Ann Med Res 2021;28(2):352-60

Annals of Medical Research
DOI: 10.5455/annalsmedres.2020.08.889

Original Article

Risk factors for anastomotic leakage and stricture following rectal cancer surgery: A retrospective cohort study

Mehmet Arif Usta, Arif Burak Cekic

Department of General Surgery, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey

Abstract

Aim: Anastomotic problems including anastomotic leakage and stricture following rectal cancer surgery are complications with indefinite risk factors. It was aimed to evaluate preoperative and postoperative risk factors for anastomotic leakage and stricture in patients who underwent rectal cancer surgery.

Materials and Methods: Patients who underwent surgical treatment after neoadjuvant treatment for middle and distal rectal tumors were retrospectively analyzed between January 2016 and September 2019. All consecutive patients who were older than 18 years and treated via low anterior resection with colorectal anastomosis or intersphincteric resection with coloanal anastomosis with diverting ileostomy were included. Patients with and without any anastomotic complications were grouped as Group 1 and 2, respectively. Subgroup analysis based on anastomotic leakage and stricture was also performed.

Results: There were 62 patients with a mean age of 60.5±12.2 years. Anastomotic complications occurred in 11 patients (17.7%). There were seven (11.3%) anastomotic leakage and six (9.7%) anastomotic stricture. Male patients were significantly higher in Group 1 (p=0.018). Anastomotic leakage was seen more commonly in male patients (p=0.035). Intersphincteric resection with hand-sewn coloanal anastomosis and the diameter of the tumor was significantly associated with anastomotic leakage (p=0.002 and p=0.004, respectively). Multivariate analysis revealed that male sex for the development of any anastomotic complication, and handsewn coloanal anastomosis, and tumor diameter for anastomotic leakage were independent risk factors.

Conclusion: Male sex, intersphincteric resection with coloanal anastomosis, and diameter of tumor can be significant risk factors for the development of any anastomotic complication including anastomotic leakage following rectal cancer surgery.

Keywords: Rectal cancer; anastomosis; surgical; anastomotic leak; anastomotic stricture; postoperative complications

INTRODUCTION

Anastomotic problems including anastomotic leakage (AL) and anastomotic stricture (AS) are essential pivotal steps for successful outcomes of sphincter-preserving rectal cancer surgery. These complications can be seen in approximately 10% for AL and up to 19% for AS in patients who underwent low anterior resection (LAR) or intersphincteric resection (ISR) for rectum cancer (1-4).

Postoperative AL is associated with increased morbidity and mortality besides poor oncological outcomes (3, 5). Although the definition of AS has not been clearly performed and there is a cause-effect relationship between AL and AS, AS is not a negligible complication due to its occurrence in a substantial proportion of the patients following LAR (1, 4). Besides, it can be regarded as a significant factor for non-reversal of diverting ileostomy (6).

Although the causes and mechanisms behind the development of these complications remain unknown, several risk factors have been proposed (7, 8). These patient-related and tumor-related factors are usually unmodifiable (1, 7). However, there are few studies describing the risk factors and the rates for both AL and AS associated with LAR (1, 3). It has been also reported that there is a close association between AL and AS (9). Thus, identification of risk factors may improve the outcomes of LAR by preventing the occurrence of both AL and AS.

This study was planned to assess the preoperative and postoperative risk factors for the development of AL and AS in patients who underwent LAR and ISR for rectal cancer.

Received: 30.08.2020 **Accepted:** 06.10.2020 **Available online:** 19.02.2021
Corresponding Author: Mehmet Arif Usta, Department of General Surgery, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkey, **E-mail:** ustausta@windowslive.com

MATERIALS and METHODS

Study

This study was a retrospective analysis of patients who underwent rectal cancer surgery between January 2016 and September 2019 in our tertiary medical center, where a high number of colorectal surgeries are performed. Written consent was taken from the patients. The study was approved by the local ethical committee (xxx xxx University, 2020/137). It was performed in accordance with the Declaration of Helsinki.

