



Patient factors may predict anastomotic complications after rectal cancer surgery

Anastomotic complications in rectal cancer



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H I G H L I G H T S

- Risk factors for anastomotic complications include malnutrition, radiation, and ischemia.
- Transfusions have been associated with increased complications.
- Hemoglobin level <11 gr/dl might be associated with increased risk of anastomotic leak.
- Presence of diverting stoma does not affect the incidence of anastomotic leaks.

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Purpose: Anastomotic complications following rectal cancer surgery occur with varying frequency. Preoperative radiation, BMI, and low anastomoses have been implicated as predictors in previous studies, but their definitive role is still under review. The objective of our study was to identify patient and operative factors that may be predictive of anastomotic complications.

Methods: A retrospective review was performed on patients who had sphincter-preservation surgery performed for rectal cancer at a tertiary medical center between 2005 and 2011.

Results: 123 patients were included in this study, mean age was 59 (26–86), 58% were male. There were 33 complications in 32 patients (27%). Stenosis was the most frequent complication (24 of 33). 11 patients required mechanical dilatation, and 4 had operative revision of the anastomosis. Leak or pelvic abscess were present in 9 patients (7.3%); 4 were explored, 2 were drained and 3 were managed conservatively. 4 patients had permanent colostomy created due to anastomotic complications. Laparoscopy approach, BMI, age, smoking and tumor distance from anal verge were not significantly associated with anastomotic complications. After a multivariate analysis chemoradiation was significantly associated with overall anastomotic complications (Wall = 0.35, $p = 0.05$), and hemoglobin levels were associated with anastomotic leak (Wald = 4.09, $p = 0.04$).

Conclusion: Our study identifies preoperative anemia as possible risk factor for anastomotic leak and neoadjuvant chemoradiation may lead to increased risk of complications overall. Further prospective studies will help to elucidate these findings as well as identify amenable factors that may decrease risk of anastomotic complications after rectal cancer surgery.

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1. Introduction

Anastomotic complications following rectal cancer surgery occur with varying frequency, from 1.8 to 19.8% [1–3]. Of these complications, anastomotic leak is the most morbid complication, with reported incidences ranging between 1.8 and 10.4% [1,4–6].

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This wide range may be due to the variable definitions used in the literature.

Male gender, preoperative radiation, BMI, hypoalbuminemia, use of defunctioning stoma and low anastomoses have been implicated as predictors in previous studies, but their definitive role is still under review and other factors have yet to be identified.

The objective of our study is to describe the risk factors associated with anastomotic complications in patients who had restorative proctectomy performed for rectal cancer. We hypothesize that anastomotic leaks are associated with conditions that affect the following factors: amount of oxygen carried in the blood stream (e.g. pulmonary diseases, smoking habits, anemia), vasculature abnormalities or inflammation (e.g. atherosclerosis, smoking habits, hypoalbuminemia), and integrity of the tissues involved in the anastomosis (e.g. type of anastomosis, technique, radiation, inflammation).

2. Methods

2.1. Study design

We conducted a retrospective analysis of a prospectively collected database of all patients who underwent elective restorative proctectomy for rectal cancer at Rush University Medical Center from January 2005–June 2011. No exclusion criteria were applied. This study was approved by the Institutional Review Board (IRB) at Rush University Medical Center (RUMC).

Laparoscopic or open approach was selected by the surgeons before the procedure, these decisions were largely based on patients comorbidities, previous surgical and medical history. The anastomotic technique involved the use of a stapler or a handsewn technique at the surgeon's discretion. Inspection of 'donuts' and intraoperative leak testing by air insufflation was performed in most of the cases. Defunctioning stoma was used in cases when technical difficulties related to anastomosis creation were present or preoperative radiation was administered. If defunctioning stoma was present, patients underwent contrast enema and/or flexible sigmoidoscopy before reversal to evaluate for anastomotic leak or stenosis. All surgeries were performed by two board-certified colorectal surgeons.

