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The Risk Factors of Anastomotic Leakage After Rectal Cancer Surgery

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Abstract

Background: Anastomotic leakage is a significant complication after colorectal anastomosis. The aim of this study was to evaluate the risk factors and preventive measures for anastomotic leakage after rectal cancer surgery.

Methods: A total of 171 patients who had undergone laparoscopic and open rectal cancer resection with a double stapling participated in this study. Twelve independent variables include age, sex, obesity, smoking, ASA grading, medical diseases, preoperative radiotherapy, preoperative chemotherapy, splenic flexure mobilization, diverting ileostomy, and the number of stapler firing were analyzed.

Results: The anastomotic leakage rate was 2.33% (4 of 171). The mean age of the patients was 58.33 years old while their mean body mass index (BMI) was calculated as 24.10 kg/m^2. In our study, 16.3% of patients were cigarette smokers. Of the 171 rectal surgeries, 69.0% of patients were diverted by loop ileostomy and 1.16% were supported by ghost ileostomy. Of 171 patients included in this study, 17.5 % of patients required a single staple firing for rectal division. In contrast, 47.9% of patients required 2 linear staplers, others, 24.5% of patients required 3 cartridges for rectal division, and 9.9% of patients required 4 cartridges in their surgeries. There were significant differences between men and women in the number of cartridges used (P = 0.023).

Conclusions: All our leakage cases were men and the higher number of stapler firings for rectal division, history of smoking; male gender, and level of anastomosis were independent risk factors for the anastomotic leak.

Keywords: Risk Factors, Anastomotic Leak, Rectal Cancer

1. Background

Anastomotic leakage is significant complication after colorectal anastomosis (1) and it often considered to be either clinical (overt) or subclinical. The reported incidence rate varies between 1% and 29%, with an average rate of 11% (2-4). The two factors having the strongest association with the leakage are the nodal involvement and height of the anastomosis above the anal verge; with a higher site location corresponding to lower inherent risk Previous reports showed that males, older patients, obese patients, patients that have undergone short-course radiotherapy, heavy alcohol consumers, and smokers are at major risk regarding anastomotic leak after undergoing low anterior resection (5).

A randomized controlled study showed that the creation of diverting stoma reduces the occurrence of anastomosis leak (6). Other studies have shown that the risk of leakage may be decreased by temporarily diverting stoma (7, 8). Besides, some reports stained that creating a diverting stoma does not reduce the post-operative anastomosis leak rate (9) with another study claiming that a temporary stoma is not a significant risk factor for leakage (10). A sufficient blood supply, a tension-free anastomosis, and healthy bowel are the basic requirements for anastomotic healing (1).

Some studies on rectal cancer surgery have shown that the short-term benefits, mid-term oncologic safety, and anastomotic leakage rate were not significantly different between open and laparoscopic surgeries (11). Regardless of the techniques employed, leakage rates are higher following low anterior resection, particularly in laparoscopic colectomy. There are controversies surrounding the impact of the number of stapler firings on anastomosis leak rate (1). Kim et al. found that more than 2 stapler firings were associated with leakage at univariate analysis (12).

In over 90% of cases, the use of one or two stapler fir-

ings for rectal division is possible and the use of 3 or more cartridges is increasingly rare. However, in approximately half of the patients, a single linear stapler has been used (13).

The negative correlation between anastomotic leakage and recurrence after rectal resection for cancer might have various explanations including that the leakage might damage local and/or systemic immunity or might be a substitute for aggressive tumors, unsatisfactory surgery, or other host-/tumor-related factors (14, 15). It would not be effective to pay excessive attention to controlling some risk factors including smoking cessation, weight loss, and good nutrition if possible (5, 16-22).

The presence of peritonitis after leakage cannot be prevented by using such techniques as the "reinforcement of anastomosis, reconstruction of post-peritoneum, and protective soma," normally considered as a protective factor in reducing the occurrence and severity of anastomotic leakage (23). Smith et al. showed that "endoscopic visual evaluation and mechanical tests such as rectal insufflation with air, betadine, or methylene blue and mechanical tests of anastomoses demonstrate intraoperative leaks in 5% to25 % of anastomoses" (24).

2. Objectives

In this study, we aimed at evaluating the risk factors and preventive measures for anastomotic leakage after rectal cancer surgery.

