

Consequences of Anastomotic Leak After Restorative Proctectomy for Cancer: Effect on Long-term Function and Quality of Life

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BACKGROUND: Long-term consequences of anastomotic leak after restorative proctectomy for rectal cancer, in terms of bowel function and quality of life, have been poorly delineated.

OBJECTIVE: The purpose of this study is to evaluate the impact of anastomotic leak, when intestinal continuity can still be maintained, on bowel function and quality of life in patients undergoing rectal cancer resection with low colorectal or coloanal anastomoses.

DESIGN: From 1980 to 2010, 864 patients undergoing restorative resection for rectal cancers were identified from a prospective cancer database. Anastomotic leak detected by a combination of clinical, radiographic, and operative means was diagnosed in 52 (6%) patients.

MAIN OUTCOME MEASURES: Patients with anastomotic leak were compared with those without anastomotic leak for functional outcomes and quality of life at 1 year and most recent follow-up (mean 3.2 years) by using Short-Form 36 questionnaires (physical and mental component scales) and the Fecal Incontinence Severity Index.

RESULTS: American Society of Anesthesiologists' class ($p = 0.48$), cancer stage ($p = 0.39$), and the use of neoadjuvant therapy ($p = 0.4$) were similar in the 2 groups. Patients with anastomotic leak were younger (56 years vs 61 years; $p = 0.007$), more likely to be

male (82% vs 64%; $p = 0.008$), and more likely to have undergone proximal diversion at proctectomy (51.9% vs 26.6%; $p = 0.001$). One year after proctectomy, patients with anastomotic leak had worse physical and mental component scores ($p = 0.01$), more frequent daytime ($p = 0.001$) and nighttime bowel movements ($p = 0.03$), and worse control of solid stool ($p = 0.01$) in comparison with those without an anastomotic leak. At most recent follow-up (leak, 3.3 years vs no leak, 2.4 years), patients with an anastomotic leak reported worse mental component scores and increased use of perineal pads.

CONCLUSION: Anastomotic leak after restorative resection for rectal cancer leads to early adverse consequences on bowel function and quality of life even when anastomotic continuity can be maintained. These findings may help counsel patients and clinicians regarding anticipated outcomes over the long term.

KEY WORDS: Rectal cancer; Proctectomy; Anastomotic leak; Quality of life.

Clinical anastomotic leak (AL) remains one of the most feared complications after restorative proctectomy in patients with colorectal cancers. With improvements in surgical technique continually allowing for more restorative procedures to be performed in this population, there are more opportunities for complications such as AL to occur, which may in turn cause difficulties in the postoperative course of these patients.¹ The consequences of AL can be disastrous and have a significant impact on important postoperative variables.²

Anastomotic leak after proctectomy is a major source of early and late morbidity and mortality in terms of cancer-related and non-cancer-related outcomes and has been the center of recent debate.³ Recent evidence in the literature has suggested that AL does significantly impact cancer-related outcomes.^{4,5} Long-term consequences of

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AL after restorative proctectomy for rectal cancer, in terms of bowel function and quality of life (QOL), have not been as clearly delineated and limited in references.

The purpose of this study is to evaluate the impact of AL, when intestinal continuity can still be maintained, on bowel function and QOL in patients undergoing rectal cancer resection with low colorectal or coloanal anastomoses.

METHODS

Patients

Patients undergoing restorative resection for rectal cancers at the Cleveland Clinic from 1980 to 2010 were identified from the Department of Colorectal Surgery cancer database. This database is prospectively maintained and approved by the Cleveland Clinic Foundation Institutional Review Board. Patients with colorectal cancer who have IBD, familial adenomatous polyposis, hereditary and non-polyposis colon cancer, and who underwent nonrestorative resections were excluded from the study.

Study Variables and Data Collection

Data were collected in a prospective manner with documentation of demographic, clinical, operative, postoperative, and pathologic characteristics. Functional and QOL data were obtained during clinic visits by using a self-administered questionnaire required during the preoperative visit and at postoperative visits at the 3-month, 6-month, and 1-, 3-, and 5-year marks. If patients did not attend clinic visits, they were contacted by telephone or mail to obtain these data. This questionnaire addressed patient descriptors of daytime and nighttime seepage, frequency, urgency, incontinence, 24-hour stool frequency, and the use of a perineal pad. Outcomes were adjusted for differences in follow-up time between groups.

