Systematic Review and Meta-Analysis of the Role of Defunctioning Stoma in Low Rectal Cancer Surgery

Norbert Hüser, MD, Christoph W. Michalski, MD,* Mert Erkan, MD,* Tibor Schuster, MSc,† Robert Rosenberg, MD,* Jörg Kleeff, MD,* and Helmut Friess, MD**

Summary Background Data: The role of a defunctioning stoma in patients undergoing low anterior resection for rectal cancer is still the subject of controversy. Recent studies suggest reduced morbidity after low anterior rectal resection with a defunctioning stoma.

Methods: Retrospective and prospective studies published between 1966 and 2007 were systematically reviewed. Randomized controlled trials (RCTs) comparing anterior resections with or without defunctioning stoma were included in a meta-analysis. The pooled estimates of clinically relevant anastomotic leakages and of reoperations were analyzed using a random effects model (odds ratio and 95% confidence interval, CI).

Results: Relevant retrospective single (n = 18) and multicenter (n = 9) studies were identified and included in the systematic review. Analysis of incoherent data of the leakage rates in these nonrandomized studies demonstrated that a defunctioning stoma did not influence the occurrence of anastomotic failure but seemed to ameliorate the consequences of the leak. Four RCTs were included in the meta-analysis. The odds ratio for clinically relevant anastomotic leakage was 0.32 (95% CI 0.17–0.59), revealing a statistically significant benefit conferred through a defunctioning stoma ($Z = 3.65$, $P = 0.0003$). The odds ratio for reoperation because of leakage-caused complications was 0.27 (95% CI 0.14–0.51), with significantly fewer reoperations in patients with a defunctioning stoma ($Z = 3.95$, $P < 0.0001$). Overall mortality rates were comparable regardless of the presence of a defunctioning stoma.

Conclusion: A defunctioning stoma reduces the rate of clinically relevant anastomotic leakages and is thus recommended in surgery for low rectal cancers.

(*Ann Surg* 2008;248: 52–60)

Through a better understanding of the distal spread of rectal cancer, there has been a shift away from abdominoperineal resection toward sphincter-preserving surgery in low rectal cancer over the last decades.

From the *Department of Surgery, and †Institute of Medical Statistics and Epidemiology, Technische Universität München, Munich, Germany.
N.H., C.W.M. and M.E. contributed equally to this study.
Reprints: Helmut Friess, MD, Department of Surgery, Technische Universität München, Ismaningerstrasse 22, 81675 Munich, Germany. E-mail: friess@chir.med.tu-muenchen.de.

ISSN: 0003-4932/08/24801-0052
DOI: 10.1097/SLA.0b013e318176bf65

Surgical resection of the tumor is the gold standard. Nevertheless, multimodal regimens, particularly for locally advanced tumors, are well established[1] and performed sequentially with surgical treatment. One of the most important surgical complications after low rectal resection is anastomotic leakage, causing morbidity and mortality. The prevention of an anastomotic leakage after rectal resection by proximal fecal diversion – achieved either by a loop colostomy or a loop ileostomy – has been a subject of controversy for many years. However, prospective and retrospective studies have not shown any superiority of either loop colostomy or ileostomy.[2–6] In a recent meta-analysis, Tilney et al did not show any differences in colorectal anastomotic leakage rates between those patients defunctioned with an ileostomy and those with a colostomy.[7]

Although, defunctioning stomas are widely performed,[8–12] prospective randomized studies assessing their association with anastomotic failure are rare. It is still not clear whether fecal diversion has any impact on anastomotic leakage rate in general.[13–15] Possibly, a defunctioning stoma – placed to protect a low pelvic anastomosis – only ameliorates the septic effects of a leak, which potentially leads to pelvic abscess formation and peritonitis.[16,17]

The literature regarding the actual effects of a defunctioning stoma is particularly difficult to interpret. In nonrandomized studies there is a general patient selection bias favoring surgery without a stoma. This bias results from the selective creation of a stoma in patients in whom complications are anticipated. In fact, the development of an anastomotic dehiscence is associated with identified general risk factors such as male gender, malnutrition, preoperative weight loss, cardiovascular disease, steroid use, preoperative alcohol abuse, perioperative blood transfusions, advanced age of the patient, obesity, and previous irradiation.[11,13,18–24] Moreover, various studies have shown an increased leakage rate the closer the anastomosis site is to the anus.[13,14,19,21,22,25–29] Therefore, after the introduction of total mesorectal excision (TME),[30,31–33] morbidity resulting from anastomotic dehiscence also increased.[10] In this context, regardless of the level of anastomosis, a Cochrane review could not demonstrate any superiority of a hand sewn versus a stapled technique, and the superiority of a double layer versus a single layer anastomosis.[34,35]

A survey of the literature, and common sense, supports several favorable local conditions essential for primary anas-

tomotic healing. These include the interrelated phenomena of sufficient microvascularization and a tension-free anastomosis. Nevertheless, because failures have even occurred in cases of technically sound anastomoses involving healthy bowels, accurate placement of sutures, or a good blood supply, proponents of a protective stoma claim that it is not possible to predict the leakage of an anastomosis.

Therefore, the aim of this study was to systematically review the literature and to perform a meta-analysis of randomized trials investigating the value of a defunctioning ileostomy/colostomy after low anterior resection for rectal cancer.

METHODS

Search Strategy

Three authors independently performed a systematic literature search of the following databases as described previously[36]: National Center for Biotechnology Information, National Library of Medicine (PubMed; January 1966 to September 2007) and the Cochrane Central Register of Controlled Trials, with the last search on September 18, 2007. The Internet and the authors' libraries were also searched. The following medical subject headings were used: rectal cancer, stoma, defunctioning stoma, protective stoma, low anterior resection, surgery, and total mesorectal excision. There was no language restriction. Because the current analysis focused only on open rectal surgery, hand-assisted or completely laparoscopic operations were not included.

The bibliographies and all potentially relevant articles were then retrieved through the consensus of the investigators. Their reference lists were cross-searched to identify additional relevant articles. Study titles, abstracts and full texts were analyzed for the study design and the studies were stratified into groups of case reports, retrospective single center and multicenter studies, and randomized trials.

