Chapter 21
Who Needs a Loop Ileostomy After Low Anterior Resection for Rectal Cancer?

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Pt population	Intervention	Comparator	Outcomes studied
Pts after LAR	Proximal diversion	No diversion	Leak rate, consequences

Introduction

The standard of care for rectal cancers has evolved over recent years to be restorative anterior proctectomy. The most feared complication after low anterior resection (LAR) is anastomotic leak. Overall risk of anastomotic leak varies between 3 and 21 % [1]. Anastomotic leak has a reported mortality of 2.1–22 % and requires intervention with methods ranging from interventional radiologic drainage to reoperation [2]. Furthermore, colonic conduit function after anastomotic leak is significantly worse than in patients without leakage [2]. Other complications from anastomotic leak include increased rate of local recurrence and decreased disease-free and overall survival [3, 4]. This increase in cancer recurrence may be due to a

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delay or abandonment of the necessary adjuvant chemoradiotherapy [4]. Because of the serious morbidity associated with anastomotic leak, measures to minimize leak rates and the morbidity from such leaks has been implemented, the most ubiquitous of these being temporary fecal diversion. However, in recent years, the dogma of mandatory fecal diversion after LAR has been called into question.

Methods

A detailed search of the Embase-Medline databases was conducted for medical literature. The following search terms were employed to identify relevant articles: ("rectal" OR "colon" OR "colorectal") AND ("resection" OR "low anterior resection" OR "proctectomy") AND ("ileostomy" OR "ostomy" OR "colostomy" OR "diversion" OR "fecal diversion"). The title and abstracts of English-language articles were assessed for relevance

Why Not Divert?

When deciding if a patient should undergo fecal diversion, it is essential to fully understand the consequences of the procedure. Despite the widespread use of fecal diversion, it is not without complications. These complications include both short- and long-term problems and range from minor, requiring only local care, to major complications requiring reoperation and prolonged hospitalization [5, 6]. The most common complication after stoma construction is peristomal skin irritation [7]. While not necessarily defined by most members of the surgical community as a "major" complication, this can have major implications for a patient's quality of life [8].

A recent retrospective review using ACS NSQIP data identified multiple complications that were increased in patients undergoing low anterior resection with fecal diversion [6]. Patients who underwent diversion were found to have a higher rate of progressive renal insufficiency (2.1 % vs. 0.8 %) without an increased risk of acute renal failure (1.3 % vs. 0.7 %). Using a risk adjusted model, this increased rate of renal insufficiency was 2.37 times more likely to occur in patients undergoing fecal diversion. Furthermore, patients with fecal diversion had a significantly higher rate of deep surgical site infections (7.5 % vs 5.3 %) and a higher rate of 30-day readmission (20.3 % vs 11 %). Although not specifically discussed in this study, the findings of renal insufficiency and readmission are not surprising following stoma creation, as one of the most commonly encountered problems with diverting ileostomy is dehydration from high ostomy output. This complication has a reported incidence of 1–16 %, is most common 4–8 days postoperatively as bowel edema is resolving, and leads to electrolyte abnormalities, hypovolemia, and readmission [9]. Further out from the index operation, parastomal hernia occurs at a rate of 15–40 % [10]. Once identified, most hernias will require operative repair, which traditionally has overall poor results.

Finally, by definition, all temporary diverting ostomies require reversal; while this is technically not a difficult procedure, it is not without risk. In a study from Pokorny et al. in 2006, 243 patients who underwent loop ileostomy closure were retrospectively reviewed for complications [5]. An overall complication rate of 19 % was identified; 3 % had anastomotic leak, 6 % developed significant postoperative ileus, 1 % had bleeding complications, and 9 % had wound infections. In total, 4 % of patients undergoing ileostomy closure required reoperation for their complication.

Does Fecal Diversion Decrease Anastomotic Leak Rate?

The key question when considering fecal diversion following low anterior resection of the rectum is whether diversion changes the rate of anastomotic leak. There have been numerous retrospective studies over the years that have reported mixed results. While the number of large retrospective studies is quite high, all of these studies are inherently biased, as surgeons concerned about a particular anastomosis will favor temporary diversion. Given the fact that there are numerous studies on both sides of the issue of fecal diversion, it is difficult to draw sound conclusions from this retrospective data. Therefore, although limited in number and patients enrolled, randomized controlled trials comparing fecal diversion to anastomosis without diversion provide more reliable data with significantly less bias.