Patients

All consecutive patients with middle or distal rectal adenocarcinoma with curative sphincter preserving surgery via LAR or ISR following neoadjuvant therapy were evaluated. The decision and the type of neoadjuvant therapy were determined based on the tumoral features of the patients (radiologically T2-T4 tumors with/without positive lymph nodes) as a multidisciplinary approach at the tumor board of the institution. Preoperative chemoradiotherapy was performed as 50.4 cGy total radiotherapy dose with 5-fluorouracil or capecitabine. After an interval of 8-10 weeks, surgical treatment by a senior surgeon who had experience in colorectal surgery was performed. Open, laparoscopic, and converted to open cases were all included. The inclusion criteria were as follows: (1) patients older than 18 years, (2) tumors less than 10 cm from the anus (middle and distal tumors), (3) surgical treatment via low anterior resection (LAR) with colorectal anastomosis (CRA) or intersphincteric resection (ISR) with coloanal anastomosis (CAA), (4) diverting ileostomy at the initial surgery.

Abdominoperineal resection (n=25), absence of neoadjuvant therapy (n=21), proximal rectal tumors (>10 cm from the anal verge) (n=18), tumors with distant metastasis (n=13) and emergency surgery (n=9) were the exclusion criteria. After that, a total of 62 patients was analyzed for the study.

Interventions and follow-up

Digital rectal examination and the findings of colonoscopy were used to determine the distance from the anal verge to the lower end of the tumor for middle and distal tumors.

Standardized laparoscopic and open surgical procedures were used (2). Specifically, tumor-specific mesorectal excision was performed for the middle and distal tumors. LAR with straight end-to-end double stapled technique (DST) CRA (DST-CRA) or total/partial ISR with hand-sewn CAA (ISR-CAA) was performed based on the discretion of the surgeon. For DST, a 29 mm or 31 mm circular stapler was used. 3/0 polyglactin sutures (Vicryl, Ethicon, Somerville, NJ, USA) were used for hand-sewn CAA. Pelvic drains were routinely applied.

Regular physical examination was performed every three months up to the closure of diverting ileostomy. The integrity of the anastomosis was controlled routinely in each patient by colonoscopy and radiological studies.

Variables

Demographic data (age, sex), clinical (American Society of Anesthesiologists (ASA) score and tumoral (location, largest diameter, T and N stages, number of total and metastatic lymph nodes, American Joint Committee on Cancer TNM stage 7th edition, differentiation grade, tumor regression grade) features, operative findings (the type of surgery and anastomosis), and complications were recorded using the medical records of the patients (10). Major surgical and clinical complications were evaluated. Postoperative paralytic ileus was defined as the dilation of the small bowel segments that was confirmed radiologically in association with a dysfunctioning diverting ileostomy. Any purulent discharge from the surgical wounds in association with hyperemia of the incision was defined as surgical site infections.

Mortality was considered as death during the postoperative 30 days following rectal surgery.

Presence of clinical findings including the discharge of pus or feces from the pelvic drains and signs of abdominal pain, tenderness, fever, or detection of anastomotic dehiscence as a visible mural defect during endoscopic examination of the anastomosis was used for the diagnosis of AL. In former cases, computed tomography with water-contrast rectal enema was used to detect the presence of an abscess with fluid/air bubbles at the level of anastomosis. Grades of AL was done using the criteria defined by Rahbari et al. (11) as grade B (symptomatic AL treated by conservative measures) and grade C (AL requiring laparotomy). Asymptomatic AL that was diagnosed by imaging techniques (grade A) was not evaluated and not taken into consideration for analysis. Any tightness or inability to insert an index finger or a standard colonoscope with a 12-mm external diameter through the anastomosis was defined as AS (1, 3).

Patients with AL and/or AS were grouped as Group 1, and Group 2 was used for patients without anastomotic complications. A subgroup analysis was also performed based on each complication as patients with and without AL as Group AL and Group non-AL, respectively, and patients with and without AS as Group AS and Group non-AS, respectively. The interventions for the treatment of both AL and AS and their outcomes were analyzed separately.

Repair of diverting ileostomy (reversal of ileostomy) was planned following the rectal surgery and after the completion of adjuvant therapy, if necessary. It was always preceded by a flexible rectoscope.

Statistical analysis

The development of anastomotic complications during both early (postoperative the first 30 days) and late postoperative periods (before the closure of diverting ileostomy) was regarded as the primary outcome. The secondary outcome was the variables predicting the development of anastomotic complications.