Data Extraction

The investigators analyzed the studies according to the type of rectal cancer surgery, whether a defunctioning stoma was applied, the overall mortality and morbidity, the number of clinically relevant anastomotic leakages, and the number of reoperations necessitated through a leak. Data collection and assessment of methodological quality were conducted following recently published protocols.[36] The conduct and reporting was in accordance with the QUOROM statement.[37] The methodological quality was assessed separately for all randomized controlled trials (RCTs) included (description of the randomization process and allocation concealment, definition of outcome parameters and complications, completeness of follow-up, and statistical analyses). Heterogeneity was evaluated by analyzing comparability of the following items: number of patients, grade or stage of disease, type of surgery performed, type of defunctioning stoma, and neoadjuvant or adjuvant treatment.

Inclusion and Exclusion Criteria

Case reports, articles presenting insufficient data on patient characteristics (specification of disease entities included, definition of anastomotic leakage, and description of the operative techniques) or outcomes (exact numbers regarding morbidity and mortality, in particular the number of anastomotic leakages, either clinical or radiologic), and studies lacking control groups were excluded.

Based on evidence mainly from nonrandomized studies, laparoscopic TME appears to have clinically measurable short term advantages in patients with primary resectable rectal cancer. These are mostly better quality of life in terms of genitourinary functions and shorter hospital stay. The most important reason for this is that by the laparoscopic approach, because of better visualization of the pelvic autonomic nerves, total preservation of these nerves without compromise of the radical extirpation of the tumor is technically feasible in the majority of patients with lower rectal cancer. Although, the long term impact on oncological endpoints awaits the findings from ongoing randomized trials, the results of large RCTs conducted on colon cancer suggest that there would also be adequate oncological results for laparoscopic approaches. In the present study, laparoscopic and hand-assisted laparoscopic surgical approaches were excluded for the analysis because these approaches are currently not used widespread, and because inclusion would further increase the heterogeneity of the included studies.

Relevant retrospective studies were included in the systematic review (Table 1). For inclusion in the meta-analysis, studies had to be randomized, comparing a defunctioning stoma with no stoma after anterior resections (standard, low, and ultralow) for rectal cancer. These studies had to report overall morbidity and mortality, particularly the number of clinically relevant anastomotic leakages and the number of reoperations because of anastomotic insufficiencies.

Statistical Analysis

A meta-analysis of anastomotic leakage and reoperations was performed as described previously[36] using the Review Manager (RevMan) software, version 4.2.8 (Cochrane Collaboration, Oxford, United Kingdom) followed by a quality of allocation concealment. Morbidity (anastomotic leakage, number of reoperations) and mortality in the respective study arms were estimated as a pooled odds ratio with 95% confidence intervals (C.I.) using the random effects model of DerSimonian and Laird.[38] Overall effects were calculated using the Z test. Statistical heterogeneity was assessed using the forest plot and I_2 statistics. Statistical significance was considered at $P < 0.05$.

RESULTS

Systematic Review of Retrospective and Prospective Nonrandomized Studies

The analyzed studies dated from January 1966 to September 2007 and contained 70 to 2729 patients. All articles reported clinically relevant – in some studies also only radiologically detected – anastomotic leakage (AL) rates, defined as the presence of abscess formation, in association with peritonitis and clinical signs such as fever, leukocytosis, and a tender abdomen. The extracted literature can be broadly divided into 3 categories: several authors advocate a selective

TABLE 1. Nonrandomised Studies Comparing Defunctioning Stoma and No Stoma

Author	Study Design	Yr	Type of Stoma	Patients (n)	Stoma/No Stoma (n)	Leaks Stoma/No Stoma (n)	Reoperations Stoma/No Stoma (n)	Irradiation (n)	Defined Criteria for Anastomotic Leakage*	Univariate/ Multivariate Analysis	Remarks
Bokey et al[51]	Retrospective single center	1995	Loop ileostomy > loop colostomy	413	109/304	21/45	n.sp.	n.sp.	Yes (clinical/ radiological)	Univariate	Patients evaluated only with anastomotic complications
Dehni et al[10]	Retrospective single center	1998	Loop ileostomy colostomy	258	152/106	8/18	6/17	Subgroup	Yes (clinical/ radiological)	Univariate	Level of anast. mentioned
Enker et al[44]	Retrospective single center	1999	Ileostomy colostomy	681	214/467	6/23	n.sp.	150 with pre-op. RCTx	Yes (clinical/ radiological)	Univariate	LAR with/without CAA
Eriksen et al[47]	Retrospective multicenter	2005	Ileostomy colostomy	1958	622/1336	64/164	n.sp.	59 preop/47 post-op.	Yes (clinical/ radiological)	Multivariate	Level of anastomosis mentioned
Fielding et al[43]	Retrospective multicenter	1984	Transverse sigmoid colostomy	2057	326/1731	58/126	n.sp.	n.sp.	Yes (clinical and radiological/ endoscopical)	Univariate	Including Intra-and extraperitoneal anastomoses
Gastinger et al[40]	Retrospective multicenter	2005	Ileostomy colostomy	2729	881/1848	128/262	32/186	119 (stoma) 80 (no stoma)	Yes (clinical/ radiological)	Multivariate	Not all TME, no difference. in overall leak rate between groups with/without stoma,protective stoma reduces incidence of AL that required surgical intervention
Giuliani et al[52]	Retrospective single center	2006	Mostly loop ileostomy	70	18/52	6/5	1/3	7 of 11 with anast. leak	Yes (clinical/ radiological)	Univariate	
Grabham et al[12]	Retrospective single center	1995	Colostomy	77	9/68	0/2	0/2	n.sp.	No	Univariate	Stoma protection only in intra-op. difficulties
Karanjia et al[13]	Retrospective single center	1994	Loop ileostomy colostomy	219	157/62	13/11	all with major leaks	n.sp.	Yes (clinical/ radiological)	Univariate	
Karanjia et al[8]	Retrospective single center	1991	Loop ileostomy colostomy	200	125/75	6/11	1/ n.i.	n.sp.	Yes (clinical/ radiological)	Univariate	
Kasperk et al[77]	Retrospective multicenter	2000	Mostly transverse colostomy	98	40/58	7/11	1/n.i.	n.sp.	Yes (clinical/ radiological)	Multivariate	
Kessler et al[53]	Retrospective multicenter	1993	n.sp.	621	115/506	10/78	n.sp.	113 pre-op.	Yes	Multivariate	High and low anterior resection
Law et al[11]	Retrospective single center	2000	Loop ileostomy	196	103/93	5/15	10 (n.sp.)	9	Yes (clinical and radiological/ endoscopycal)	Multivariate	TME only

