Diverting ileostomy versus no diversion after low anterior resection for rectal cancer: A prospective, randomized, multicenter trial

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Background. *This study sought to determine whether a protective diverting ileostomy improves short-term outcomes in patients with rectal resection and colonic J-pouch reconstruction for low anastomoses. Criteria for the use of a proximal stoma in rectal resections with colonic J-pouch reconstruction have not been defined sufficiently.*

Methods. *In a multicenter prospective study, rectal cancer patients with anastomoses below 8 cm treated with low anterior resection and colonic J-pouch were randomized to a defunctioning loop ileostomy or no ileostomy. The primary study endpoint was the rate of anastomotic leakage, and the secondary endpoints were surgical complications related to primary surgery, stoma, or stoma closure.*

Results. *From 2004 to 2014, a total of 166 patients were randomized to 1 of the 2 study groups. In the intention-to-treat analysis, the overall leakage rate was 5.8% in the stoma group and 16.3% in the no stoma group (*P = *.0441). However, some patients were not treated according to randomization and only 70% of our patients with low anastomoses received a pouch. Therefore, we performed a second analysis as to actual treatment. In this analysis, as well, leakage rates (*P = *.044) and reoperation rates for leakage (*P = *.021) were significantly higher in patients without a stoma. In multivariate analysis, male gender (*P = *.0267) and the absence of a stoma (*P = *.0092) were significantly associated with anastomotic leakage.*

Conclusion. *Defunctioning loop ileostomy should be fashioned in rectal cancer patients with anastomoses below 6 cm, particularly in male patients, even if reconstruction was done with a J-pouch. (Surgery 2016;159:1129-39.)*

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Low anterior rectal resection and abdominoperineal excision are the most effective treatments for localized rectal cancer. The introduction of total mesorectal excision (TME) was a major advance in the surgical strategy for rectal cancer, resulting in a reduction of local recurrence without adjuvant therapy. In radically operated patients, the local recurrence rates with TME after 5 and 10 years have been reported to be <10%, with a 5-year survival rate of 80%.[1-4]

Recent years have seen a decrease in the frequency of abdominoperineal resection in favor of sphincter-sparing procedures.[5] Although patient satisfaction and quality of life may be superior after sphincter-preserving surgery,[6] significant morbidity and mortality may occur, with anastomotic dehiscence being the primary concern.[7,8] The incidence of anastomotic leakage after anterior resection varies from 2 to 25%, depending on the level of anastomosis,[9] tumor diameter, tumor location, and absence of a protective stoma[10] or the method of reconstruction.[11-13] In patients with leaks and generalized abdominal sepsis,

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mortality rates of ≤50% have been reported,[2,14] whereas patients surviving the immediate consequences of anastomotic failure may expect a poor functional outcome owing to stenosis and reduced compliance of the neorectum.[15]

Therefore, it is the major goal of dedicated colorectal surgeons to prevent complications caused by anastomotic leaks subsequent to rectal surgery. For this purpose, several studies have suggested to fashion a protective stoma in patients undergoing TME with neoadjuvant treatment, in obese patients and those with low anastomoses and after technically demanding procedures.[16-18] However, the literature yields inadequate definitions as to the precise criteria for the use of a proximal stoma after elective rectal resections.

The role of a temporary diverting stoma in patients undergoing low anterior resection remains controversial. Some authors have considered the risk of leakage to be sufficiently low such that patients do not require diversion routinely.[19] Selective or nonroutine use of a fecal diversion is supported by the knowledge that both the application of a stoma and stoma reversal may cause significant morbidity and even mortality. Moreover, stoma reversal also implies a secondary hospital stay and several temporary stomas become permanent.[20,21]

Another technique reported to reduce possibly leakage rates is to perform a colonic J-pouch for reconstruction in low anastomoses.[12,13] A pouch may improve leakage rates most likely owing to an improved blood supply to the apex of the pouch[22] and may help to avoid a protective stoma.

The objective of this study was to determine whether a protective diverting ileostomy reduces the anastomotic leakage rate in patients with operable rectal cancer treated by mesorectal excision and colonic J-pouch for low anastomoses.