Statistical analysis was performed using a commercially available statistical software package (SPSS Inc., Chicago, IL). The Kolmogorov-Smirnov and/or Shapiro-Wilk tests were applied to determine the normal distribution of continuous variables. Mean ± standard deviation and median (interquartile range) were used to express continuous variables with and without normal distribution, respectively. Categorical variables were expressed as frequencies and percentages. The Pearson chi-square, Fisher's exact, and Kruskal-Vallis tests were used for categorical variables. The Mann-Whitney U test was applied to compare continuous variables without normal distribution. The t-test and one-way analysis of variance (ANOVA) were used for the comparison of continuous variables with the normal distribution. Binary logistic regression with backward stepwise elimination was used for multivariate analysis considering the statistical significance of the variables in univariate analysis. The data were expressed as odds ratios (OR) with a 95% confidence interval (CI). A p-value of < 0.05 was considered significant.

RESULTS

There were 62 patients in the study group. The mean age was 60.5±12.2 years. Of them, 36 patients (58.1%) were male. Demographic and laboratory features are given in Table 1.

Anastomotic complications occurred in 11 patients (17.7%). There were seven (11.3%) AL and six (9.7%) AS in the study group. In the treatment group, there were two patients in whom both AL and AS developed. The median time for the diagnosis of AL after the surgery was 7 days (range 4-21 days). Grade B and Grade C AL were seen in five (8.1%) and two patients (3.2%), respectively.

Comparison of the groups with (Group 1) and without anastomotic complications (Group 2) revealed that the percentage of male patients was higher in Group 1 (p=0.018) (Table 1). Although AL was significantly associated with male sex (p=0.035), grouping based on AS revealed no significant sex distribution (Table 2). Other demographic and laboratory variables were similar in Group 1 and Group 2, and the groupings based on AL and AS.

Table 1. Demographic and clinical features of the groups

Variable		Overall (n=62)	Group 1 (n=11)	Group 2 (n=51)	p
Age (year) †		60.5±12.2	59.5±7.0	60.1±13.1	0.764
Sex‡	Male	36 (58.1)	10 (90.9)	26 (51.0)	0.018
	Female	26 (41.9)	1 (9.1)	25 (49.0)	
ASA groups‡	1-2	30 (48.4)	7 (63.6)	23 (45.1)	0.329
	>3	32 (51.6)	4 (36.4)	28 (54.9)	
Hemoglobin (g/dL) †		12.3±1.8	12.34±1.9	12.30±1.9	0.952
Albumin (mg/dL) §		4.1 (3.75-4.3)	4.1 (3.8-4.2)	4.1 (3.6-4.3)	0.839

†: mean ± standard deviation, ‡: n(%), §: median (interquartile range)
ASA: American Society of Anesthesiologists

Table 2. Demoraphic and clinical features of the groups based on AL and AS

Variable		Overall (n=62)	Group AL (n=7)	Group non-AL (n=55)	p	Group AS (n=6)	Group non-AS (n=56)	p
Age (year) †		60.5±12.2	57.9±5.8	60.8±12.8	0.551	62.8±7.1	60.2±12.6	0.621
Sex‡	Male	36 (58.1)	7 (100)	29 (52.7)	0.035	5 (83.3)	31 (55.4)	0.387
	Female	26 (41.9)	0 (0)	26 (47.3)		1 (16.7)	25 (44.6)	
ASA groups‡	1-2	30 (48.4)	5 (71.4)	25 (45.5)	0.249	3 (50.0)	27 (48.2)	1.0
	>3	32 (51.6)	2 (28.6)	30 (54.5)		3 (50.0)	29 (51.8)	
Hemoglobin (g/dL) †		12.3±1.8	12.34±1.9	12.30±1.9	0.983	12.05±2.3	12.34±1.8	0.415
Albumin (mg/dL) §		4.1 (3.75-4.3)	4.1 (3.8-4.2)	4.1 (3.6-4.3)	1.0	4.1 (3.2-4.2)	4.1 (3.8-4.3)	0.553

†: mean ± standard deviation, ‡: n(%), §: median (interquartile range)
AL: Anastomotic leakage, AS: Anastomotic stricture, ASA: American Society of Anesthesiologists

In Group 2, there were significantly more patients with DST-CRA (p=0.004) (Table 3). Other tumoral and operative features were similar in both groups. The median diameter of the tumors was significantly higher in patients with AL (p=0.004) (Table 4). Besides, ISR-CAA was seen more commonly in patients with AL (p=0.002).