(*Continued*)

TABLE 1. (*Continued*)

Author	Study Design	Yr	Type of Stoma	Patients (n)	Stoma/No Stoma (n)	Leaks Stoma/No Stoma (n)	Reoperations Stoma/No Stoma (n)	Irradiation (n)	Defined Criteria for Anastomotic Leakage*	Univariate/ Multivariate Analysis	Remarks
Law and Chu[48]	Retrospective single center	2004	Loop ileostomy loop colostomy	622	310/312	17/18	n.sp.	21 pre-op. 21 post-op.	Yes (clinical and radiological/ endoscopycal)	Multivariate	TME and PME
Lefebure et al[50]	Retrospective single center	2007	n.sp.	132	42/90	3/10	0/3	68 pre-op.	Yes (clinical followed by radiological)	Univariate	
Leester et al[42]	Retrospective single center	2002	Loop ileostomy	249	74/175	7/9	0/8	Subgroup	Yes (clinical followed by radiological)	Univariate	
Marusch et al[9]	Retrospective multicenter	2002	Ileostomy colostomy	482	148/334	16/35	2/23	Subgroup	Yes (clinical/ radiological)	Multivariate	Stoma in relation to level of anastomosis, no differenc in overall leak rate between groups with/without stoma, protective stoma reduces incidence of AL that required surgical intervention
Matthiessen et al[16]	Retrospective multicenter	2004	Ileostomy colostomy	432	72/360	11/42	1/32	n.sp.	Yes (clinical followed by radiological)	Multivariate	Multicenter, random sample of patients
Merad et al[45]	Retrospective multicenter	1998	Ileostomy colostomy	705	55/650	10/25	4/8	n.sp.	Yes (clinical/ radiological)	Univariate	Not all cancer patients
Pakkastie et al[27]	Retrospective single center	1994	7× loop transverse colostomy 1× loop ileostomy	134	8/126	1/15	n.sp	No	Yes (clinical followed by radiological or endoscopical)	Univariate	Level of anastomosis mentioned. Stoma protection only if intra-op. difficulties
Peeters et al[49]	Retrospective multicenter	2005	Ileostomy colostomy	924	523/401	43/64	n.sp	Subgroup	Yes (clinical followed by radiological)	Multivariate	
Poon et al[46]	Retrospective single center	1999	Ileostomy colostomy	148	61/87	2/11	0/7	n.sp.	Yes (clinical/ radiological)	Univariate	
Rudinskaite et al[20]	Retrospective single center	2005	n.sp.	269	45/224	7/13	n.sp	61	Yes (clinical followed by radiological)	Multivariate	Low and high anastomoses
Rullier et al[21]	Retrospective single center	1998	Ileostomy colostomy	272	114/158	20/12	6/7	Subgroup	Yes (clinical followed by radiological)	Multivariate	
Shukla and Pandey[78]	Retrospective single center	2005	n.sp.	168	63/105	6/9	2/10	n.sp.	No	n.i.	Level of anastomosis mentioned
Wong and Eu[39]	Retrospective single center	2005	Ileostomy (702) colostomy (40)	1066	742/324	28/13	39 (n.sp.)	No	Yes (clinical/ radiological)	Univariate	

*Clinical leakage is the leakage with fever, abscess, fecal discharge in drainage and/or sepsis signs requiring either surgical intervention or conservative therapy (antibiotics and parenteral nutrition). Radiological leakage is the leakage found on contrast enema and/or CT scan.

n.sp. indicates not specified; n.i., not indicated; LAR, low anterior resection; CAA, coloanal anastomosis; PME, partial mesorectal excision.

usage of defunctioning stomas, whereas some clearly reject, and some others suggest routine fecal diversion.

Studies on Selective Usage of Defunctioning Stomas

Recent studies have shown that a diverting stoma minimizes morbidity and complications but does not prevent the leakage itself. Therefore, Wong et al concluded from their study that a diverting stoma should not be performed routinely.[39] This was also recommended by Gastinger et al,[40] who found no difference in overall leakage rates between groups with/without a stoma but a significantly lower surgical intervention rate in those with a protective stoma ($P < 0.001$).

Karanjia et al recommended fecal stream diversion for low anastomosis; nevertheless they showed similar total leakage rates for patients with stoma and those who were not diverted.[13] However, they reported that more clinically verified, major leaks occurred in patients without a defunctioning stoma, suggesting colostomy as a precaution in case of TME with anastomoses within 6 cm or less of the anal verge.[8] Moreover, fecal peritonitis was seen in 8% of patients who had undergone anterior resection without a stoma, in contrast to a rate of 0.8% in patients with defunctioning colostomy.

In a Swedish investigation comparing the surgical outcomes of 2 hospitals which used similar operative techniques for resection of rectal cancer but had different policies regarding the use of a routine diverting stoma, there was no significant difference between the centers with regard to mortality, number of reoperations, or AL.[41]

According to a retrospective study performed by Pakkastie et al, a diverting stoma did not show a significant benefit for cancers of the midrectum. In contrast, in lower anastomoses (within 7 cm of the anal verge) without protective stoma, the leakage rate was higher (29%) than in patients with a stoma (13%).[27] The authors mentioned that all stomas were created due to technical difficulties and therefore reflect the surgeon's preference.[27]

This strategy was also applied by Grabham et al,[12] with an AL of 3% (n = 2) out of 77 patients undergoing low anterior resection. Seven patients were covered with a defunctioning stoma, and clinically relevant AL occurred in only 2 patients who had not received a defunctioning stoma. Consequently, a transverse colostomy had to be performed in these 2 patients.

Similarly, as demonstrated in retrospective analyses by Leester et al (249 patients),[42] Rudinskaite et al (269 patients),[20] and Rullier et al (272 patients)[21] creation of a defunctioning stoma did not prevent anastomotic insufficiency. Nevertheless, these groups collectively concluded that a protecting stoma is generally not recommended but should be used for patients in whom a higher risk of anastomotic failure is anticipated.

