kg/m²)    |                     |                       |
| <25                        | 214                 | 35 (16.4) 1           |
| ≥25                        | 61                  | 10 (16.4)             |
| Ischemic disease           |                     |                       |
| No                         | 261                 | 43 (16.5) 1           |
| Yes                        | 14                  | 2 (14.3)              |
| Diabetes                   |                     |                       |
| No                         | 235                 | 40 (17.0) 0.644       |
| Yes                        | 14                  | 5 (12.5)              |
| ASA                        | 1, 2                | 245 40 (16.3) 1       |
| 3, 4                       | 30                  | 5 (16.7)              |
| Blood transfusion          |                     |                       |
| No                         | 266                 | 42 (15.8) 0.168       |
| Yes                        | 9                   | 3 (33.3)              |
| Tumor size (cm)            |                     |                       |
| <5                         | 157                 | 20 (12.7) 0.070       |
| ≥5                         | 118                 | 25 (21.2)             |
| Tumor location from AV (cm)|                     |                       |
| ≥5                         | 137                 | 16 (11.7) 0.049 1.98 (0.86-4.53) 0.107 |
| <5                         | 138                 | 29 (21.0)             |
| Anastomotic height from AV (cm)|       |                       |
| ≥4                         | 56                  | 5 (8.9) 0.107         |
| ≤4                         | 219                 | 40 (18.3)             |
| Circumferential occupation |                     |                       |
| No                         | 229                 | 36 (15.7) 0.516       |
| Yes                        | 46                  | 9 (19.6)              |
| Tumor depth                |                     |                       |
| T1, T2                     | 106                 | 15 (14.2) 0.504       |
| T3, T4                     | 169                 | 30 (17.8)             |
| Regional lymph node metastasis|                 |                       |
| No                         | 146                 | 21 (14.4) 0.415       |
| Yes                        | 129                 | 24 (18.6)             |
| Distant metastasis         |                     |                       |
| No                         | 243                 | 42 (17.3) 0.318       |
| Yes                        | 32                  | 3 (9.4)               |

(Continues)
As a result of poor healing after anastomotic leakage in male patients in the current study, it may be desirable to form a diverting stoma in males until identification of reliable predictors of a low risk of anastomotic leakage after low anastomosis. For patients with risk factors of local recurrence, the introduction of preoperative adjuvant therapy and precise assessment of tumor extension by high-resolution magnetic resonance imaging (MRI) could offer oncological safe sphincter-preserving surgery and justify inevitable abdominoperineal resection.

There are several limitations in the present study. First, it was carried out as a single-center retrospective observational study, and only a small number of patients treated with currently accepted laparoscopic surgery were included. The high rate of anastomotic leakage in this single center suggested that there might have been some technical problems which could be a limitation of this study. Second, only about 50% of patients responded to the questionnaire on evaluation of anal function, and the presence of a bias as a result
of non-respondents cannot be ruled out. Third, the subjects were patients who did not receive preoperative treatment. Such treatment for low rectal cancer is not specified as a standard approach in current Japanese guidelines, but preoperative chemoradiotherapy is standard treatment in Western countries. Our institution has formed a diverting stoma in patients treated with preoperative radiotherapy based on poor healing of the anastomosis region, and a diverting stoma may be significant for prevention of anastomotic leakage in female patients treated with preoperative radiotherapy. In contrast, favorable local outcomes have been reported in Europe for rectal cancer treated with surgery alone without preoperative treatment, with selection of patients based on preoperative high-resolution MRI. Patients similar to the subjects in the current study are likely to increase worldwide, and thus our results may be significant, despite the above limitations.

5 | CONCLUSIONS

Sphincter-preserving surgery for low rectal cancer without diverting stoma formation may be indicated for female patients. Male gender was a risk factor for anastomotic leakage in this procedure, with a permanent stoma as a result of anastomotic leakage formed in one in three male patients.

ACKNOWLEDGMENTS

The authors thank Motoi Koyama, Asuka Kamimura and Chiharu Yamada for their support of data collection.