Graffner et al. were the first to design such a trial in 1983 and randomized 50 patients to fecal diversion versus no diversion [11]. 25 patients were in each group and there was a low overall leakage rate (4 % in the stoma group versus 12 % in the no stoma group). The next study was performed in 1997 by Pakkastie et al. In this study of 134 patients, there was a clinically detected 16 % leak rate in the stoma group versus a 32 % leak rate in the no stoma group. Importantly, there was also a lower re-operation rate in the stoma group, as only one of three leaks required re-operation compared to all six leaks requiring return to the OR in the no stoma group [12].

The next major study to address this issue was published in 2007 by Matthiessen et al. [13]. Importantly, this was a large multicenter trial, which enrolled a total of 234 patients for randomization, 116 in the stoma group and 118 in the no stoma group. Postoperatively, patients were monitored clinically for signs of anastomotic leak. There was a significantly higher leak rate in patients without a stoma (28.2 %) compared to those with a stoma (10.3 %; $p < 0.001$). Furthermore, there was a significantly higher rate of reoperation in the no stoma group with overall 25.4 % of patients requiring any reoperation versus 8.6 % in the stoma group. The largest of such studies, published in 2008 by Chude et al., included 256 patients, 120 without diversion and 136 with diversion [14]. Postoperatively, 12 of the 120 patients without diversion developed anastomotic leak (10 %) versus only 3 patients in the diverted group (2.2 %). Furthermore, two of the non-diverted patients required return to the OR for their anastomotic leak whilst none of the diverted patients required reoperation.

Another small study was performed by Ulrich et al. and reported in 2009 [15]. This study was much smaller than the other two published around the same time, with only 34 patients randomized. Again, there was a significantly higher rate of clinically detected anastomotic leaks in the no stoma group (37.5 %) compared to the stoma group (5.5 %, p = 0.02). All patients who developed a leak in the no stoma group required reoperation while none of the stoma patients with a leak returned to the OR. The differences in the study were in fact so dramatic that the study was halted after 34 patients were accrued due to clear superiority in the diverted group.

All of the above randomized trials were analyzed in a meta-analysis performed by the Cochrane Database and reported in 2010 [16]. When the results from these individual studies were combined, there was found to be a dramatic reduction in anastomotic leakage using fecal diversion (RR 0.33; 95 % CI [0.21, 0.53]). Furthermore, diverted patients had a decreased rate of urgent reoperation (RR 0.23; 95 % CI [0.12, 0.42]). Despite these differences, there was no significant decrease in terms of overall mortality (RR 0.58; 95 % CI [0.14, 2.33]). The conclusion of the review was that fecal diversion is an effective method in reducing the rates of anastomotic leak in patients undergoing low anterior resection and therefore the procedure can be offered routinely. This review did note significant limitations in all of the above studies and found that the methodology was overall poor; it was also observed that there was a lack of reporting of long-term mortality and quality of life.

Since the Cochrane Review was completed, at least one further study has been performed in a prospective, randomized fashion [17]. Thoker et al. reported in 2014 on 78 patients undergoing LAR randomized to stoma versus no stoma. In their study, they demonstrated a lower leak rate in the diverted group at 6 % compared to a rate of 11 % in the non-diverted group. Of note, they also followed patients for stoma related complications and found a higher rate of electrolyte imbalance in the postoperative period, as well as significant stomal complication rate of 25.4 %. Finally, they demonstrated that stoma closure was associated with an overall complication rate of 67.7 %.

Taken together, these data demonstrate that fecal diversion offers a clear benefit in LAR in lowering anastomotic leak rate and need for reoperation. While early retrospective studies arrived at varying conclusions, prospective randomized trials have all demonstrated a clear benefit to fecal diversion. Therefore, at this point, it is clear that at a population level, fecal diversion should be the default operation in combination with LAR. However, what these studies fail to address is which patients are at decreased risk of anastomotic leak and therefore could avoid defunctioning stoma placement.

Who Is at Highest Risk for Developing a Leak?

There are multiple risk factors for development of anastomotic leak, some which are associated with wound healing in general, and some which are specific to rectal cancer. Patient factors that increase the risk of developing an anastomotic leak are

risk factors that are associated with poor wound healing in general. Patients that have malnutrition, preoperative weight loss, preoperative steroids, and obesity are at higher risk for developing an anastomotic leak [18]. In a retrospective analysis from 2010 which reviewed 1495 consecutive patients who underwent LAR, an overall leak rate of 11 % was observed [19]. In reviewing specific patient factors associated with anastomotic leak, distance from anal verge was found to have the strongest association with leak rate (OR = 2.0 for anastomosis 10 cm from anal verge, OR = 3.6 for anastomosis 7 cm from anal verge, and OR = 5.4 for anastomosis 5 cm from anal verge). This finding that anastomoses close to the anal verge were at high risk for anastomotic leak was also observed by Rullier et al. [20]. Their study examined outcomes in 272 consecutive patients undergoing LAR and found by multivariate analysis that anastomoses within 5 cm of the anal verge were six times more likely to develop an anastomotic leak. Further operative factors related to anastomotic leak include male gender (OR = 2.36), and intraoperative blood loss (OR = 1.05).