Studies That Reject the Use of Defunctioning Stomas

Fielding et al[43] found that 15.8% of their rectal cancer patients received a protective stoma and observed that there was a higher leakage rate in patients with a defunctioning stoma (17.8% out of 326 patients with stoma vs. 7.1% out of 1731 patients without, $P < 0.05$). Because there were no differences in mortality rates, they suggested that surgeons with an individual AL rate less than 5% need not create a defunctioning stoma at all.

Other groups also support the notion that the routine use of a diverting stoma in low anterior resection is not advisable. In a study of 681 consecutive patients, Enker et al showed that a diverting stoma did not reduce the incidence of AL in patients undergoing low or ultra low anterior resection.[44] No leaks developed in patients with coloanal anastomosis and a stoma, and 2 of 45 patients without diversion had an anastomotic failure.

There was also no statistically significant difference reported by Matthiessen et al,[16] who assessed the outcomes in patients with a temporary stoma (432 randomly selected patients) out of a total of 6833 patients who underwent selective anterior resection in Sweden (15% with vs. 12% without a temporary stoma).

Merad et al investigated the role of omentoplasty in the prevention of AL after colonic/rectal resection.[45] Patients who underwent fecal diversion paradoxically had 4 times the AL rate ($P < 0.0005$). However, diverting stomas were selectively placed, particularly according to the surgeon's preference, suggesting a selection bias toward patients in whom complications were anticipated.[45]

In a comparative study by Dehni et al on patients with low colorectal anastomoses, the clinical leakage rate was 6% with temporary stoma compared with 17% without a stoma.[10] The latter group was also significantly more likely to require unscheduled reoperation ($P = 0.006$) and to develop an AL ($P = 0.01$). Overall, the authors compared leakage rates of 258 consecutive patients with midrectal cancer localized 6–11 cm from the anal verge.

Studies Which Advocate Routine Use of Defunctioning Stomas

An analysis by Poon et al reported a clinical leakage rate of 3.3% for patients with versus 12.6% without a stoma.[46] The results of a study by Eriksen et al[47] and a multicenter trial involving 75 German hospitals[9] also indicated a protective effect of a stoma for low anastomosis in reducing clinical AL.

In case of low anterior resection and TME, Law et al furthermore suggested the routine use of a protective stoma, based on their experience in 2 retrospective studies of 196[11] and 622[48] patients. The gender of the patients and the presence of a stoma ($P = 0.008$,[11]) were identified as the most important and independent risk factors for AL.

In a Dutch TME trial, the presence of 1 or more pelvic drains after surgery, and placement of a protective stoma, was significantly associated with decreased clinical leakage rates in patients undergoing TME for rectal cancer ($P < 0.001$,[49]). Nevertheless, Peeters et al pointed out that this trial was not set up to answer questions regarding AL, and therefore these observations have to be viewed critically.[49]

Results of a recent retrospective study by Lefebure et al indicate a protective effect of diverting stoma for low anterior resection, confirmed by a reduced clinical AL rate.[50] With a low rate of clinically significant AL in the diverting stoma

group in an Australian study by Bokey et al,[51] the authors called for the general use of a diverting stoma in rectal cancer resection. However, there was no statistically significant difference in the frequency of clinically relevant leaks in patients with or without proximal stoma, but a significantly higher incidence of localized leaks in patients with a stoma. Thus, it is likely that if a stoma had not been present in these patients, many might have developed severe complications.

In an analysis of a smaller group of patients, Giuliani et al reported that less surgical intervention was required in the group of patients with a defunctioning stoma; therefore, they recommended a defunctioning stoma for all patients with low rectal cancer in whom TME is performed after neoadjuvant radiochemotherapy.[52]

In a German multicenter study, an AL was observed in only 8.7% of the defunctioned patients (10 of 115) as compared with 15.4% if a protective stoma was not placed (78 of 506).[53] Although, these findings were not statistically significant, Kessler et al advised that a protective stoma be used.[53]

Meta-analysis of Randomized Controlled Trials

Four randomized controlled trials were suitable for meta-analysis.[54–57] In the first study by Graffner et al, 50 patients were randomized into 2 groups: 25 received a defunctioning colostomy and 25 received no stoma.[54] Clinically relevant anastomotic leaks developed in 3 patients who were not defunctioned and in 1 patient who had received a protective colostomy. All 3 patients with an anastomotic leak received emergency colostomies because of abscess formation and sepsis. The overall leakage rate was 8% (4% in the stoma group and 12% in the no-stoma group).

Pakkastie et al showed a clinical leakage rate of 16% in the colostomy group (3/19), whereas 32% of patients without a defunctioning stoma developed clinically evident leakage (6/19;[55]). Although all patients with a leak in the no-stoma group had to be reoperated, only 1 reoperation was necessary in the patients with a defunctioning colostomy.

The study by Pimentel et al has so far only been published in abstract form.[56] Therefore, an assessment of methodological quality was not possible. Because figures for leakage rates and reoperations were described, this study could be included in the meta-analysis. A total of 36 patients with distal rectal cancer undergoing low anterior resection with total mesorectal excision (plus colonic J-pouch) were randomized into 2 groups of 18 patients. Two patients in the nondefunctioned group developed an anastomotic leak, whereas only 1 patient in the group of patients with a stoma had an insufficiency. The overall leakage rate was 11.1% (5.6% in the stoma group and 16.6% in the nondefunctioned group). The nondefunctioned patients with a clinically relevant leak had to be reoperated and a stoma was constructed.