DISCLOSURE

The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and conforms to the provisions of the Declaration of Helsinki. The study was approved by the Ethics Committee of our institution (2016-1006, 2016-1033). Conflict of Interest: Authors declare no conflicts of interest for this article.

REFERENCES

1. Marusch F, Koch A, Schmidt U, et al. Value of a protective stoma in low anterior resections for rectal cancer. Dis Colon Rectum. 2002;45:1164–71.
2. Eriksen MT, Wibe A, Norstein J, Haffner J, Wiig JN; Norwegian Rectal Cancer Group. Anastomotic leakage following routine mesorectal excision for rectal cancer in a national cohort of patients. Colorectal Dis. 2005;7:51–7.
3. Tan WS, Tang CL, Shi L, Eu KW. Meta-analysis of defunctioning stomas in low anterior resection for rectal cancer. Br J Surg. 2009;96:462–72.
4. Shiomi A, Ito M, Maeda K, et al. Effects of a diverting stoma on symptomatic anastomotic leakage after low anterior resection for rectal cancer: a propensity score matching analysis of 1,014 consecutive patients. J Am Coll Surg. 2015;220:186–94.
5. Huh JW, Park YA, Sohn SK. A diverting stoma is not necessary when performing a handsaw coloanal anastomosis for lower rectal cancer. Dis Colon Rectum. 2007;50:1040–6.
6. Koyama M, Murata A, Sakamoto Y, et al. Long-term clinical and functional results of intersphincteric resection for lower rectal cancer. Ann Surg Oncol. 2014;21(Suppl 3):S422–8.
7. Koyama M, Murata A, Sakamoto Y, et al. Risk factors for anastomotic leakage after intersphincteric resection without a protectivedefunctioning stoma for lower rectal cancer. Ann Surg Oncol. 2016;23(Suppl 2):S249–56.
8. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240:205–13.
9. Rahbari NN, Weitz J, Hohenberger W, et al. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. Surgery. 2010;147:339–51.
10. Celerier B, Denost Q, Van Geluwe B, Pontallier A, Rullier E. The risk of definitive stoma formation at ten years after low and ultra-low anterior resection for rectal cancer. Colorectal Dis. 2016;18:59–66.
11. Colvijn H, Mizushima T, Eguchi H, Takiguchi S, Doki Y, Mori M. Gastroenterological surgery in Japan: the past, the present and the future. Ann Gastroenterol Surg. 2017;1:5–10.
12. Shirouzu K, Murakami N, Akagi Y. Intersphincteric resection for very low rectal cancer: a review of the updated literature. Ann Gastroenterol Surg. 2017;1:24–32.
13. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum. 1993;36:77–97.
14. Hashimoto H, Shiokawa H, Funahashi K, et al. Development and validation of a modified fecal incontinence quality of life scale for Japanese patients after intersphincteric resection for very low rectal cancer. J Gastroenterol. 2010;45:928–38.
15. Kanda Y. Investigation of the freely available easy-to-use software ‘EZR’ for medical statistics. Bone Marrow Transplant. 2013;48:452–8.
16. Chun LJ, Haigh PI, Tam MS, Abbas MA. Defunctioning loop ileostomy for pelvic anastomoses: predictors of morbidity and nonclosure. Dis Colon Rectum. 2012;55:167–74.
17. Lindgren R, Hallbook O, Rutegard J, Sjodahl R, Matthiessen P. What is the risk for a permanent stoma after low anterior resection of the rectum for cancer? A six-year follow-up of a multicenter trial. Dis Colon Rectum. 2011;54:41–7.
18. Junghering T, Gonner U, Trinh TT, Lollert A, Oberholzer K, Berres M. Permanent stoma after low anterior resection for rectal cancer. Dis Colon Rectum. 2010;53:1632–9.
19. Dinnewitzer A, Jager T, Nawara C, Buchner S, Wolfgang H, Ofner D. Cumulative incidence of permanent stoma after sphincter preserving low anterior resection of mid and low rectal cancer. Dis Colon Rectum. 2013;56:1134–42.