METHODS

Study design. The study was designed as a 2-arm, randomized, open-label, multicenter study in patients with operable rectal cancer. Preoperative screening and patient recruitment were performed in 3 participating colorectal centers in Austria. Patients were stratified by gender, anastomotic height, and preoperative radiochemotherapy to be operated either by rectal resection and coloanal/rectal anastomosis with a diverting ileostomy (group A) or rectal resection and coloanal/rectal anastomosis without protective ileostomy (group B). Patients in both groups with low anastomoses (<8 cm) were planned to receive a colonic J-pouch reconstruction. In accordance with the study protocol, all randomized patients were assessed preoperatively and during their hospital stay for primary surgery. Patients randomized for a diverting ileostomy were assessed additionally at the time of stoma reversal 8–10 weeks after the primary operation. Patients without protective stoma underwent a follow-up visit 10 weeks after the initial rectal resection. The study protocol was approved by the local ethics committees and institutional review boards of each participating center. Additionally, the study was registered in the International Standard Registered Clinical/Social Study Number registry under ISRCTN15655996.

Patient population and randomization. Patients aged 19–85 years with biopsy-proven and operable rectal cancer, with or without preoperative radiochemotherapy, a distal border of the tumor <16 cm from the anal verge as demonstrated by rigid rectoscopy, and a World Health Organization performance status of ≤2 were eligible for study inclusion. Patients with previous rectal surgery, emergency cases, planned laparoscopic resections, and those suffering from metastatic disease or synchronous colon cancer were excluded.

After completing preoperative rectal cancer staging and obtaining written informed consent, patients were randomized before surgery to either of the 2 groups using an Internet-based electronic randomization and documentation system. Randomization was performed using a dynamic 1:1 balanced allocation procedure with a block size of 4 (2 per group) and stratified by study site, gender, preoperative radiotherapy/chemotherapy, and anastomotic height (≤ 60 vs > 60 mm). The corresponding treatment group was obtainable after baseline assessments were performed and registered in the system. The data collected from each patient were documented using this online system and supported by automatic plausibility and completeness checks. The following data were gathered and collected prospectively: preoperative data (gender, age, body height and weight, body mass index, smoking habits, preoperative radiochemotherapy, tumor location, cTNM, blood chemistry including serum albumin, World Health Organization performance status), intraoperative data (anastomotic height, performance of a pouch, intraoperative blood loss, duration of surgery), postoperative data during primary hospitalization (anastomotic leakage, treatment of leakage, postoperative complications and morbidity, pTNM stage, duration of hospital stay) and data from hospital stay for ileostomy closure (days until closure, duration of stay, complications).

Study procedures. All patients underwent preoperative mechanical bowel preparation and received adequate thrombosis prophylaxis. Prophylactic intravenous single-shot antibiosis was given 30–60 minutes before the operation. A surgeon or stoma therapist marked the site of the stoma preoperatively in all patients.

The technique of surgical resection was constant; all of the operations were accomplished or assisted by only 3 surgeons. In both groups, surgery started with median laparotomy, followed by routine abdominal exploration to rule out distant metastasis. Complete mobilization of the left colonic flexure, high ligation of the inferior mesenteric vein, and flush ligation of the inferior mesenteric artery at the aorta, preserving the hypogastric nerves, was performed in all cases. Tumors of the mid and low rectum were resected by TME to the pelvic floor, whereas partial mesorectal excision with a resection margin of 5 cm below the tumor was considered sufficient for tumors of the upper rectal third (12–16 cm from the anal verge). In patients with anastomoses <8 cm from the anal verge, a colonic J-pouch was fashioned.[22] Double-stapled reconstruction was performed for most anastomoses; some very low anastomoses were hand sewn transanally. After completion of the anastomosis, anastomotic integrity was tested by underwater air insufflation. Patient withdrawal from the study was warranted if a primary leak of the anastomosis was identified intraoperatively. Each patient suffering from a primary leak after air insufflation underwent anastomotic repair and fecal diversion. Drainage was used optionally at the discretion of the surgeon.

In the postoperative course, a diatrizoic acid (Gastrografin) enema and/or computed tomography scan and/or sigmoidoscopy were performed immediately in patients with clinical signs of anastomotic leakage and further management was planned at the discretion of the surgeon in charge. In diverted patients suffering from leakage and in those primarily not defunctioned undergoing fecal diversion owing to anastomotic leakage in their postoperative course, follow-up visits to investigate anastomotic integrity were performed and stoma closure was performed after complete healing of the anastomoses. In all other patients, a Gastrografin enema was performed before release from the hospital. Stoma closure in an uneventful course was scheduled 8–10 weeks after the primary operation.