Medical records were reviewed and the following factors were extracted and entered into a database: age, gender, body mass index (BMI), history of coronary artery disease, diabetes mellitus, American Society of Anesthesiologist (ASA) classification, distance of tumor from anal verge, neoadjuvant chemoradiation therapy, type of surgery, approach, length of surgery, method of anastomosis, level of anastomosis from the anal verge, use of defunctioning stoma, and pathology features.

The primary outcome of the study was incidence of anastomotic complications which were classified as anastomotic leakage or stenosis. Anastomotic leakage was defined as total or partial breakdown of the connection and subsequent leakage of gastrointestinal contents or abscess formation demonstrated clinically or radiographically (computed tomography scan or barium enema). Stenosis was defined as narrowing of the anastomotic site characterized by an inability to pass the surgeon's index finger or a colonoscope, or narrowing demonstrated on a contrast study.

2.2. Statistical analysis

All quantitative variables are reported as a mean with an associated range. All patients included in the prospectively collected database were included in the analysis, and no sample size calculation was performed. Chi square was used to compare nominal variables (e.g.: neoadjuvant chemoradiation, gender, approach,

stoma creation). Independent *t*-tests or non-parametric Mann–Whitney test were performed as appropriate to compare continuous variables in univariate analyses (e.g.: age, hemoglobin, length of surgery, length of stay). All *p* values were 2-tailed, and $p < 0.05$ was the criterion for statistical significance. Factors with a *p* value < 0.10 in the univariate analyses were entered into the stepwise multivariate logistic regression. No subgroup or sensitivity analyses were performed. In case of missing data, only cases with complete data in the variable of study were included in the analysis; no imputation system for missing data was used. All statistical analyses were conducted using SPSS computer program (IBM SPSS 21).

3. Results

One-hundred twenty-three patients were included in this study. The mean age was 59 years (26–86); 58% were male and 42% were female. Stapled anastomoses were performed in 110 patients (89%), 12 were handsewn and one used a compression ring. The characteristics of patients are summarized in [Table 1](#).

There were 33 complications in 32 patients (27%). The mean length of follow-up time after surgery was 23 months (range 0–70 months); the median was 17 months. Overall, eight patients required surgery for any anastomotic complication, and four patients had a permanent colostomy created due to anastomotic complications.

Stenosis was the most frequent complication (24/33, 72%). The average time to diagnosis of anastomotic stenosis was 204 days (range 17–890 days). Eleven patients required dilatation, four had operative revision of the anastomosis, and the nine remaining patients required only finger dilatation.

Anastomotic leak or pelvic abscess were present in nine patients (7.3%); five (4%) were diagnosed clinically within 14 days of surgery (mean 9 days, range 6–14 days). Four were diagnosed radiographically after surgery (mean 198 days, range 94–254 days); these were asymptomatic and identified during routine exam before ileostomy reversal. Four patients required exploration (exploratory laparotomy/laparoscopic with peritoneal lavage, ileostomy formation), two were drained percutaneously and three were treated with antibiotics and observation.

[Table 2](#) shows the univariate and multivariate analyses for anastomotic complications. Neoadjuvant chemoradiation was

Table 1
Demographics.

Variable	Overall (N = 123)
Age (Mean ± SD)	59.24 ± 12.7 (range 26–86)
Gender	
• Male	71 (57.7%)
• Female	52 (42.3%)
Body mass index (Mean ± SD)	27.24 ± 5.7 (range 26.17)
Approach	
• Open	77 (63.1%)
• Laparoscopy	45 (36.9%)
ASA	
• 1	2 (1.6%)
• 2	57 (46.3%)
• 3	34 (27.6%)
• 4	2 (1.6%)
Technique	
• Stapled	110 (89%)
• Handsewn	12 (9.75%)
• Anastomotic ring	1 (0.81%)
Anastomotic complications	32 Patients (27%)
• Stenosis	24 (19.5%)
• Leakage or abscess	9 (7.3%)
○ Clinical	5 (4%)
○ Radiographic	4 (3.3%)

associated with increased risk of overall anastomotic complications ($\chi^2 = 4.14$ $p = 0.04$). Stenosis was not significantly associated with any of the examined variables (Table 3). Table 4 shows the variables associated with anastomotic leak; hemoglobin level appears to be an independent predictor ($t = -2.29$, $p = 0.01$). Further analysis demonstrated that hemoglobin levels <11 mg/dl increase the risk of anastomotic leak 6.5- fold.