Assessment Tools

Patient QOL data were evaluated by the Cleveland Global Quality of Life, a validated tool in which patients rate QOL and health, and current energy level from 0 to 10, with 10 representing excellent function.⁶ A mathematical calculation produced the overall Cleveland Global Quality of Life score in which rating level was divided by 30 to produce a score between 0 and 1. Quality of life was assessed with Short-Form 36 questionnaires (physical and mental component scales, PCS and MCS; Medical Outcomes Trust, Waltham, MA), and bowel function with the Fecal Incontinence Severity Index.⁷

Definition of AL

Patients were designated as having AL when clinical, radiographic, or intraoperative findings guided the primary surgeon to document this diagnosis in the medical record.

Clinically, the presence of pus, gas, or stool evacuated in a drain, similar discharge from the operative wound, or a rectovaginal fistula or peritonitis signified AL. Only patients with clinically evident AL were included in the study; AL was identified by means of a distal contrast study at the time of ostomy closure; and unless AL was clinically evident, patients were not included.

Details of Surgery

Restorative resections in the study were performed by multiple surgeons at a single center with a closed colorectal department who received similar specialty colorectal fellowship training. Comparable operative principles were used with respect to strict adherence to complete mesorectal excision and high ligation of the vascular pedicle. The decision to perform fecal diversion at the time of oncologic resection was left to the discretion of the operating surgeon. We defined coloanal anastomosis as one that lies less than or equal to 3 cm from the anal verge.⁷ We included patients with tumors less than 15 cm from the anal verge, based on preoperative measurements.

Statistical Analysis

Patients with and without AL were compared with respect to categorical characteristics and outcomes by using the Fisher exact and χ^2 tests. Comparisons with respect to quantitative characteristics and outcomes were performed with Wilcoxon rank sum tests. Analyses were performed by using R version 2.11.1 (R-project.org). Comparisons with respect to outcomes, adjusting for follow-up time as a covariate, were performed with linear regression models.

RESULTS

Demographics and Clinical Presentation

From 1983 to 2007, 864 patients underwent restorative resection for colorectal cancer at the Cleveland Clinic Foundation and participated in perioperative follow-up questionnaires regarding QOL and bowel function. The mean age was 61 years, and 65% of patients were male. Mean length of follow-up was 3.2 years (range, 1–6 years).

Anastomotic leak detected by a combination of clinical, radiographic, and operative means was diagnosed in 52 of 864 (6%) patients. Patients with AL were compared with those who did not have AL for functional outcomes and QOL at 1 year and most recent follow-up (AL, 3.3 years vs no AL, 2.4 years).

Table 1 depicts background factors of patients with and without AL after restorative resection. ASA class ($p = 0.48$), cancer stage ($p = 0.39$), and the use of neoadjuvant therapy ($p = 0.4$) were similar in the 2 groups. Patients with AL were younger (56 years vs 61 years; $p = 0.007$), more likely to be male (82% vs 64%; $p = 0.008$), and more likely to have undergone proximal diversion at

TABLE 1. Patient characteristics, with and without anastomotic leak

	Leak, n (%)	No leak, n (%)	<i>p</i>
Number (%)	52 (6)	812 (94)	
Age	56.9	61.3	0.01
Sex, male	43 (83)	519 (64)	0.01
Anastomotic type			0.1
Stapled	42 (81)	712 (89)	
Handsewn	10 (19)	92 (11)	
Proximal diversion			0.01
Yes	27 (52)	216 (27)	
No	25 (48)	596 (74)	
Use of neoadjuvant therapy	23 (67.6)	206 (55.5)	0.4
ASA class			0.1
ASA I	2 (4)	8 (1)	
ASA II	19 (40)	395 (50)	
ASA III	26 (54)	369 (47)	
ASA IV	1 (2)	18 (2)	
ASA V	0	0	
Cancer stage			0.4
Stage I	55 (30)	6 (23)	
Stage II	67 (36)	8 (31)	
Stage III	47 (26)	8 (31)	
Stage IV	15 (8)	3 (12)	
Level of anastomosis, cm from anal verge	5.7	5.8	0.98
Level of primary tumor, cm from anal verge	9.7	13.6	0.001