Endpoints. The primary efficacy endpoint of the present study was the overall anastomotic leakage rate as defined by one of the following: (1) radiologic leak: radiologic evidence of a leak in a Gastrografin enema and/or computed tomography scan without clinical signs of anastomotic leakage; (2) clinical leak: radiologic evidence of a leak in a Gastrografin enema and/or computed tomography scan and/or sigmoidoscopy with one or more of the following clinical signs: elevated temperature (>38°C), leukocytosis, peritonitis, putrid or fecal discharge over the drainage, or fistulas (rectovaginal).

Secondary endpoints were surgical complications related to the primary operation, to the stoma before closure, and to secondary surgery for stoma closure, and postoperative mortality defined as death on account of any cause during the hospital stay owing to the primary operation or stoma closure and the duration of hospital stay in days for the primary operation and stoma closure.

Statistical analyses. A maximum sample size of 210 patients was calculated as necessary to achieve 80% power with a 2-sided significance level of 5% and an expected leakage rate of 5% with and 17% without diverting ileostomy. Interim analyses were planned and accounted for in the sample size calculation. Together with an expected dropout rate of 5% before the end of the operative procedure, recruitment of 222 patients (111 group A, 111 group B) was calculated as necessary.

Interim analyses to detect a possible statistical difference in the primary endpoint (leak rate) were planned after one-quarter, one-half, and three-quarters of recruiting the planned sample size. The analyses were planned to reject the null hypothesis only with a Lan–DeMets alpha-spending function resembling an O'Brien-Fleming boundary for group sequential tests.

Patient characteristics were summarized with frequencies and percentages (for categorical variables) or with mean values ± standard deviation, median values, quartiles, range, and minimum and maximum values (for continuous variables). Statistical analysis was performed primarily according to the intention-to-treat (ITT) principle, that is, patients were analyzed according to their randomized treatment group.

Frequencies were compared by Fisher's exact test and differences in means were investigated with the Wilcoxon–Mann–Whitney *U* test for unpaired observations. Univariate and multivariate logistic regression was applied to assess the influence of patient characteristics on the leakage rate. Two-sided 95% CI were calculated and all reported *P*-values are 2-sided. Calculations were performed with SAS 9.2 software (SAS, Inc., Cary, NC).

Table I. Study population demography and surgical details (ITT)

	Randomized to stoma (n = *86*)	*Randomized to no stoma* (n = *80*)	P *value*
Age (y), median (range)	64 (37–84)	61 (30–84)	NS*
Gender (male/female)	49/37	48/32	NS†
Body height (cm), median (range)	170 (150–200)	170 (152–192)	NS*
Weight (kg), median (range)	75 (54–112)	76 (46–127)	NS*
BMI (kg/m^2), median (range)	26.1 (19.8–38.3)	25.8 (18.4–38.8)	NS*
Radiochemotherapy, *n* (%)	45 (52.3)	41 (51.3)	NS†
Tumor height (mm), median (range)	78 (38–150)	80 (40–150)	NS*
pT stage, *n* (%)			NS†
T1/2	32 (37.7)	37 (47.5)	
T3/4	45 (53.0)	38 (48.8)	
WHO performance status, *n* (%)			NS†
Grade 0	77 (89.5)	75 (93.8)	
Grade 1	9 (10.5)	4 (5.0)	
Grade 2	—	1 (1.3)	
ASA score, *n* (%)			NS†
I	6 (13.3)	11 (22.9)	
II	31 (68.9)	31 (64.6)	
III	8 (17.8)	6 (12.5)	
Anastomosis height (mm), median (range)	47 (28–95)	51(32–97)	NS*
J-pouch, *n* (%)	54 (62.8)	46 (58.2)	NS†
Intraoperative blood loss (mL), median (range)	230 (20–670)	240 (50–900)	NS*
Duration of surgery (min), median (range)	198 (95–650)	186 (75–735)	NS*

*Wilcoxon test.
†Fisher's exact test.
ASA, American Association of Anesthesiologists; *BMI*, body mass index; *NS*, not significant; *WHO*, World Health Organization.