4. Discussion

Our analysis showed that neoadjuvant chemoradiation was associated with the development of complications in the post-operative period. This finding may be due to the local effects of radiation on the tissues as well as represent a marker of the location of the tumor. Most locally advanced rectal cancers located in the mid and lower receive neoadjuvant radiation. Tumors located in the lower third of the rectum (between 5 and 8 cm from the anal verge) have been associated with higher rates of anastomotic leaks [7–9]. Radiation has been associated with decrease oxygen delivery to the tissues and decrease healing as well.

4.1. Anastomotic leak

Anastomotic leaks are present in 1.8–12% of the cases of rectal surgery [1,4–6]; however, these rates vary according to the definition used. When leaks were diagnosed by radiology (CT, MRI, Gastrofin enema), higher rates were reported [2].

Some of the identified risk factors for anastomotic leaks are male gender, nutritional status, the location of the anastomosis, diverting stoma, and previous history of radiation [3,7,10,11]. Males have narrower configuration of the pelvis resulting in increased technical difficulty during the operation, and subsequent increased risk of leak [6–8]. However, our study did not have adequate power to identify this association (Post-hoc achieved power: 23%).

We did not find significant associations between previously implicated factors (e.g. BMI, location of the anastomosis) and anastomotic leak. Although some studies have identified laparoscopic surgery as a risk factor for anastomotic leaks [6], our study showed no association between the approach and its incidence, similar to other reports in the literature [12–14].

Several studies have shown an association between leaks and fecal diversion [4], but other studies, including ours, suggest that diverting stoma does not affect the incidence of leak, but rather decreases the associated morbidity [7,11,14].

Ischemia has been described as a risk factor for leaks; therefore, adequate blood flow is a priority during the creation of the anastomosis. Currently this is a subjective assessment, based on the characteristics of the tissue and blood loss, which does not take into account factors such as hemoglobin concentration or tissue oxygenation. In our study we showed that patients with a hemoglobin level <11 g/dl have an increased risk of leak, explained by a decreased capacity to transport oxygen to the tissues and subsequent risk of ischemia. Although this association has not been described to date, operative blood loss can be considered a surrogate measure of decreased hemoglobin levels [5,6].

Table 2
Univariate and multivariate analysis for anastomotic complication.

	Anastomotic complication		Univariate analysis		Multivariate analysis	
	Yes N = 32	No N = 91	χ^2	p-value	Wald	p-value
Age (Mean \pm SD)	58.9 \pm 10.7	59.3 \pm 13.3	46.48	0.33		
Gender						
• Male	22 (31%)	49 (69%)	2.16	0.14		
• Female	10 (19.2%)	42 (80.8%)				
BMI (Mean \pm SD)	26.8 \pm 4.9	27.3 \pm 5.9	109.33	0.42		
Hgb (Mean \pm SD)	11.9 \pm 1.7	12.1 \pm 1.5	64.07	0.09	0.01	0.92
Chemoradiotherapy						
• Yes	26 (31.7%)	56 (68.3%)	4.14	0.04	0.35	0.05
• No	6 (14.6%)	35 (85.4%)				
Tumor location (cm)	7.32 \pm 3.98	8.37 \pm 4.14	1.43	0.23		
Approach						
• Laparoscopy	11 (24.4%)	34 (75.65%)	0.12	0.73		
• Open	21 (27.3%)	56 (72.7%)				
ASA						
• 1	1 (50%)	1 (50%)	1.69	0.64		
• 2	14 (24.6%)	43 (75.4%)				
• 3	7 (20.6%)	27 (79.4%)				
• 4	1 (50%)	1 (50%)				
OR time (Mean \pm SD)	279.4 \pm 92.7	246.9 \pm 94.5	104.38	0.47		
Technique						
• Stapled	26 (24.1%)	82 (75.9%)	1.75	0.19		
• Hand-sewn	5 (41.7%)	7 (58.3%)				
Mobilization of splenic flexure						
• Yes	20 (32.3%)	42 (67.7%)	2.94	0.09	1.07	0.30
• No	11 (18.6%)	48 (81.4%)				
Air testing leak						
• Yes	2 (12.5%)	14 (87.5%)	1.00	0.32		
• No	17 (23.9%)	54 (76.1%)				
Asymmetric donuts						
• Yes	2 (66.7%)	1 (33.35)	3.66	0.06	1.14	0.28
• No	20 (20.4%)	78 (19.6%)				
Fecal diversion						
• Yes	26 (32.5%)	54 (67.5%)	4.99	0.03	0.11	0.71
• No	6 (14%)	37 (86%)				