The largest study on the role of a defunctioning stoma in rectal cancer surgery was recently published by Matthiessen et al.[57] Two hundred and thirty-four patients were randomized into 2 arms: defunctioning stoma versus no stoma (ileostomy or colostomy was chosen by the operating surgeon). An anastomotic leak developed in 10.3% (12/116) of patients with a stoma and in 28% (33/118) of nondefunctioned patients. This difference was statistically significant ($P < 0.001$). As expected, the number of reoperations was significantly higher in the group of patients without a stoma (30/118, vs. 10/116 with a stoma; $P < 0.001$). Therefore, although the first 3 studies revealed only a trend towards a protective role of a defunctioning stoma, there was a significantly lower number of clinically symptomatic leakages and fewer reoperations in the group of patients with a defunctioning stoma in the study by Matthiessen et al.[57]

These results are further underlined by our meta-analysis showing an odds ratio of 0.32 (95% C.I. 0.17–0.59) for anastomotic leakage. This reveals a statistically significant benefit conferred through a defunctioning stoma ($Z = 3.65$, $P = 0.0003$; Fig. 1). Regarding the number of reoperations, the meta-analysis demonstrated an odds ratio of 0.27 (95% C.I. 0.14–0.51) for reoperation because of leakage-caused complications, with significantly fewer reoperations in patients with a defunctioning stoma ($Z = 3.95$, $P < 0.0001$; Fig. 2). The perioperative mortality rates were comparable between the groups (Fig. 3). However, the study by Graffner et al had to be excluded from the mortality meta-analysis because the authors did not report to which group the patient who died in the postoperative course had been randomized.[54] Furthermore, Matthiessen et al showed that mortality after elective reversal of the stoma was also low (1/111, 0.9%).[57]

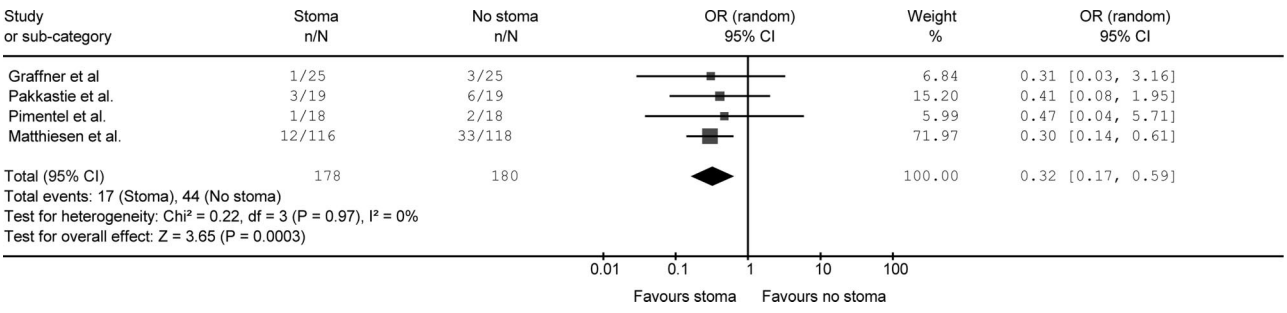

FIGURE 1. Meta-analysis of leakage rates in the RCTs. Odds ratio estimates for leakage rates in the groups of patients with a defunctioning stoma versus no stoma were calculated using the random effects model. The diamond represents the overall treatment effect from the pooled studies spanning the 95% CI. The leakage rate is significantly higher in the no-stoma groups ($P = 0.003$). Test for heterogeneity: $\chi^2 = 0.22$, 3 d.f., $P = 0.97$, $I^2 = 0\%$. Test for overall effect: $Z = 3.65$, $P = 0.0003$. Values in parentheses are 95% CIs.

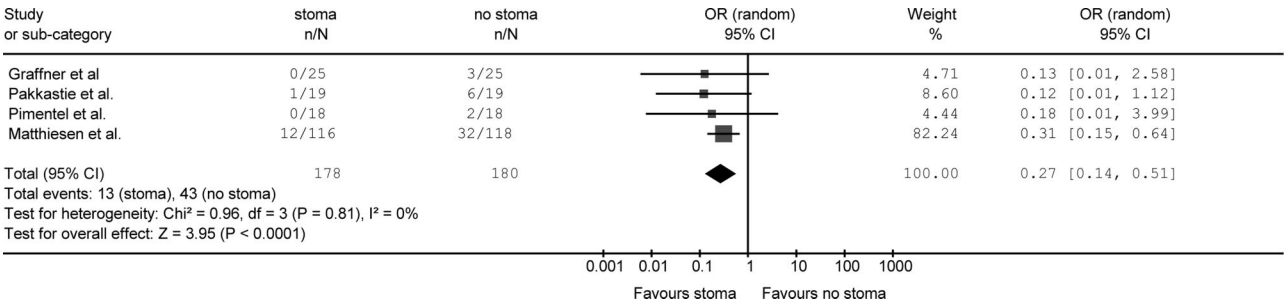

FIGURE 2. Meta-analysis of the number of reoperations in the RCTs. Odds ratio estimates for the number of reoperations in the groups of patients with a defunctioning stoma versus no stoma were calculated using the random effects model. The diamond represents the overall treatment effect from the pooled studies spanning the 95% CI. The number of reoperations is significantly higher in the no-stoma groups ($P < 0.0001$). Test for heterogeneity: $\chi^2 = 0.96$, 3 d.f., $P = 0.81$, $I^2 = 0\%$. Test for overall effect: $Z = 3.95$, $P < 0.0001$. Values in parentheses are 95% CIs.

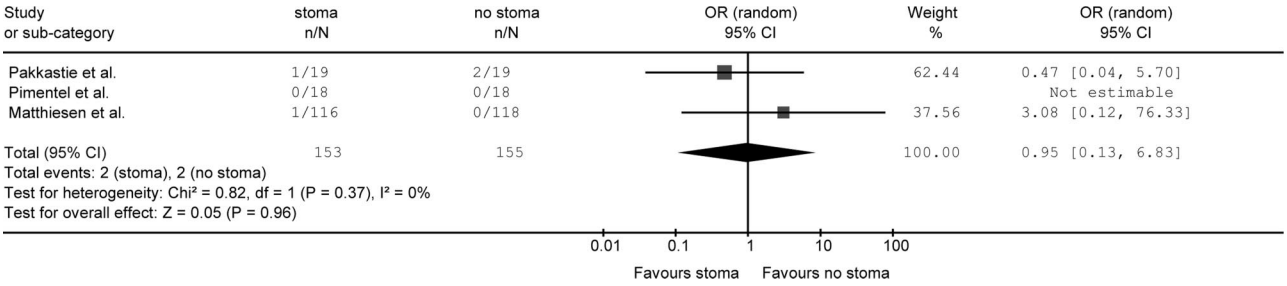

FIGURE 3. Meta-analysis of mortality in the RCTs. Odds ratio estimates for overall mortality in the groups of patients with a defunctioning stoma versus no stoma were calculated using the random effects model. The study by Graffner et al had to be excluded from the mortality meta-analysis because it did not report to which group the patient who died in the postoperative course had been randomized. Overall mortality is comparable in both groups. Test for heterogeneity: $\chi^2 = 0.82$, 1 d.f., $P = 0.37$, $I^2 = 0\%$. Test for overall effect: $Z = 0.05$, $P = 0.96$. Values in parentheses are 95% CIs.