RESULTS

Between January 2004 and August 2014, a total of 242 patients were screened for study inclusion in 3 Austrian colorectal service centers. Adhering to the inclusion and exclusion criteria, 166 patients were randomized after giving written informed consent.

The first and second interim analyses showed no difference regarding leakage rates. In September 2014, 166 patients (three-quarters of the planned sample size) were recruited and were included in the planned interim ITT analysis. Of these patients, 86 (51.8%) were randomized to group A (with diverting ileostomy) and 80 (48.2%) were randomized to group B (without diverting ileostomy). The analysis showed a significant difference in the leak rates. Owing to the significance reached after analyzing that sample size, and according to the protocol, the study was closed at that time.

ITT analysis. Overall, 166 randomized patients were included in the ITT analysis. Group comparisons between patients randomized to group A (with protective stoma) and to group B (without protective stoma) showed a well-balanced distribution of demographic and intraoperative variables (Table I).

Overall, anastomotic leakage occurred in 18 of 166 patients (10.8%). The leakage rate was significantly higher in patients without protective stoma. Five patients in group A versus 13 in group B developed a leak. Another analysis according to anastomotic height showed that 17 of 133 patients (12.8%) with anastomoses <60 mm from the anal verge and only 1 of 33 patients (3.0%) with an anastomosis >60 mm developed leakage. The leakage rate in patients with low anastomoses was also significantly higher in patients without defunctioning stoma. There was no difference in leak rates between participating hospitals. The reoperation rate was significantly higher in patients without protective ileostomy. Data are summarized in Table II.

Surgical details. Contrary to the study protocol, a diverting ileostomy was not performed in 13 patients (15%) randomized to group A (stoma group) who had changed their decision after randomization. In 21 patients (26%) randomized into group B (no stoma group), a protective ileostomy was performed based on the responsible

Table II. Anastomotic leakage (intention to treat)

Variable	*Randomized to stoma* (n = *86*), n (*%*)	*Randomized to no stoma* (n = *80*), n (*%*)	P *value*
Leakage overall	5 (5.8)	13 (16.3)	.0441*
Leakage by anastomotic height (mm)†			
≤60	4 (6.0)	13 (19.7)	.0206*
>60	1 (5.3)	—	NS
Treatment of leakage‡			.0006*
Conservative	4 (80.0)	1 (7.7)	
Surgical	1 (20)	12 (92.3)	

*Fisher's exact test.
†Percentages are based on the number of observations within each stratum.
‡Percentages are calculated in relation to the overall leakage rate in each group.
NS, Not significant.

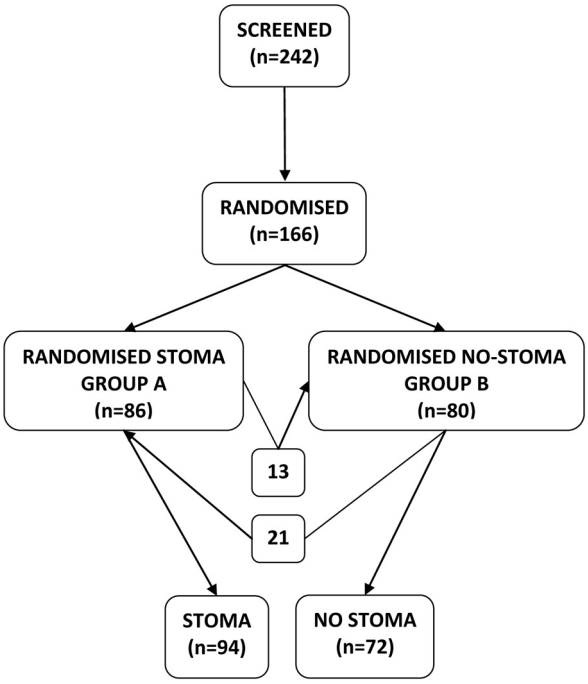

Fig. Study flow chart.

surgeon's intraoperative decision (Fig). Surgeons tended to defunction some patients with very low anastomoses or after neoadjuvant treatment despite randomization. Finally, 94 patients were treated with a protective ileostomy and 72 patients were not defunctioned. In addition, a colonic J-pouch could only be performed in 75% of patients with anastomoses <6 cm (98 of 133 patients) owing to technical reasons, such as a fatty colonic mesentery or a short colonic limb.