Bold values mean they are statistically significant.

Table 3
Univariate and multivariate analysis for anastomotic stenosis.

	Stenosis		Univariate analysis		Multivariate analysis	
	Yes N = 24	No N = 99	X ²	p value	Wald	p value
Age (Mean ± SD)	57.3 ± 11.7	59.7 ± 12.8	46.41	0.33		
Gender						
• Male	15 (21%)	56 (78.9%)	0.28	0.59		
• Female	9 (17%)	43 (82.7%)				
BMI (Mean ± SD)	26.24 ± 4.7	27.47 ± 5.9	108.72	0.44		
Hgb (Mean ± SD)	12.28 ± 1.5	12.03 ± 1.5	60.21	0.15		
Chemoradiotherapy						
• Yes	19 (23.2%)	63 (76.8%)	2.09	0.15		
• No	5 (12.2%)	26 (87.8%)				
Tumor location (cm)	6.9 ± 3.9	8.3 ± 4.1	16.96	0.53		
Approach						
• Laparoscopy	9 (20%)	36 (80%)	0.01	0.94		
• Open	15 (19.5%)	62 (80.5%)				
ASA						
• 1	1 (50%)	1 (50%)	6.34	0.09	5.01	0.17
• 2	13 (22.8%)	44 (77.2%)				
• 3	2 (5.9%)	32 (94.1%)				
• 4		2 (100%)				
OR time (Mean ± SD)	288 ± 101	247.4 ± 91	101.25	0.56		
Technique						
• Stapled	19 (17.6%)	89 (82.4%)	1.73	0.19		
• Hand-sewn	4 (33.3%)	8 (66.7%)				
Mobilization of splenic flexure						
• Yes	15 (24.2%)	42 (75.8%)	2.22	0.14		
• No	8 (13.6%)	48 (86.4%)				
Air testing leak						
• Yes	1 (6.3%)	15 (93.8%)	1.16	0.28		
• No	12 (16.9%)	59 (83.1%)				
Asymmetric donuts						
• Yes	2 (66.7%)	1 (33.3%)	5.99	0.01	1.36	0.24
• No	14 (14.3%)	84 (95.7%)				
Fecal diversion						
• Yes	20 (25%)	60 (75%)	4.388	0.036	1.76	0.19
• No	4 (9.3%)	39 (90.7%)				

Some randomized clinical trials have suggested that hemoglobin values of 7–9 g/dl are safe and do not increase mortality [15], but the effects of these guidelines on the morbidity of rectal anastomosis have not been described. More analyses are required to determine if blood transfusions before or during the surgery can be used to decrease leak rates without increased risk of other complications.

4.2. Anastomotic stenosis

Anastomotic stenosis is less frequently described in the literature. Some studies report an incidence of 5–13% [10,11,16,17], which is lower than the results in our study (19%). Our definition of stenosis is broad and included patients with benign stenosis that resolved after finger dilation; traditionally anastomotic stenosis are defined as narrowing of the lumen that require mechanical dilation with balloon or more invasive interventions. This difference might explain our high incidence, however, we decided to analyze technical factors unique to our practice that might be related with our higher than normal rate of stenosis.