Finally, intraoperative assessment of the anastomosis may play an important role in reducing the leak rate and in deciding on the need for proximal diversion. Common methods of evaluating a colorectal anastomosis include air leak testing, saline leak, methylene blue leak tests and endoscopic assessment. Two randomized trials have evaluated the validity of performing an intraoperative leak test and have found that the risk of leak in those tested was significantly lower than the untested controls (5.8 % versus 16 %, $p < 0.05$) [21, 22]. Therefore, intraoperative leak testing should be performed and patients found to have concerning findings on exam should undergo repair, revision, or anastomotic resection.

One area of continued controversy is the role of neoadjuvant radiotherapy in promoting anastomotic leak. The largest study which compared preoperative radiotherapy to selective postoperative chemoradiotherapy was published in 2009 by Sebag-Montefiore et al. [23]. In this multicenter randomized trial, 1350 patients with rectal cancer were randomized to neoadjuvant radiotherapy versus adjuvant chemoradiotherapy. While the purpose of the study was to identify best timing of treatment in relation to overall and disease-free survival, one of the data points collected was the rate of anastomotic leak. After low anterior resection with fecal diversion, 9 % of patients treated with neoadjuvant therapy developed an anastomotic leak compared to 7 % in the adjuvant group, which was not statistically significant. However, the application of these findings is limited by the fact that both groups underwent fecal diversion and only clinically significant leaks were reported; therefore leaks which may have been clinically significant if not diverted were not detected.

In a retrospective study published in 2012 by Nisar et al., 1862 patients who underwent resection between 1980 and 2010 were stratified into two groups based on preoperative radiotherapy and assessed for anastomotic leak [24]. An overall leak rate of 6.3 % was identified with no difference between the two groups (8 % neoadjuvant group versus 5.7 % in the no radiotherapy group, $p = 0.06$). On multivariate analysis, neoadjuvant therapy was not found to be associated with increased leak rate (OR = 1.44; CI 0.85, 2.46; $p = 0.18$). However, there were significant preoperative differences between the groups, including a rate of defunctioning ostomy

of 87 % in the neoadjuvant group versus 44 % in the no radiotherapy group. These differences make interpretation of the data difficult.

To further evaluate this issue, a recent meta-analysis was performed by Qin et al. and included seven randomized controlled trials comparing preoperative radiotherapy to no preoperative therapy [25]. Pooling these studies, a total of 1660 patients formed the preoperative radiotherapy group while 1715 patients formed the control group. In this analysis, rates of anastomotic leak were not increased in the preoperative radiotherapy group (OR = 1.02; CI 0.80, 1.30; p = 0.88). This study, however, is once again limited by the use of clinically detected anastomotic leaks in the individual trials making up the analysis, which may underreport anastomotic leaks that would be clinically significant if no defunctioning stoma were in place. Because of the lack of studies which truly examine the rate of all leaks, not only clinically significant leaks in the presence of a defunctioning stoma, making strong recommendations in patients who received preoperative radiotherapy remains difficult.

What Type of Diverting Ostomy Should We Use?

When considering fecal diversion, there are two common options; loop ileostomy or loop colostomy. Four randomized trials have compared these two options to each other, with two studies favoring the use of loop colostomy [26, 27] and two favoring loop ileostomy [28, 29]. In 2007, a Cochrane review was conducted which found five randomized studies involving 334 patients: 168 in the loop Ileostomy group and 166 in the loop colostomy group [30]. There was a very large difference in rates of stomal prolapse, with a rate of only 2 % in the ileostomy group versus 19 % in the colostomy group ($p < 0.01$), however, there were no other differences noted. Given the large difference in rates of prolapse, current recommendations are to create a loop ileostomy when possible.

Personal View of the Data

While it is clear that proximal diversion is not without risks, the consequences of an anastomotic leak are such that the benefits often outweigh the risks. Therefore, proximal fecal diversion following anterior resection for rectal cancer should be considered standard practice in all but a select few patients. This group of patients should include those at the lowest risk for developing an anastomotic leak such as non-smoking women with high rectal lesions who have not had preoperative radiation therapy. After creation, all colorectal anastomoses should be tested for the presence of an anastomotic leak. A positive test may necessitate a revision of the anastomosis followed by proximal diversion.

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