proctectomy (51.9% vs 26.6%; $p = 0.001$). Preoperative tumor distance from the anal verge was significantly different between the groups (AL, 9.9 cm vs no AL, 11.6 cm; $p = 0.001$). Level of anastomosis from the anal verge was equivalent between groups (AL, 5.8 cm vs no AL, 5.7 cm; $p = 0.98$). Preoperative tumor distance in patients with AL was closer to the anal verge in comparison with those without AL (AL, 9.7 cm vs no AL: 13.6 cm; $p = 0.001$).

Functional Outcomes

Bowel Frequency and Continence. One year after proctectomy, patients with AL had more frequent daytime ($p = 0.001$) and nighttime bowel movements ($p = 0.03$), and worse control of solid stool ($p = 0.01$) compared to those without AL. At most recent follow up, patients with AL reported increased use of perineal pads, but other bowel function parameters were equivalent to the group without AL (Table 2).

Quality of Life. Quality-of-life data are listed in Table 2. At 6 months and 1 year after proctectomy, patients with AL had worse PCS ($p = 0.01$) in comparison with patients without AL. MCS scores at 6-month, 1-year, and 3-year visits were also significantly reduced in patients with AL ($p = 0.01, 0.01, 0.02$). At most recent follow-up (AL, 3.3 years vs no AL, 2.4 years), patients with AL reported worse MCS scores, but PCS scores equivalent to the group without AL (Table 3).

TABLE 2. Functional outcomes

	Patients with AL (n = 52)	Patients without AL (n = 812)	<i>p</i>
Daytime frequency			
1 year	4.9	2.8	0.001
Most recent	3.6	3.0	0.48
Nighttime frequency			
1 year	1.8	1.2	0.03
Most recent	1.7	1.3	0.6
Control of gas ^a			
1 year	3.0	2.6	0.06
Most recent	2.4	2.6	0.30
Control of solids ^a			
1 year	2.6	2.0	0.01
Most recent	2.2	2.1	0.6
Control of liquids ^a			
1 year	1.9	1.8	0.5
Most recent	1.9	1.9	0.8
Urgency to evacuate			
1 year	1.5	1.5	0.75
Most recent	1.5	1.6	0.83
Use of pad ^b			
1 year	2.7	1.8	0.001
Most recent	2.3	1.8	0.04

AL = anastomotic leak.

^aScores reflect responses given indicating frequency of incontinence to listed parameters. A score of 0 = never, 1 = less than 1/month, 2 = 1 to 3 times/month, 3 = 1 to 2 times/week, 4 = 1 to 2 times/day incontinence to the specific parameter.

^bScores reflect frequency of use. A score of 0 = never, 1 = rarely, 2 = sometimes, 3 = usually, and 4 = always.

DISCUSSION

Anastomotic leak is a significant complication after proctectomy for colorectal cancer and is a major cause of both postoperative morbidity and adverse cancer-related outcomes in the long term.^{1,2} In terms of oncologic outcomes after resection, a number of recent studies have shown clear associations between the presence of AL and worsened oncologic outcome. Eberhardt et al⁴ in 2009 showed that the occurrence of AL does increase overall and cancer-specific mortality and local recurrence in patients undergoing rectal cancer resection. Similarly, a meta-analysis in 2011 by Mirnezami et al⁵ showed that AL has a negative prognostic impact on local recurrence and suggested an association between AL and reduced long-term survival. Other studies describe opposing data. Jorgren et al,³ in 2010, submitted

TABLE 3. Patient quality of life

	Patients with AL (n = 52)	Patients without AL (n = 812)	<i>p</i>
SF-36 PCS			
1 year	43.7	49.0	0.007
Most recent	44.6	46.8	0.23
SF-36 MCS			
1 year	44.5	49.8	0.007
Most recent	44.8	48.5	0.02

AL = anastomotic leak; PCS = Physical Component Scale; MCS = Mental Component Scale.