Therefore, we performed a secondary statistical analysis for the 2 groups as to actual treatment. In this analysis, patient and tumor characteristics and intraoperative parameters were unevenly distributed. There were significantly more patients with neoadjuvant treatment and lower tumor height in the stoma group. Anastomotic height was lower, intraoperative blood loss was greater, and duration of surgery was longer. In addition, significantly more pouches were fashioned in defunctioned patients (Table III).

In the as-treated analysis and the ITT analysis, a protective stoma was seen to lead to significantly reduced leakage and reoperation rates (Table IV). Anastomotic leaks occurred in 6 of 94 patients with a stoma versus 12 of 72 patients without a stoma ($P = .044$). Conservative treatment of anastomotic leakage was possible in 5 patients (3.0%) and included pharmacologic therapy and radiologically guided pelvic drainage or transanally applied Endo-Sponge therapy. Revision surgery was necessary in 13 of 166 patients (7.8%) and included the application of a protective stoma in patients without diversion after primary surgery, anastomotic renewal, oversewing of the leakage, or abdominoperineal resection with end colostomy and application of intraabdominal vacuum-assisted closure systems in cases of severe leakage with peritonitis. The reoperation rate for leakage was significantly lower in stoma patients compared with nonstoma patients ($P = .0217$).

In the subgroup of patients that had anastomoses <6 cm and J-pouch reconstruction (65 of 94 patients in group A and 33 of 72 patients in group B), a significant decrease in the number of leaks was seen in defunctioned patients. In the group with pouch and stoma, 4 of 65 patients developed a leak versus 7 of 33 patients with a pouch and no stoma ($P = .0399$).

Predictors of anastomotic leakage. Univariate and multivariate analyses of patient and tumor characteristics (age, gender, body mass index,

Table III. Study population demography and surgical details as actually treated

	Treated with stoma (n = *94*)	*Treated without stoma* (n = *72*)	P *value*
Age (y), median (range)	62.5 (41–84)	63 (30–84)	NS*
Gender (male/female)	59/35	38/34	NS†
Body height (cm), median (range)	172 (154–200)	169 (150–192)	NS*
Weight (kg), median (range)	76.5 (54–127)	75 (46–115)	NS*
BMI (kg/m^2), median (range)	26.1 (19.8–38.8)	25.8 (18.4–38.4)	NS*
Radiochemotherapy, *n* (%)	58 (61.7)	28 (38.9)	.0047†
Tumor height (mm), median (range)	70 (38–150)	90 (40–150)	.0014*
pT stage, *n* (%)			NS†
T1/2	38 (40.4)	31 (43.1)	
T3/4	48 (51.1)	35 (48.6)	
WHO performance status, *n* (%)			NS†
Grade 0	85 (90.4)	67 (93.1)	
Grade 1	9 (9.6)	4 (5.6)	
Grade 2	—	1 (1.4)	
ASA score, *n* (%)			NS†
I	8 (16.3)	9 (20.5)	
II	34 (69.4)	28 (63.6)	
III	7 (14.3)	7 (15.9)	
Anastomosis height (mm), median (range)	40 (28–99)	50 (30–99)	.0003*
J-pouch, *n* (%)	66 (70.2)	34 (47.9)	.0041†
Intraoperative blood loss (mL), median (range)	250 (0–670)	200 (50–900)	.0037*
Duration of surgery (min), median (range)	198 (95–650)	179 (75–330)	.0030*
Duration of hospital stay‡ (d), median (range)	17.0 (7.0–49.0)	12 (7.0–47.0)	.0002*

*Wilcoxon test.
†Fisher's exact test.
‡Duration of stay includes primary operation and stoma closure.
ASA, American Association of Anesthesiologists; *BMI*, body mass index; *NS*, not significant; *WHO*, World Health Organization.