DISCUSSION

AL increases the postoperative mortality rate because of septicaemia and peritonitis, at a rate between 6% and 22%.[21,28,58] Furthermore, it has been shown to decrease long-term survival and to increase local tumor recurrence.[59,60] In an effort to overcome these problems, some surgeons have advocated the usage of fecal diversion.

However, the value of a defunctioning stoma has been the subject of controversy for a long time. Earlier randomized studies were rather inconclusive but showed a trend toward fewer anastomotic leaks and reoperations after low anterior resection with a defunctioning stoma. This meta-analysis showed a clear benefit conferred by constructing a defunctioning stoma, with significantly lower leakage and reoperation rates, whereas mortality rates remained comparable between the groups. Because of the low patient numbers in the 3 previously published RCTs, this meta-analysis was mostly influenced by the recently published and largest randomized trial – that of Matthiessen et al.[57] Therefore, we have to mainly base our conclusions upon this particular study. Interestingly, when calculating the meta-analysis without the Matthiessen study and when analyzing the rate of anastomotic leakages, there was still a trend in favor of the application of a stoma ($P = 0.11$); in addition, regarding reoperations, our recalculated meta-analysis revealed a statistically significant difference in favor of a defunctioning stoma ($P = 0.01$). Furthermore, with regard to morbidity, all studies favored the creation of a defunctioning stoma, which reduced the leakage rates and number of reoperations.

No clear conclusion can be drawn from the nonrandomized studies. This is primarily due to their considerable selection bias. Because construction of a stoma was largely left to the discretion of the surgeon, it is likely that more patients in whom a "risky" anastomosis was anticipated were included in the defunctioning stoma group. However, there was no general trend toward giving up the use of a stoma. In fact, such studies provide further evidence in favor of the stoma: despite the positive selection bias toward no stoma, patients with a defunctioning stoma fared no worse.

Because the sample size in some (retrospective) studies is rather low, there is likely a lack of power for some of the studies. However, inasmuch as retrospective studies were included only into the systematic review, we aimed to provide both, a general survey about the results of all retrospective studies and evidence about an expected underlying "true effect." Thus, even the less powered trials (in combination with the larger trials) seem to have an impact on the overall estimation of the effect of a diverting stoma and its degree of confidence by increasing the total sample size. Furthermore, the study by Matthiessen et al[57] which was included in the meta-analysis is based on a large number of patients, and this

number was more than sufficient to show a statistically significant benefit of construction of a defunctioning stoma.

However, a number of points remain to be evaluated critically. First, routine creation of a stoma will reduce the quality of life in the subgroup of patients in whom no complications would occur. Second, selective or nonroutine use of fecal diversion is supported by the knowledge that stoma placement itself is a source of morbidity[61,62] reported to be as high as 30%.[4,61,63–67] These complications may even lead to mortality after elective reversal of the stoma (ie, 0–2.3%[46,57,63,66,68–70]). Furthermore, the closure of a diverting stoma requires a second hospital stay and additional surgery and is accompanied by considerable patient management costs.[71]

Finally, although there are no clear data on the long term functional results after an anastomotic leak/pelvic sepsis in low rectal cancer, there is a convincing body of evidence stemming from studies on J-pouch reservoirs in inflammatory bowel diseases.[72–76] These studies indicate that pelvic sepsis not only affects the pouch itself, but also distorts the pelvic apparatus, creating continence-related problems. Such concerns most likely will apply for low/ultra-low anastomosis after cancer surgery. Moreover, the increased risk of local and metastatic recurrence after pelvic sepsis is another reason why pelvic sepsis should be avoided as much as possible by fecal diversion.[70]

In conclusion, this meta-analysis shows that a defunctioning stoma reduces the rate of clinically relevant anastomotic leaks and thus is recommended in surgery for low rectal cancers.