Ischemia and tension at the level of the anastomosis had been described as possible risk factors, therefore we used splenic flexure mobilization as a surrogate factor for tension in the anastomosis, which did not show a significant difference, possibly because some patients had tension-free anastomosis without requiring mobilization of the splenic flexure. Other technical factors like high division of inferior mesenteric artery (IMA) and inferior mesenteric vein (IMV) were not analyzed in our study.

Luchtefeld et al. described that incomplete donuts were an independent predictor of stenosis [16]. This association might be related to the redundant tissue left at the anastomotic site, which might compromise blood flow and subsequently result in ischemia and fibrosis at the site of the anastomosis.

Fecal diversion has been described as a risk factor for stenosis [10]. Feces in the lower rectum produces distention, therefore its absence may induce atrophy of the muscle cells with subsequent stenosis. Another risk factor that has been described in the literature is handsewn anastomosis; our study was not powered to identify an association due to the low use of handsewn technique, but recent systematic reviews suggest that it might not be a factor [18,19].

4.3. Limitations

The limitations of our study are those inherent to any retrospective analysis. Although most data was collected prospectively, some variables were included at the time of this study, therefore increasing the risk of missing data. We did not identify significant association of previously reported risk factors. This may be related to the amount of patients included in the study; larger populations may be required to identify these differences.

4.4. Conclusion

The identification of amenable risk factors for anastomotic complications may help to change techniques and preoperative management in order to decrease the associated morbidity of

Table 4
Univariate and multivariate analysis for anastomotic leak.

	Anastomotic leak		Univariate analysis		Multivariate analysis	
	Yes N = 9	No N = 114	X ²	p value	Wald	p value
Age (Mean ± SD)	62.4 ± 6.18	58.99 ± 13	0.79	0.43		
Gender						
• Male	8 (11.3%)	63 (88.7%)	3.86	0.05	2.49	0.12
• Female	1 (1.9%)	51 (98.1%)				
BMI (Mean ± SD)	28.34 ± 5	27.16 ± 5.7	0.63	0.56		
Hgb (Mean ± SD)	10.7 ± 1.8	12.1 ± 1.5	−2.29	0.01	4.09	0.04
Chemoradiotherapy						
• Yes	7 (8.5%)	75 (91.5%)	0.54	0.46		
• No	2 (4.9%)	39 (95.1%)				
Tumor location (cm)	8.5 ± 4.3	8 ± 4.12	0.24	0.81		
Approach						
• Laparoscopy	2 (4.4%)	43 (95.6%)	0.89	0.34		
• Open	7 (9.1%)	70 (90.95)				
ASA						
• 1		2 (100%)	8.19	0.04	4.61	0.20
• 2	2 (3.5%)	55 (96.5%)				
• 3	5 (14.7%)	29 (85.3%)				
• 4	1 (50%)	1 (50%)				
OR time (Mean ± SD)	262.4 ± 60	254.8 ± 97	0.35	0.73		
Technique						
• Stapled	7 (6.5%)	101 (93%)	0.06	0.81		
• Hand-sewn	1 (8.3%)	11 (9.17%)				
Mobilization of splenic flexure						
• Yes	5 (8.1%)	57 (91.9%)	0.07	0.78		
• No	4 (6.8%)	55 (93.2%)				
Air testing leak positive						
• Yes	2 (12.5%)	14 (87.5%)	0.55	0.61		
• No	5 (7%)	66 (93%)				
Asymmetric donuts						
• Yes	—	3 (100%)	0.23	1.00		
• No	7 (7.1%)	91 (92.9%)				
Fecal diversion						
• Yes	6 (7.5%)	74 (92.5%)	0.01	1.00		
• No	3 (7%)	40 (93%)				

Bold values mean they are statistically significant.

anastomotic leak and stenosis. Although some of the classic risk factors were not identified, preoperative anemia was a risk factor for anastomotic leak, which may influence guidelines on preoperative transfusion or iron supplementation, if these results are demonstrated in larger prospective studies. Our findings also suggest that neoadjuvant chemoradiation might be associated with increased risk of complications. This may support the argument against administration of preoperative radiation unless strongly indicated by clinical exam or evidence of local invasion.

Conflict of interest

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Disclaimers

None.

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