Table IV. Anastomotic leakage (study population as actually treated)

Variable	*Treated with stoma* (n = *94*)	*Treated without stoma* (n = *72*)	P *value*
Leakage overall, *n* (%)	6 (6.4)	12 (16.7)	.0443*
Leakage by anastomotic height (mm), *n* (%)†			
≤60	6 (7.3)	11 (21.6)	.0300*
>60	—	1 (4.8)	NS
Treatment of leakage, *n* (%)‡			.0217*
Conservative	4 (66.7)	1 (8.3)	
Surgical	2 (33.3)	11 (91.7)	

*Fisher's exact test.
†Percentages are based on the number of observations within each stratum.
‡Percentages are calculated in relation to the overall leakage rate in each group.
NS, Not significant.

World Health Organization status, neoadjuvant therapy, serum albumin tumor height, pT stage) and surgery details (blood loss, duration of surgery, J-pouch, anastomotic height, stoma) showed that a protective stoma and female gender were the only parameters significantly associated with decreased leakage rates. Anastomotic height showed borderline significance. Logistic regression analyses to investigate predictive factors of anastomotic leakage are shown in Table V.

Complications, reoperation, and mortality. Postoperative complications within 30 days after primary surgery or stoma reversal occurred in 64 of 166 patients (38%). According to the Clavien-Dindo classification for surgical complications,[23,24] 102 patients (62%) did not show postoperative complications, 32 patients (19%) suffered from minor (grades I and II) and 32 patients (19%) from major complications (grades III and IV); no patient died.

Table V. Predictors of anastomotic leakage

Variable	*Univariate analysis*		*Multivariate analysis*	
	OR (95% CI)	P *value*	*OR (95% CI)*	P *value*
Age (y)	0.98 (0.94–1.03)	.3948	1.01 (0.93–1.08)	.8740
Gender (female vs male)	2.74 (0.86–8.72)	.0878	10.48 (1.31–83.68)	.0267
BMI (kg/m^2)	0.95 (0.84–1.07)	.3821	0.95 (0.78–1.17)	.6449
RCT* (yes vs no)	0.65 (0.24–1.78)	.4054	0.19 (0.02–1.57)	.1242
Tumor height (≤60 vs >60 mm)	1.05 (0.37–2.97)	.9243	2.70 (0.36–20.35)	.3354
pT stage (pT1/pT2 vs pT3/pT4)	0.52 (0.18–1.54)	.2375	0.41 (0.09–1.83)	.2401
Intraoperative blood loss (≤250 vs >250 mL)	1.18 (0.42–3.35)	.7532	2.15 (0.24–19.25)	.4955
Duration of surgery (≤180 vs >180 min)	0.76 (0.28–2.03)	.5808	0.72 (0.11–4.72)	.7352
J-pouch (pouch vs no pouch)	0.82 (0.29–2.35)	.7152	5.06 (0.49–52.57)	.1746
Anastomotic height (≤60 vs >60 mm)	0.21 (0.03–1.66)	.1404	0.02 (0.00–1.12)	.0574
Defunctioning stoma (no stoma vs stoma)	0.34 (0.12–0.96)	.0413	0.01 (0.00–0.34)	.0092

*Radiochemotherapy.
BMI, Body mass index; *OR*, odds ratio; *RCT*, randomized controlled trial.

Table VI. Postoperative complications and reoperations related to primary surgery and stoma closure* (study population as actually treated)

Variable	*Group A (stoma),* n = *94*		*Group B (no stoma),* n = *72*	
	Complication (n)	*Reoperation* (n)	*Complication* (n)	*Reoperation* (n)
Anastomotic leakage	6	2	12	11
Bowel obstruction	15	7	2	2
Wound infection	7	1	6	0
Cholecystitis	1	1	1	0
Fecal incontinence	1	0	—	—
SSRI related to port-a-cath infection	1	1	—	—
Bleeding	2	1	—	—
High-output stoma	2	0	—	—
Perianal thrombosis	1	0	—	—
Acute renal failure	1	0	—	—
Early postoperative hernia	—	—	2	2
Epilepsy (grand mal)	—	—	1	0
Pneumonia	2	0	—	—
Enterocutaneous fistula	1	0	—	—
Polyuria	1	0	—	—
Urinary tract infection	—	—	1	0
Diarrhea	—	—	1	0
Fixed drainage	—	—	1	1
Pulmonary edema	—	—	1	0
Thrombopenia (ITP)	—	—	1	1
Atrial fibrillation	—	—	1	0
Peritonitis	—	—	1	1
Pulmonary embolism	—	—	1	0

*Seven patients suffered from >1 complication.
ITP, Idiopathic thrombocytopenic purpura; *SIRS*, systemic inflammatory response syndrome.