Table 3. Tumoral and operative findings of the study groups

Variable		Overall (n=62)	Group 1 (n=11)	Group 2 (n=51)	p
Location ‡	Middle	34 (54.8)	4 (36.4)	30 (58.8)	0.200
	Distal	28 (45.2)	7 (63.6)	21 (41.2)	
Diameter (mm)		47.5 (40.0-55.75)	58.0 (40.0-78.0)	46.0 (40.0-55.0)	0.181
Type of surgery ‡	Open	42 (67.7)	9 (81.8)	33 (64.7)	0.483
	Laparoscopic	17 (27.4)	2 (18.2)	15 (29.4)	
	Converted	3 (4.8)	0 (0)	3 (5.9)	
Type of surgery ‡	Open	45 (72.6)	9 (81.8)	36 (70.6)	0.712
	Laparoscopic	17 (27.4)	2 (18.2)	15 (29.4)	
Type of anastomosis ‡	DST-CRA	50 (80.6)	5 (45.5)	45 (88.2)	0.004
	ISR-CAA	12 (19.4)	6 (54.5)	6 (11.8)	
Differentiation grade ‡	Well	44 (71.0)	6 (54.5)	38 (74.5)	0.059
	Moderate	8 (12.9)	1 (9.1)	7 (13.7)	
	Poor-mucinous	3 (4.8)	1 (9.1)	2 (3.9)	
	Complete response	7 (11.3)	3 (27.3)	4 (7.8)	
T stage ‡	0	9 (14.5)	3 (37.3)	6 (11.8)	0.624
	1	3 (4.8)	0 (0)	3 (5.9)	
	2	12 (19.4)	2 (18.2)	10 (19.6)	
	3	36 (58.1)	6 (54.5)	30 (58.8)	
	4	2 (3.2)	0 (0)	2 (3.9)	
N stage ‡	0	38 (61.3)	8 (72.7)	30 (58.8)	0.497
	1	14 (22.6)	1 (9.1)	13 (15.7)	
	2	10 (16.1)	2 (17.7)	8 (15.7)	
TNM stage ‡	0	8 (12.9)	3 (27.3)	5 (9.8)	0.422
	1	10 (16.1)	1 (9.1)	9 (17.6)	
	2	22 (35.5)	4 (36.4)	18 (35.3)	
	3	22 (35.5)	3 (27.3)	19 (37.3)	
Total lymph nodes §		13 (8-17.25)	13 (7-17)	13 (8-18)	0.671
Metastatic lymph nodes §		0 (0-2)	0 (0-3)	0 (0-2)	0.658
Tumor regresyon grade ‡	Complete response	8 (12.9)	3 (27.3)	5 (9.8)	0.413
	Partial response	9 (14.5)	2 (18.2)	7 (13.7)	
	Residual tumor	8 (12.9)	1 (9.1)	7 (13.7)	
	No response	7 (11.3)	0 (0)	7 (13.7)	
	Unknown	30 (48.4)	5 (45.5)	25 (49.0)	
Length of hospital stay (day) §		9.0 (7.0-11.5)	13.0 (9.0-21.0)	9.0 (7.0-11.0)	0.014

‡: n(%), §: median (interquartile range).
DST-CRA: Double stapler technique-colorectal anastomosis, ISR-CAA: Intersphincteric resection-coloanal anastomosis