3. Methods

3.1. Patients

This descriptive cross-sectional study was conducted at the Colorectal Research Center of Faghihi Hospital, Shiraz, Iran on all of the patients having already undergone laparoscopic and open rectal resection for all stages (1 to 4) of rectal cancer with a double stapling colorectal or coloanal anastomosis between January 2011 and October 2020. The patients with a recurrence history of rectal cancer and patients with inflammatory bowel disease and corticosteroids consumers were excluded. Regarding neoadjuvant therapy, 60.8% (43 women and 61 men) of patients had received radiotherapy, while 53.8% (39 women and 53 men) had received chemotherapy and surgery at least 2 months after the chemoradiotherapy. During this period, 171 patients (of these 155 were patients treated by laparoscopic approach, 13 had converted to open surgery, while 16 patients had started with laparotomy). The ethics code was IR.SUMS.REC.1399.999 according to the Shiraz University of Medical Sciences Ethics Committee.

The level of anastomosis is related to the site of surgery. Patients were divided into 3 groups: upper rectal cancer, middle rectal cancer, and lower rectal cancer. A primary rectal carcinoma was determined by rigid sigmoidoscopy and digital rectal examination. The tumors were defined into the following categories: lower rectum (0 - 7 cm), middle rectum (7.1 - 12 cm), and upper rectum (12.1 - 17 cm). Of all the patients, 90.6% (93 men and 62 women) underwent laparoscopy, 7.6% (3 women and 10 men) converted to open surgery due to multiple factors (anatomical-related factors, bleeding, and local tumor extension); and 9.3% (10 women and 6 men) had first undergone laparotomy due to previous operation and comorbidities.

The preoperative workup consisted of a clinical assessment (history and examination), carcinoembryonic antigen (CEA), total colonoscopy, pelvic MRI, chest x-ray, abdominal ultrasonography, and computed tomography of the abdomen, chest, and pelvis.

3.2. Surgical Procedures

The day before each operation, the bowel was prepared with polyethylene glycol. Each patient also received antibiotics, deep vein thrombosis prophylaxis, and stoma nurse consultation.

For low anterior resections of the rectum, we adopted the TME technique in the extrafascial plane, dissecting down to the pelvic floor. We used extrafascial dissection for high anterior resections, dividing the mesorectum at 5 cm below the distal extent of the tumor and the rectum at 2 cm distal to the tumor. We performed splenic flexure mobilization in the majority of our cases. The anastomotic technique involved the use of double stapling. A diverting ileostomy was used in cases where we observed poor bowel preparation, anastomotic tension, leakage on testing or incomplete doughnuts, or technical difficulties in performing low rectal anastomosis caused by the patient's anatomy; this was also done for all cases of coloanal anastomoses and patients with a history of radiotherapy and steroid use.

3.3. Anastomotic Leakage

Anastomotic leakage is often considered to be either clinical (overt) or subclinical. Symptomatic anastomotic leakage showed by pus or fecal discharge from the pelvic drain, peritonitis, or extravasation of administered contrast on radiography or computed tomography. Asymptomatic radiological anastomotic leakages were not considered valid in our study because routine contrast enema was not performed after the operation.

3.4. Statistical Analysis

This study analyzed 12 independent variables including age, sex, obesity, smoking, ASA grading, medical diseases, preoperative radiotherapy, preoperative chemotherapy, level of anastomosis from the anal verge, splenic flexure mobilization, diverting ileostomy, and number of stapler firings. The Pearson chi-square test was performed for analyzing the data.

4. Results

The results of our work on 171 (72 women and 99 men) patients showed that the patients had a mean age of 58.33 $\pm$ 11.95 years old, while their mean BMI was calculated as 24.10 $\pm$ 4.41 kg/m^2 (Table 1).

Table 1. Demographical Data of Patients

Parameters	Mean $\pm$ SD/No.	Range (Min.-Max.)/% of No.
Age (y)	58.33 $\pm$ 11.95	30 - 94
BMI (kg/m^2)	24.10 $\pm$ 4.41	14.7 - 41.5
Cartridge usage	2.27 $\pm$ 0.87	1 - 4
Cigarette smokers	27 men and 1 woman	16.3
Positive test for opium	12 men	7.01
Anterior resection	3 women and 2 men	2.9
High anterior resection	One man	0.5
Low anterior resection	47 women and 66 men	66.1
Ultra-low anterior resection	22 women and 30 men	30.4
Diverted by loop ileostomy	46 women and 72 men	69.0
Ghost ileostomy	2 men	1.16

Of the 171 patients included in this study, 17.5 % (20 women and 10 men) required a single staple firing for rectal division, while 47.9% (32 women and 50 men) required 2 linear staplers, and 24.5% (15 women and 27 men) required 3 cartridges for rectal division, while 9.9% (5 women and 12 men) required 4 cartridges in their surgeries. There were significant differences between men and women in the number of cartridges used (P = 0.023) (Table 2).

Splenic flexure mobilization was performed in 71.3% (50 women and 72 men) of patients, two of which had anastomotic leakage. In our study, anastomotic leaks had occurred in 2.33% (4 men) of patients after 5 postoperative days.