20. Lim SW, Kim HJ, Kim CH, Huh JW, Kim YJ, Kim HR. Risk factors for permanent stoma after low anterior resection for rectal cancer. Langenbecks Arch Surg. 2013;398:259–64.
21. Kim MJ, Kim YS, Park SC, et al. Risk factors for permanent stoma after rectal cancer surgery with temporary ileostomy. Surgery. 2016;159:721–7.
22. Ashburn JH, Stocchi L, Kiran RP, Dietz DW, Remzi FH. Consequences of anastomotic leak after restorative proctectomy for cancer: effect on long-term function and quality of life. Dis Colon Rectum. 2013;56:275–80.
23. Bittorf B, Stadelmaier U, Merkel S, Hohenberger W, Matzel KE. Does anastomotic leakage affect functional outcome after rectal resection for cancer? Langenbecks Arch Surg. 2003;387:406–10.
24. Morgin C, Maggiori L, Agostini J, Ferron M, Panis Y. Does anastomotic leakage impair functional results and quality of life after laparoscopic sphincter-saving total mesorectal excision for rectal cancer? A case-matcheld study. Int J Colorectal Dis. 2014;29:459–67.
25. Law W, Chu KW, Ho JW, Chan CW. Risk factors for anastomotic leakage after low anterior resection with total mesorectal excision. Am J Surg. 2000;179:92–6.
26. Shimada H, Fukagawa T, Haga Y, Oba K. Does postoperative morbidity worsen the oncological outcome after radical surgery for gastrointestinal cancers? A systematic review of the literature. Ann Gastroenterol Surg. 2017;1:11–23.
27. Rullier E, Laurent C, Garrelon JL, Michel P, Saric J, Parmeix M. Risk factors for anastomotic leakage after resection of rectal cancer. Br J Surg. 1998;85:355–8.
28. Matthias P, Hallbook O, Andersson M, Rutegard J, Sjodahl R. Risk factors for anastomotic leakage after anterior resection of the rectum. Colorectal Dis. 2004;6:462–9.
29. Park JS, Choi GS, Kim SH, et al. Multicenter analysis of risk factors for anastomotic leakage after laparoscopic rectal cancer excision: the Korean laparoscopic colorectal surgery study group. Ann Surg. 2013;257:665–71.
30. Akiyoshi T, Ueno M, Fukunaga Y, et al. Incidence of and risk factors for anastomotic leakage after laparoscopic anterior resection with intracorporeal resection and double-stapling technique anastomosis for rectal cancer. Am J Surg. 2011;202:259–64.
31. Katsuno H, Shiomi A, Ito M, et al. Comparison of symptomatic anastomotic leakage following laparoscopic and open low anterior resection for rectal cancer: a propensity score matching analysis of 1014 consecutive patients. Surg Endosc. 2016;30:2848–56.
32. Jafari MD, Wexner SD, Martz JE, et al. Perfusion assessment in laparoscopic left-sided/anterior resection (PILLAR II): a multi-institutional study. J Am Coll Surg. 2015;220:82–92.
33. Penna M, Hompes R, Arnold S, et al. Transanal total mesorectal excision: international registry results of the first 720 cases. Ann Surg. 2017;266:111–7.
34. Battersby NJ, How P, Moran B, et al. Prospective validation of a low rectal cancer magnetic resonance imaging staging system and development of a local recurrence risk stratification model: the MERCURY II study. Ann Surg. 2016;263:751–60.
35. Glimelius B, Tiret E, Cervantes A, Arnold D. Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2013;24(Suppl 6):vi81–8.
36. Peeters KC, Tollenaar RA, Marijnen CA, et al. Risk factors for anastomotic failure after total mesorectal excision of rectal cancer. Br J Surg. 2005;92:211–6.
37. Taylor FG, Quirke P, Heald RJ, et al. Preoperative magnetic resonance imaging assessment of circumferential resection margin predicts disease-free survival and local recurrence: 5-year follow-up results of the MERCURY study. J Clin Oncol. 2014;32:34–43.