Table 4. Comparison of functional studies

Author	Year of study	Type of study	No. of patients	Follow-up	Results	Conclusions
Hallböök and Sjö Dahl ⁸	1996	Case-matched	19/19 patients	30 mo	Sphincter function maintained Reduced neorectal volume, increased frequency and urgency of bowel movements	Function outcome is compromised
Nesbakken et al ⁹	2001	Case-matched	11/11	24 mo	Sphincter function maintained Reduced MTV	Function outcome is compromised
Bittorf et al ¹⁰	2003	Retrospective	150/22 (with AL)	~ 2 y	AL reported less incontinence No significant difference in urgency or MTV, or patient satisfaction	Functional outcome is not compromised
Our study	2012	Retrospective	812/52	3.2 y	Increased frequency and incontinence/ pad use at 1 y QOL compromised at 1 y and most recent follow-up (3.2 y)	Function outcome is compromised

AL = anastomotic leak; QOL = quality of life; MTV = maximum tolerated volume.

results from a small meta-analysis looking at the impact of AL on oncologic outcomes and showed no relationship between AL and worsened oncologic outcome. Despite these opposing views, much attention has been given to the debate regarding the effect of AL on cancer-related outcomes. There is a lack of data, however, regarding the impact of AL on long-term functional outcomes and QOL after restorative proctectomy for colorectal cancer.

Three reports in the past 2 decades have directly addressed this question (Table 4), as evidenced by a PubMed search using key terms of “anastomotic leakage,” “rectal cancer,” and “function.” In 1996, Hallböök and Sjö Dahl⁸ published a small series of 283 patients undergoing low anterior resection for cancer. Thirty-four patients (12%) experienced AL, and 19 of these patients were identified and assessed for frequency and urgency of bowel movements and manovolumetric characteristics over a median follow-up of 30 months. These data showed a reduced neorectal volume and increased frequency of bowel movements after AL. When variables were evaluated separately, there was no significant difference in urgency or incontinence. The authors suggested that AL was associated with decreased neorectal volume and compliance and proposed that AL leads to worsened functional outcome after proctectomy. Patient QOL was not investigated in this study. With similar results, Nesbakken et al⁹ reported that AL correlated with a reduction in maximum tolerated volume and difficult evacuation. Urgency and incontinence were slightly worse after AL, but differences were not significant. Both studies agreed that overall functional outcome was negatively affected by AL. In the third study, Bittorf et al¹⁰ performed a retrospective evaluation of 150 patients, 22 with AL. They suggested that there was no functional difference between groups, although urgency and maximum tolerated volume were lower in the AL group, albeit not significantly so. They also reported that patient satisfaction was equivalent between groups.

We know from published studies in the ileal pouch literature that there may be a relationship between

postoperative AL and long-term pelvic pouch function and pouch loss, although controversy exists. In a recent 2012 study, Kiely et al¹¹ reported on 3000 patients who had pelvic pouches, 6.2% with postoperative pelvic sepsis, over a median follow-up of 7 years. Patients in this study with pelvic sepsis reported increased daytime seepage ($p = 0.03$) and lower QOL scores ($p < 0.001$) than those without pelvic sepsis. Other studies with smaller numbers of patients have also reported compromised bowel function in patients with postoperative pelvic sepsis or abscess.¹²

Based on the results of these functional studies, we hypothesized that bowel function and QOL after proctectomy for colorectal cancer may be adversely affected after AL. To investigate this, we retrospectively studied outcomes of more than 850 patients undergoing restorative resection over a 20-year period by using data from a prospectively maintained database. Patients experiencing AL were compared with those without AL, with an emphasis on postoperative bowel function and QOL, to better understand a possible relationship between AL and functional outcome in these patients.

Six percent (52/864) of patients experienced an AL after proctectomy. At 1 year after proctectomy, patients with AL reported more frequent daytime and nighttime bowel movements than patients without AL. These patients also reported worse control of solid stool and a greater need for daily perineal pad use. Control of flatus was not statistically different among groups, although differences neared significance. Our results show that, at 1 year after proctectomy, patients with AL have comparatively worse bowel function than their counterparts without AL.