The type and frequency of postoperative complications and the frequency of reoperations are shown in Table VI. Complications related to stoma closure occurred in 14 patients, reoperation was necessary in 2 of 3 patients for mechanical bowel obstruction, in 1 of 2 patients with postoperative bleeding, and in 1 of 7 patients for severe wound infection. Moreover, 1 patient developed acute renal failure and 1 patient an enterocutaneous fistula, which was treated conservatively after stoma closure. A comparison of overall complications and reoperation rates for complications (primary operation and ileostomy closure) between both groups failed to show differences. The total duration of stay was longer in stoma patients (17 vs 12 days; $P = .0002$).

Stoma reversal. Ninety-four patients received a stoma upon primary surgery; 92 patients had their stoma reversed after a median of 66 days (range, 21–309); 2 patients were not reoperated at the time of analysis. Two male patients who had not been defunctioned initially and developed leakage with severe sepsis underwent abdominoperineal excision and end colostomy.

DISCUSSION

Sphincter-sparing surgery represents the treatment of choice in rectal cancer surgery. Despite possible severe and life-threatening postoperative complications and the risk to develop a number of functional problems such as low anterior resection syndrome, quality of life seems to be improved in patients undergoing sphincter preservation.[6,25,26] However, short- and long-term postoperative outcomes and quality of life may be severely jeopardized by anastomotic leakage. Thus, it is a major goal to prevent leakages in sphincter-sparing surgery.[7,8] Despite excellent results in rectal surgery in terms of survival and local recurrence, leakage rates have not changed over the past decades and remain an unresolved surgical problem.

Several nonrandomized studies have argued that applying a defunctioning stoma may prevent anastomotic leakage and reduce the negative consequences of leakage, such as the rate of reoperations.[17,18] To date, only a few prospective trials have investigated the significance of fecal diversion after sphincter-sparing rectal resections.[16,27-32] Most of these studies are limited by small patient numbers[27-29] or deficient randomization,[30,31] leading to inconsistent results and conclusions.

The randomized multicenter trial authored by Matthiessen et al[16] was the first study to show a significant difference in leakage rates, with 28% in patients without defunctioning stoma compared with 10.3% in those who had been defunctioned. These investigators recommended the use of a defunctioning stoma in low anterior resection of the rectum, taking into account all aspects of a defunctioning stoma in terms of the need of secondary hospitalization and reoperation for stoma closure, complications caused by the stoma, and the fact that some protecting stomas become permanent. Forty percent of their patients were reconstructed with a colonic pouch. The overall higher leakage rate compared with our results can be explained by the fact that their study only included mid and low rectal cancer patients. Comparable leakage rates were identified in our patients with mid and low rectal tumors.

Another randomized trial also recommended a defunctioning loop ileostomy as routine procedure in patients undergoing lower rectal cancer surgery. In this trial, 256 patients were randomized to either of 2 arms. The anastomotic leak rate was significantly lower in defunctioned patients. However, this investigation only included patients with straight anastomoses.[32]

Very recently, an analysis of >1,000 patients performed in Japan reported that a diverting stoma failed to have a significant relationship with symptomatic leaks, whereas a stoma served to mitigate the consequences of leakage reducing the need for urgent abdominal reoperations. However, in their conclusion, these authors stated that it was not possible to present clear guidelines regarding criteria for stoma construction. Furthermore, they did not explore pouch rates in their study population.[33]

In contrast with our study, all these trials failed to investigate the influence of a colonic J-pouch in their study populations. To date, no randomized trial investigating the relevance of a protective stoma after anterior resection has considered the possible benefit of a J-pouch.

The application of a J-pouch may lead to decreased anastomotic complications owing to an improved blood supply to the apex of the pouch. Hallböök et al[22] performed a blood flow measurement study in rectal resections, comparing straight and colonic J-pouch reconstructions. Based on their results, these authors concluded that unaffected blood flow at the site of the anastomosis of the pouch may be a favorable factor for anastomotic healing.[22]

There is evidence that the application of a colonic J-pouch results not only in more favorable functional outcomes, but also in a slightly lower risk of anastomotic dehiscence compared with a straight colorectal or coloanal anastomosis.[12,13]

Based on this evidence, the construction of a J-pouch in all patients with anastomoses <80 mm from the anal verge was part of our study protocol. According to our protocol, we performed ITT analyses for the primary endpoint after randomization of one-quarter, one-half, and three-quarters of the calculated total sample size. The third interim analysis showed a significant difference in leak rates between the groups, and we terminated the study according to the protocol.