REFERENCES

1. Morton DG, Sebag-Montefiore D. Defunctioning stomas in the treatment of rectal cancer. *Br J Surg*. 2006;93:650–651.
2. Williams NS, Nasmyth DG, Jones D, et al. De-functioning stomas: a prospective controlled trial comparing loop ileostomy with loop transverse colostomy. *Br J Surg*. 1986;73:566–570.
3. Rullier E, Le Toux N, Laurent C, et al. Loop ileostomy versus loop colostomy for defunctioning low anastomoses during rectal cancer surgery. *World J Surg*. 2001;25:274–277; discussion 277–278.
4. Gooszen AW, Geelkerken RH, Hermans J, et al. Temporary decompression after colorectal surgery: randomized comparison of loop ileostomy and loop colostomy. *Br J Surg*. 1998;85:76–79.
5. Rutegard J, Dahlgren S. Transverse colostomy or loop ileostomy as diverting stoma in colorectal surgery. *Acta Chir Scand*. 1987;153:229–232.
6. Khoury GA, Lewis MC, Meleagros L, et al. Colostomy or ileostomy after colorectal anastomosis? a randomised trial. *Ann R Coll Surg Engl*. 1987;69:5–7.
7. Tilney HS, Sains PS, Lovegrove RE, et al. Comparison of outcomes following ileostomy versus colostomy for defunctioning colorectal anastomoses. *World J Surg*. 2007;31:1142–1151.
8. Karanjia ND, Corder AP, Holdsworth PJ, et al. Risk of peritonitis and fatal septicaemia and the need to defunction the low anastomosis. *Br J Surg*. 1991;78:196–198.
9. Marusch F, Koch A, Schmidt U, et al. Value of a protective stoma in low anterior resections for rectal cancer. *Dis Colon Rectum*. 2002;45:1164–1171.
10. Dehni N, Schlegel RD, Cunningham C, et al. Influence of a defunctioning stoma on leakage rates after low colorectal anastomosis and colonic J pouch-anal anastomosis. *Br J Surg*. 1998;85:1114–1117.
11. Law WI, Chu KW, Ho JW, et al. Risk factors for anastomotic leakage after low anterior resection with total mesorectal excision. *Am J Surg*. 2000;179:92–96.
12. Grabham JA, Moran BJ, Lane RH. Defunctioning colostomy for low anterior resection: a selective approach. *Br J Surg*. 1995;82:1331–1332.
13. Karanjia ND, Corder AP, Bearn P, et al. Leakage from stapled low anastomosis after total mesorectal excision for carcinoma of the rectum. *Br J Surg*. 1994;81:1224–1226.
14. Mealy K, Burke P, Hyland J. Anterior resection without a defunctioning colostomy: questions of safety. *Br J Surg*. 1992;79:305–307.
15. Antonsen HK, Kronborg O. Early complications after low anterior resection for rectal cancer using the EEA stapling device. A prospective trial. *Dis Colon Rectum*. 1987;30:579–583.
16. Matthiessen P, Hallbook O, Andersson M, et al. Risk factors for anastomotic leakage after anterior resection of the rectum. *Colorectal Dis*. 2004;6:462–469.
17. Schmidt O, Merkel S, Hohenberger W. Anastomotic leakage after low rectal stapler anastomosis: significance of intraoperative anastomotic testing. *Eur J Surg Oncol*. 2003;29:239–243.
18. Makela JT, Kiviniemi H, Laitinen S. Risk factors for anastomotic leakage after left-sided colorectal resection with rectal anastomosis. *Dis Colon Rectum*. 2003;46:653–660.
19. Schrock TR, Deveney CW, Dunphy JE. Factor contributing to leakage of colonic anastomoses. *Ann Surg*. 1973;177:513–518.
20. Rudinskaite G, Tamelis A, Saladzinskas Z, et al. Risk factors for clinical anastomotic leakage following the resection of sigmoid and rectal cancer. *Medicina* (*Kaunas*). 2005;41:741–746.
21. Rullier E, Laurent C, Garrelon JL, et al. Risk factors for anastomotic leakage after resection of rectal cancer. *Br J Surg*. 1998;85:355–358.
22. Vignali A, Fazio VW, Lavery IC, et al. Factors associated with the occurrence of leaks in stapled rectal anastomoses: a review of 1,014 patients. *J Am Coll Surg*. 1997;185:105–113.
23. Kapiteijn E, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med*. 2001;345:638–646.
24. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med*. 2004;351:1731–1740.
25. Merad F, Hay JM, Fingerhut A, et al. Is prophylactic pelvic drainage useful after elective rectal or anal anastomosis? A multicenter controlled randomized trial. French Association for Surgical Research. *Surgery*. 1999;125:529–535.
26. Malmberg M, Graffner H, Ling L, et al. Recurrence and survival after anterior resection of the rectum using the end to end anastomotic stapler. *Surg Gynecol Obstet*. 1986;163:231–234.
27. Pakkastie TE, Luukkonen PE, Jarvinen HJ. Anastomotic leakage after anterior resection of the rectum. *Eur J Surg*. 1994;160:293–297; discussion 299–300.
28. Fielding LP, Stewart-Brown S, Blesovsky L, et al. Anastomotic integrity after operations for large-bowel cancer: a multicentre study. *Br Med J*. 1980;281:411–414.
29. Morgenstern L, Yamakawa T, Ben-Shoshan M, et al. Anastomotic leakage after low colonic anastomosis. Clinical and experimental aspects. *Am J Surg*. 1972;123:104–109.
30. Heald RJ. A new approach to rectal cancer. *Br J Hosp Med*. 1979;22:277–281.
31. Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet*. 1986;1:1479–1482.
32. Enker WE, Pilipshen SJ, Heilweil ML, et al. En bloc pelvic lymphadenectomy and sphincter preservation in the surgical management of rectal cancer. *Ann Surg*. 1986;203:426–433.
33. Enker WE, Thaler HT, Cranor ML, et al. Total mesorectal excision in the operative treatment of carcinoma of the rectum. *J Am Coll Surg*. 1995;181:335–346.
34. Lustosa SA, Matos D, Atallah AN, et al. Stapled versus handsewn methods for colorectal anastomosis surgery: a systematic review of randomized controlled trials. *Sao Paulo Med J*. 2002;120:132–136.
35. Lustosa SA, Matos D, Atallah AN, et al. Stapled versus handsewn methods for colorectal anastomosis surgery. *Cochrane Database Syst Rev*. 2001:CD003144.
36. Michalski CW, Kleeff J, Wente MN, et al. Systematic review and meta-analysis of standard and extended lymphadenectomy in pancreaticoduodenectomy for pancreatic cancer. *Br J Surg*. 2007;94:265–273.