One major goal of our study was to investigate the possible effect of AL on postoperative QOL in patients undergoing proctectomy. This has not been previously extensively addressed in the literature. We found that patient QOL is significantly affected by AL, because patients with AL reported worse PCS and MCS 1 year after surgery than patients without AL. We conclude that AL has a significant

effect on both bowel function and patient QOL at 1 year after surgery.

One limitation of our study was the incomplete follow-up at time points longer than 1 year after surgery. Our data depended on a patient's availability to complete questionnaires at follow-up clinic visits, and many patients may have been lost to follow-up or were seeing local physicians for surveillance at visits after the 1-year mark. We believe that the major reason for this, despite having a database spanning 3 decades, is primarily because most patients do not live locally and are often seen by local physicians after the immediate postoperative period. This has limited our ability to perform a complete evaluation of functional outcome in these patients. To account for this limitation, we additionally examined functional data and QOL scores at the most recent follow-up time point for each group (AL, 3.3 years vs no AL, 2.4 years). We found that patients with AL reported increased daily use of perineal pads at most recent follow-up in comparison with patients without AL. Other bowel function parameters were equivalent between the groups. With regard to patient QOL at most recent follow-up, MCS scores were worse in patients with AL, whereas PCS scores were similar between groups.

These data suggest that the effects of AL development in these patients may impact more than just the inpatient course requiring transabdominal or transanal drainage or home infusion of antibiotic therapy. These patients may develop compromised bowel function after the immediate postoperative period that may be associated with changes in bowel function lasting beyond the first year after surgery. Similarly, patients reported feelings of worse QOL that parallel this time of compromised bowel function, suggesting that both components may be negatively affected by development of AL.

Interestingly, we do not note such a marked difference in function and QOL at the most recent follow-up. We identify 2 reasons for this. First, patients whose postoperative questionnaires were complete to 5 years were included in the study; those with incomplete follow-up were omitted, and therefore result in fewer numbers at later time points. Differences may exist but may not be evident because of much lower numbers of patient follow-up after 1 year. This type II error may be remedied with better capturing of patient follow-up in clinic visits later in the postoperative period.

Second, the near resolution of differences in bowel function at the most recent follow-up may be indicative of an improvement over time in patients initially experiencing AL. A possible pathophysiology of this compromise is not entirely clear. Several studies have proposed the negative effect of pelvic sepsis as a cause of fibrosis contributing to poor anorectal function.^{13,14} Anastomotic leak leads to pelvic fibrosis, causing reduced neorectal compliance and capacity and resulting in compromised postoperative continence.^{13,14} The Hallböök and Nesbakken studies

support this observation, because they proposed that AL affects neorectal reservoir function, thus leading to compromised bowel function. One possible explanation of our most-recent follow-up results may be that there are structural or functional aberrations causing poor bowel function that may be predominant in the first few years after surgery, and slowly improve over time.

We also noted that patients with AL were more likely to be male and have undergone proximal diversion at the time of proctectomy. A possible hypothesis for this observation is that these patients may have required a more extensive or technically difficult operation because of unfavorable body habitus or pelvic anatomy increasing the risk for AL, thus prompting the operating surgeon to opt for temporary diversion at the time of surgery.

Despite these improvements over time, some changes do still exist, as seen at the most recent follow-up with lower MCS scores and daily use of perineal pads in patients with AL. Awareness of these potential differences in function, especially in the short term, allows the surgeon to identify and predict patients' outcomes in the first few years after restorative resection. Thus, the surgeon and patient are able to come together to set reasonable and achievable goals for recovery in the long term, soon after AL is discovered.

CONCLUSION

Anastomotic leak after restorative resection for rectal cancer may lead to early adverse consequences on bowel function and QOL, even when anastomotic continuity can be maintained. Despite some improvement over time, some effects may persist after the immediate postoperative period. These findings may help counsel patients and clinicians regarding anticipated outcomes over the long term and support the careful consideration of strategies to avoid the development of this complication.

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