Table 4. Tumoral and operative findings of the study groups based on AL and AS								
Variable		Overall (n=62)	Group AL (n=7)	Group non-AL (n=55)	p	Group AS (n=6)	Group non-AS (n=56)	p
Location ‡	Middle	34 (54.8)	2 (28.6)	32 (58.2)	0.228	3 (50.0)	31(55.4)	1.0
	Distal	28 (45.2)	5 (71.4)	23 (41.8)		3 (50.0)	25 (44.6)	
Diameter (mm) §		47.5 (40.0-55.75)	64.0 (58.0-82.0)	46.0 (40.0-55.0)	0.004	40.0 (38.0-55.0)	48.5 (41.0-56.5)	0.332
Type of surgery ‡	Open	42 (67.7)	6 (85.7)	36 (65.5)	0.271	4 (66.7)	38 (67.9)	0.977
	Laparoscopic	17 (27.4)	1 (14.3)	16 (29.1)		2 (33.3)	15 (26.8)	
	Converted	3 (4.8)	0 (0)	3 (5.5)		0 (0)	3 (5.5)	
Type of surgery ‡	Open	45 (72.6)	6 (85.7)	39 (70.9)	0.662	4 (66.7)	41 (73.2)	0.662
	Laparoscopic	17 (27.4)	1 (14.3)	16 (29.1)		2 (33.3)	15 (26.8)	
Type of anastomosis ‡	DST-CRA	50 (80.6)	2 (28.6)	48 (87.3)	0.002	3 (50.0)	47 (83.9)	0.081
	ISR-CAA	12 (19.4)	5 (71.4)	7 (12.7)		3 (50.0)	9 (16.1)	
Differentiation grade ‡	Well	44 (71.0)	3 (42.9)	41 (74.5)	0.060	5 (83.3)	39 (69.6)	0.602
	Moderate	8 (12.9)	1 (14.3)	7 (12.7)		0 (0)	8 (14.3)	
	Poor-mucinous	3 (4.8)	1 (14.3)	2 (3.6)		0 (0)	3 (5.4)	
	Complete response	7 (11.3)	2 (28.6)	5 (9.1)		1 (16.7)	6 (10.7)	
T stage ‡	0	9 (14.5)	2 (28.6)	7 (12.7)	0.960	1 (16.7)	8 (14.3)	0.602
	1	3 (4.8)	0 (0)	3 (5.5)		0 (0)	3 (5.4)	
	2	12 (19.4)	0 (0)	12 (21.8)		2 (33.3)	10 (17.9)	
	3	36 (58.1)	5 (71.4)	31 (56.4)		3 (50.0)	33 (58.9)	
	4	2 (3.2)	0 (0)	2 (3.6)		0 (0)	2 (3.6)	
N stage ‡	0	38 (61.3)	5 (71.4)	33 (60.0)	0.608	4 (66.7)	34 (60.7)	0.826
	1	14 (22.6)	1 (14.3)	13 (23.6)		1 (16.7)	13 (23.1)	
	2	10 (16.1)	1 (14.3)	9 (16.4)		1 (16.7)	9 (16.1)	
TNM stage ‡	0	8 (12.9)	2 (28.6)	6 (10.9)	0.391	1 (16.7)	7 (12.5)	0.422
	1	10 (16.1)	0 (0)	10 (18.2)		1 (16.7)	9 (16.1)	
	2	22 (35.5)	3 (42.9)	19 (34.5)		2 (33.3)	20 (35.7)	
	3	22 (35.5)	2 (28.6)	20 (36.4)		2 (33.3)	20 (37.7)	
Total lymph nodes §		13 (8-17.25)	14 (7-19)	13 (8-17)	0.913	14 (8-17)	13 (8-18)	0.954
Metastatic lymph nodes §		0 (0-2)	0 (0-3)	0 (0-2)	0.862	0 (0-3)	0 (0-2)	0.972
Tumor regresyon grade ‡	Complete response	8 (12.9)	2 (28.6)	6 (10.9)	0.255	1 (16.7)	7 (12.5)	0.517
	Partial response	9 (14.5)	2 (28.6)	7 (12.7)		1(16.7)	8 (14.3)	
	Residual tumor	8 (12.9)	1 (14.3)	7 (12.7)		0 (0)	8 (14.3)	
	No response	7 (11.3)	0 (0)	7 (12.7)		0 (0)	7 (13.7)	
	Unknown	30 (48.4)	2 (28.6)	28 (50.9)		4 (66.7)	26 (46.4)	
Length of hospital stay (day) §		9.0 (7.0-11.5)	13.0 (10.0-30.0)	9.0 (7.0-11.0)	0.006	12.0 (8.0-16.0)	9.0 (7.0-11.0)	0.394

‡: n(%), §: median (interquartile range)
AL: Anastomotic leakage, AS: Anastomotic stricture, DST-CRA: Double stapler technique-colorectal anastomosis, ISR-CAA: Intersphincteric resection-coloanal anastomosis.