However, a number of patients were not treated as randomized. Twenty-six percent of patients randomized to the no stoma group received a stoma and 15% of the patients randomized to a stoma did not receive an ileostomy. Several patient

and tumor characteristics were distributed unevenly between the groups. Furthermore, 30% of our patients did not receive a pouch. Therefore, we performed additional analyses looking at the actual treatment of our patients. This as-treated analysis likewise showed a significant benefit for a protective ileostomy regarding leak rates and reoperation rates. This was also the case in the subgroup of pouch patients. The lacking impact of a pouch reconstruction on leakage rates was reported as well in a very recent metaanalysis by Hüttner et al.[34]

Intraoperative blood loss, duration of surgery, and total duration of stay were increased significantly for stoma patients. We not only found a significantly lesser leakage rate in patients with stoma compared with patients without diversion, but also demonstrated that anastomotic leakage in patients with stoma could be treated conservatively in the vast majority of cases. Only 1 patient in our stoma group required a revision operation.

Multivariate analysis showed that a defunctioning stoma and gender were the only factors associated significantly with anastomotic leakage, which is in accordance with other investigations.[35,37-39] Anastomotic height showed borderline significance. A pouch did not inhibit leakage.

Several factors of our study deserve mention. Overall the recruitment period was 10 years and several changes in the treatment of rectal cancer were introduced over the past years. Recruitment over time in our study was slow but constant; however, the treatment was standardized throughout the trial. Laparoscopy was an exclusion criterion because at the time the study was designed, there were not enough data to regard this approach as oncologically safe for rectal cancer. Neoadjuvant radiochemotherapy was standardized throughout the study following the protocol of the German trial CAO/ARO/AIO-94 by Sauer et al[40] and has not changed over the years. Fast track protocols[41,42] were adopted during the trial, yet this was the case in both groups at the same time and should not have influenced the results. A limiting factor of our study is that the full number of patients was not reached owing to the planned interim analysis. This could have led to a lack of significance of the secondary endpoints such as the influence of J-pouch in logistic regression. Furthermore, we were unable to perform a J-pouch in more than three-quarters of our patients, and several patients did not receive the treatment to which they were randomized. Despite these limitations, the impact of our study is supported by the prospective randomized approach and the thorough statistical methodology. The ITT analysis, the as-treated analysis, and the logistic regression showed consistent results regarding the impact of a protective stoma on leak rates and the lacking protective effect of a pouch.

We agree that the main advantages of a protecting stoma, such as decreased leakage rates and decreased rates of reoperations owing to leakage, should be well-balanced against the potential morbidity and mortality caused by stoma closure or the stoma itself.[16,18]

In our series, we found a low stoma-related complication rate. Postoperative complications owing to stoma reversal occurred in 14% of all patients who received a stoma, and reoperations for stoma complications were necessary in 4%. No patient died after stoma closure. These findings are comparable with other studies investigating the morbidity and mortality rates of diverting stomas.[16-21] Additionally, several risk factors leading to a permanent stoma in initially defunctioned patients after rectal resection must be considered.[35,36] In our series, only 2 patients were not reversed at the time of analysis.

Overall, particularly for male patients with low anastomoses, we argue in favor of the benefits of a protecting stoma, even in patients with colonic pouch reconstruction. Decreased anastomotic leakage and reoperation rates for leakage prevail over the risk of stoma-related morbidity and mortality and prolonged total duration of hospital stay.

In conclusion, and based on the results of our randomized multicenter trial, we recommend the application of a protective stoma in patients undergoing low anterior resection for carcinoma with anastomosis <6 cm, in particular in male patients. Even in patients treated with a J-pouch, a stoma should be performed, because an independent influence of diverting ileostomy has been demonstrated on anastomotic dehiscence. Possible stoma-related complications should not prevent surgeons from performing an ileostomy under defined conditions, because acceptable low stoma-related complication rates can be achieved.

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