Our study showed that smoking is an important risk factor in causing anastomosis leaks (P = 0.016; Table 3) and

Table 2. Relation Between Number of Cartridge and Gender

Gender	No. of Cartridge				P-Value
	1	2	3	4	
Female	20	32	15	5	0.023 [a]
Male	10	50	27	12	
Total	30	82	42	17	

[a] Pearson chi-square test

the anastomotic leakage group did not show any significant comorbidities associated with the incidence of the leak.

In the present study, three patients presented with perianal abscess and were examined under anaesthesia and treated by incision and drainage. One patient that presented with peritonitis was treated by laparoscopic exploration and irrigation with normal saline and drainage.

5. Discussion

Leakage of anastomosis is a serious complication in rectal surgery with significant morbidity. We conducted this study to identify the risks and find preventive measures. The level of anastomosis is related to the site of surgery and the more distal it is, the greater the chance of leakage (25), which is why ileostomy is indicated even if the patient has not been neoadjuvant and has been given a coloanal anastomosis. Due to referral cases from other centers, most of our cases were mid- and lower-rectal cancer and these patients have more difficulty managing. The level of anastomosis is dependent on anterior resection, low anterior resection, and ultra-low anterior resection. In the present study, the low anterior resection had the most frequency (66.1%, Table 1).

In this study, anastomotic leaks had occurred in 2.33% (4 men) of patients after 5 postoperative days. Concerning the timing of leakage after surgery, early leakage (within 0 - 4 postoperative days) may be due to technical factors (23) but in all participants in this research leakage occurred after 5 postoperative days, pointing to factors other than technical issues as the cause but after 5 days it could be due to comorbidities and immune deficiency.

Most of the studies revealed that the higher number of stapler firings for rectal division increases the chance of leakage (1) and the mean number of cartridge usage in the current research was 2.27 $\pm$ 0.87 (Table 1) and the relation between the number of cartridges and the chance of leakage was not statistically significant, perhaps due to the low number of cases of leakage (P = 0.280; Table 3).

Splenic flexure mobilization was performed in 71.3% (50 women and 72 men) of patients, two of which had anas-

Table 3. Leakage After 5 Days of Surgery Relation to Number of Cartridges and Smoking

	Leakage After 5 Days (No.)	P-Value
Number of cartridges		0.280
1	0	
2	2	
3	1	
4	1	
Smoker (cigarette or opium)	3	0.016 [a]

[a] Pearson chi-square test

tomotic leakage in our study. Most of authors recommend splenic flexure mobilization to decrease the tension in colorectal anastomosis since it will decrease the leakage risk (26). Despite the fact that splenic flexure was mobilized, the incidence of anastomotic leak in most of our cases showed that other factors may be responsible rather than tension.

Of the 171 rectal surgeries, 69.0% of patients were diverted by loop ileostomy and 1.16% of were supported by ghost ileostomy. The remaining 29.8% of the patients did not undergo ileostomy (Table 1). There is no consensus on whether ileostomy should protect the distal anastomosis or be useful in treating leakage. In this study, most cases had an ileostomy and our results were inconclusive, perhaps due to the low number of cases.

Smoking is the main risk factor for anastomotic leak in low rectal resection (5) and, in the present study; some of our cases had a history of smoking (16.1%; Table 1). Findings showed that smoking is an important risk factor in causing anastomosis leaks (P = 0.016; Table 3). In our study, the anastomotic leakage group did not show any significant comorbidities associated with the incidence of the leak. There were significant differences between men and women in the number of cartridges used (P = 0.023; Table 2) and it could be related to the anatomical difference between them.

5.1. Conclusions

The higher number of stapler firings for rectal division, history of smoking, level of anastomosis, and male sex were seen to be independent risk factors for the anastomotic leak.

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Footnotes

Authors' Contribution: S.V.H. conceived and designed the evaluation and drafted the manuscript. A.E.K.A. participated in designing the evaluation, performed parts of the statistical analysis, and helped to draft the manuscript. H.Kh. and A.B. re-evaluated the clinical data, revised the manuscript and performed the statistical analysis, and revised the manuscript. F.B. and S.M.K.T. collected the clinical data, interpreted them, and revised the manuscript. M.H. and F.H. re-analyzed the clinical and statistical data and revised the manuscript. All authors read and approved the final manuscript.

Conflict of Interests: There was not any financial or non-financial competing interest in this study.

Data Reproducibility: The dataset presented in the study is available on request from the corresponding author during submission or after publication. The data are not publicly available due to privacy of patients.

Ethical Approval: The ethics code was IR.SUMS.REC.1399.999 according to the Shiraz University of Medical Sciences Ethics Committee (Link: ethics.research.ac.ir/ProposalCertificateEn.php?id=171560).

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Informed Consent: This is a real retrospective study and the informed consent is not gathered from patients.

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