In the overall study group, surgical site infections and postoperative paralytic ileus were the two most common complications that were seen in 17 (27.4%) and 10 patients (16.1%). Other complications are detailed in Table 5. There was no perioperative mortality in the study group.

Multivariate analysis of the variables associated with the anastomotic complications is shown in Table 6. Male sex (OR=14.531 (95% CI 1.246-169.413), p=0.033) was independently associated with the development of any anastomotic complication. ISR-CAA (OR=28.783 (95% CI 1.775-466.788, p=0.018) and the diameter of the tumor (OR=1.083 (95% CI 1.007-1.165, p=0.033) were shown to be associated with the development of AL. However, multivariate analysis revealed no significant independent risk factor for AS.

Clinical features and treatment outcomes of the patients with AL and AS are described in Table 7. Laparotomy was needed in two patients with AL. Re-anastomosis and Hartmann's procedure was performed in each. Besides, percutaneous abscess drainage was needed in three patients during the conservative treatment of AL.

Three patients with AL remained with a permanent stoma due to AS in two and peritoneal carcinomatosis in one. Besides, one patient with AL refused the reversal of ileostomy and remained with the Hartmann's procedure. AS was treated in three patients with digital dilatation approaches either manually or using Hegar dilators. But, one patient refused the treatment for AS.

Adjuvant treatment was needed in 29 patients (46.8%). The reversal of ileostomy was performed with a mean interval of 23.9±11.3 weeks. Permanent stoma was required in a total of six patients in the study group with an overall rate of 9.7%. Due to the development of lung metastasis, the non-reversal of ileostomy was not performed in one patient without anastomotic complications.

Table 5. Distibution of the complications in patients with and without AL

Complication		Overall (n=62)	Group AL (n=7)	Group non-AL (n=55)
Surgery-related	Incisional SSI	17	3	14
	Organ/space SSI	4	3	1
	Postoperative paralytic ileus	12	2	10
	Anastomotic leakage	7	7	0
Cardiovascular system	Arrhythmia, hypentensive attack	5	2	3
Respiratory system	Pulmonary embolism, pneumonia, plevral effusion	4	1	3
Central nervous system	Cerebrovascular accident	1	0	1
Urinary system	Urinary tract infection	2	1	1

AL: Anastomotic leakage, SSI: Surgical site infection

Table 6. Multivariate analysis of variables probably associated with the development of anastomotic complications

Complication	Variable	OR	95% CI	p
AL and AS	Sex (male vs female)	14.531	1.246-169.413	0.033
	Anastomosis type (ISR-CAA vs DST-CRA)	7.321	0.946-56.684	0.057
AL	Sex (male vs female)	0.0	0.007-0.848	0.998
	Anastomosis type (ISR-CAA vs DST-CRA)	28.783	1.775-466.788	0.018
	Diameter (mm)	1.083	1.007-1.165	0.033
AS	Sex (male vs female)	3.277	0.309-34.789	0.325
	Anastomosis type (ISR-CAA vs DST-CRA)	2.250	0.282-17.930	0.444

AL: Anastomotic leakage, OR: Odds ratio, CI: Confidence interval, AS: Anastomotic stricture, DST-CRA: Double stapler technique-colorectal anastomosis, ISR-CAA: Intersphincteric resection-coloanal anastomosis

Table 7. Demographic and clinical features and treatment outcomes of the patients with anastomotic complications