37. Turpin DL. CONSORT and QUOROM guidelines for reporting randomized clinical trials and systematic reviews. *Am J Orthod Dentofacial Orthop*. 2005;128:681–685; discussion 686.
38. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7:177–188.
39. Wong NY, Eu KW. A defunctioning ileostomy does not prevent clinical anastomotic leak after a low anterior resection: a prospective, comparative study. *Dis Colon Rectum*. 2005;48:2076–2079.
40. Gastinger I, Marusch F, Steinert R, et al. Protective defunctioning stoma in low anterior resection for rectal carcinoma. *Br J Surg*. 2005;92:1137–1142.
41. Machado M, Hallbook O, Goldman S, et al. Defunctioning stoma in low anterior resection with colonic pouch for rectal cancer: a comparison between two hospitals with a different policy. *Dis Colon Rectum*. 2002;45:940–945.
42. Leester B, Asztalos I, Polnyib C. Septic complications after low anterior rectal resection–is diverting stoma still justified? *Acta Chir Iugosl*. 2002;49:67–71.
43. Fielding LP, Stewart-Brown S, Hittinger R, et al. Covering stoma for elective anterior resection of the rectum: an outmoded operation? *Am J Surg*. 1984;147:524–530.
44. Enker WE, Merchant N, Cohen AM, et al. Safety and efficacy of low anterior resection for rectal cancer: 681 consecutive cases from a specialty service. *Ann Surg*. 1999;230:544–552; discussion 552–554.
45. Merad F, Hay JM, Fingerhut A, et al. Omentoplasty in the prevention of anastomotic leakage after colonic or rectal resection: a prospective randomized study in 712 patients. French Associations for Surgical Research. *Ann Surg*. 1998;227:179–186.
46. Poon RT, Chu KW, Ho JW, et al. Prospective evaluation of selective defunctioning stoma for low anterior resection with total mesorectal excision. *World J Surg*. 1999;23:463–467; discussion 467–468.
47. Eriksen MT, Wibe A, Norstein J, et al. Anastomotic leakage following routine mesorectal excision for rectal cancer in a national cohort of patients. *Colorectal Dis*. 2005;7:51–57.
48. Law WL, Chu KW. Anterior resection for rectal cancer with mesorectal excision: a prospective evaluation of 622 patients. *Ann Surg*. 2004;240:260–268.
49. Peeters KC, Tollenaar RA, Marijnen CA, et al. Risk factors for anastomotic failure after total mesorectal excision of rectal cancer. *Br J Surg*. 2005;92:211–216.
50. Lefebure B, Tuech JJ, Bridoux V, et al. Evaluation of selective defunctioning stoma after low anterior resection for rectal cancer. *Int J Colorectal Dis*. 2008;23:283–288.
51. Bokey EL, Chapuis PH, Fung C, et al. Postoperative morbidity and mortality following resection of the colon and rectum for cancer. *Dis Colon Rectum*. 1995;38:480–486; discussion 486–487.
52. Giuliani D, Willemsen P, Van Elst F, et al. A defunctioning stoma in the treatment of lower third rectal carcinoma. *Acta Chir Belg*. 2006;106:40–43.
53. Kessler H, Hermanek P Jr, Wiebelt H. Operative mortality in carcinoma of the rectum. Results of the German Multicentre Study. *Int J Colorectal Dis*. 1993;8:158–166.
54. Graffner H, Fredlund P, Olsson SA, et al. Protective colostomy in low anterior resection of the rectum using the EEA stapling instrument. A randomized study. *Dis Colon Rectum*. 1983;26:87–90.
55. Pakkastie TE, Ovaska JT, Pekkala ES, et al. A randomised study of colostomies in low colorectal anastomoses. *Eur J Surg*. 1997;163:929–933.
56. Pimentel JM, Duarte A, Patricio J. The role of a protecting stoma in low anterior resection with TME and colonic J-pouch for rectal cancer; results of a prospective randomized trial. *Colorectal Dis*. 2003;5(suppl. 2):83.
57. Matthiessen P, Hallbook O, Rutegard J, et al. Defunctioning stoma reduces symptomatic anastomotic leakage after low anterior resection of the rectum for cancer: a randomized multicenter trial. *Ann Surg*. 2007;246:207–214.
58. McArdle CS, Hole D. Impact of variability among surgeons on postoperative morbidity and mortality and ultimate survival. *Bmj*. 1991;302:1501–1505.
59. Fujita S, Teramoto T, Watanabe M, et al. Anastomotic leakage after colorectal cancer surgery: a risk factor for recurrence and poor prognosis. *Jpn J Clin Oncol*. 1993;23:299–302.
60. Akyol AM, McGregor JR, Galloway DJ, et al. Anastomotic leaks in colorectal cancer surgery: a risk factor for recurrence? *Int J Colorectal Dis*. 1991;6:179–183.
61. Chen F, Stuart M. The morbidity of defunctioning stomata. *Aust N Z J Surg*. 1996;66:218–221.
62. Londono-Schimmer EE, Leong AP, Phillips RK. Life table analysis of stomal complications following colostomy. *Dis Colon Rectum*. 1994;37:916–920.
63. Rosen L, Friedman IH. Morbidity and mortality following intraperitoneal closure of transverse loop colostomy. *Dis Colon Rectum*. 1980;23:508–512.
64. Pittman DM, Smith LE. Complications of colostomy closure. *Dis Colon Rectum*. 1985;28:836–843.
65. Wexner SD, Taranow DA, Johansen OB, et al. Loop ileostomy is a safe option for fecal diversion. *Dis Colon Rectum*. 1993;36:349–354.
66. Edwards DP, Leppington-Clarke A, Sexton R, et al. Stoma-related complications are more frequent after transverse colostomy than loop ileostomy: a prospective randomized clinical trial. *Br J Surg*. 2001;88:360–363.
67. Law WL, Chu KW, Choi HK. Randomized clinical trial comparing loop ileostomy and loop transverse colostomy for faecal diversion following total mesorectal excision. *Br J Surg*. 2002;89:704–708.
68. Hallbook O, Matthiessen P, Leinskold T, et al. Safety of the temporary loop ileostomy. *Colorectal Dis*. 2002;4:361–364.
69. Wheeler MH, Barker J. Closure of colostomy–a safe procedure? *Dis Colon Rectum*. 1977;20:29–32.
70. Laurent C, Nobili S, Rullier A, et al. Efforts to improve local control in rectal cancer compromise survival by the potential morbidity of optimal mesorectal excision. *J Am Coll Surg*. 2006;203:684–691.
71. Koperna T. Cost-effectiveness of defunctioning stomas in low anterior resections for rectal cancer: a call for benchmarking. *Arch Surg*. 2003;138:1334–1338; discussion 1339.
72. Fukushima T, Sugita A, Koganei K, et al. The incidence and outcome of pelvic sepsis following handsewn and stapled ileal pouch anal anastomoses. *Surg Today*. 2000;30:223–227.
73. Hallberg H, Stahlberg D, Akerlund JE. Ileal pouch-anal anastomosis (IPAA): functional outcome after postoperative pelvic sepsis. A prospective study of 100 patients. *Int J Colorectal Dis*. 2005;20:529–533.
74. Farouk R, Dozois RR, Pemberton JH, et al. Incidence and subsequent impact of pelvic abscess after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Dis Colon Rectum*. 1998;41:1239–1243.
75. Breen EM, Schoetz DJ Jr, Marcello PW, et al. Functional results after perineal complications of ileal pouch-anal anastomosis. *Dis Colon Rectum*. 1998;41:691–695.
76. Dayton MT, Larsen KP. Outcome of pouch-related complications after ileal pouch-anal anastomosis. *Am J Surg*. 1997;174:728–731; discussion 731–732.
77. Kasperk R, Philipps B, Vahrmeyer M, et al. Risk factors for anastomosis dehiscence after very deep colorectal and coloanal anastomosis. *Chirurg*. 2000;71:1365–1369.
78. Shukla PJ, Pandey D. Protective defunctioning stoma in low anterior resection for rectal carcinoma (*Br J Surg* 2005;92:1137–1142). *Br J Surg.*. 2005;92:1565–1566.