No	Complication	Age	Sex	Type of anastomosis	Management	Outcome	Reversal of ileostomy	Reason for nonreversal
1	AL	62	M	DST-CRA	ENPT	Closure	Yes	
2	AL	56	M	ISR-CAA	Primary repair	Closure	Yes	
3	AL	49	M	ISR-CAA	Primary repair	Closure	Yes	
4	AL+AS	62	M	ISR-CAA	Primary repair	AS	No	AS
5	AL	55	M	ISR-CAA	ENPT	Closure	No	Peritoneal carcinomatosis
6	AL	55	M	DST-CRA	Laparotomy-Hartmann's procedure	--	No	Refusal to treatment
7	AL+AS	66	M	ISR-CAA	Laparotomy-reanastomosis	AS	No	AS
8	AS	52	M	DST-CRA	Digital dilatation	Healing	Yes	
9	AS	59	M	DST-CRA	Digital dilatation	Healing	Yes	
10	AS	72	F	DST-CRA	Digital dilatation	Healing	Yes	
11	AS	67	M	ISR-CAA	Refusal to treatment	--	No	Refusal to treatment

AL: Anastomotic leakage, AS: Anastomotic stricture, M: Male, F: Female, DST-CRA: Double stapler technique-colorectal anastomosis, ISR-CAA: Intersphincteric resection-coloanal anastomosis, ENPT: Endoscopic negative pressure therapy

DISCUSSION

In this retrospective study, we have shown that male sex and the type of anastomosis as ISR-CAA are the independent risk factors for the development of both AL and AS in patients who underwent low anterior resection with or without ISR following neoadjuvant chemoradiotherapy. Male sex, ISR-CAA, and the diameter were shown to be significantly associated with AL. Although all these factors were unmodifiable in nature, these two complications were also the main factors affecting stoma reversal.

In earlier studies, AL and AS have been regarded as important sequelae of the rectum surgery. The rates of AL and AS show great variability in the previous studies with reported rates upwards of 30% (12, 13). The heterogeneity of the study groups regarding the diverse inclusion criteria such as different approaches and types of surgery and lack of standardized definitions for both AL and AS can partly explain the considerable variations (1, 4, 12, 14-16). So, any comparison between the outcomes of the studies seems to be difficult.

Among the important complications of the rectum surgery, only AL has been studied in most of the previous studies (2, 5, 8, 14-20). A significant correlation between AL and AS has been also shown by Kim's study indicating the reciprocal consequences between AL and AS (1). Considering this relation, we believe that the evaluation of AL and AS in the same study group helps physicians to identify the risk factors.

Depending on the type of surgery and patient characteristics, the rate of AL has varied by up to 20% (8, 10, 12, 17, 19). This difference can be attributed to the different ratios of the colon and rectal surgery and the inconsistent inclusion criteria (19). Several authors reported that AL occurred in up to 14.7% of patients who underwent surgery for rectal cancer (8, 15). But, they included all grades of AL. In a nationwide study of colorectal cancer from the Netherlands, there was an AL rate of 4.16% (20). But, colon cancer comprised almost 80% of the study group and rectal cancer was shown to be an independent risk factor for AL. Therefore, we can not use this low rate as a standard for other studies. In Zheng's study (19), the rate of clinical AL was 14.3% for the patients who received neoadjuvant therapy. They included only Grade B and Grade C AL cases. In the present study, our clinical AL rate (Grade B and Grade C) was 11.3% as inconsistent with the results mentioned above (15, 17, 19).

In Zhu's study (6), the authors reported a rate of 21.1% for both AS and anastomotic stiffness following low anterior resection with CRA. Zhang et al. (9) detected anastomotic strictures in 13.2% of the cases who underwent laparoscopic ISR. Reif de Paula et al. (13) found a rate of 3.6% for AS and 3.4% for AL in patients with left-sided CRA. In a study in which ultra-low LAR or ISR was performed, the authors detected AS in 7.8% of the patients (4). In the present study, our AS rate was 9.7% that was regarded as comparable with the values described in previous reports (4, 6, 9, 13). Based on the reported rates, we can conclude that both AL and AS can be seen in a substantial proportion of the patients following rectal cancer surgery.

Several risk factor including preoperative or postoperative radiotherapy, male sex, ultra-low rectal cancer, hand-sewn CAA and size and the number of staplers have been analyzed in the previous studies, but, the results have not reached a consensus yet (2, 4, 5, 7, 12, 13). Male sex has been shown as a significant risk factor for the development of anastomotic complications after rectal cancer surgery (12, 15, 15, 18, 19). But, there have been also controversial results. In Reif de Paula's study (13), there was no significant association of gender on AL and AS. It has been also reported that male patients are more prone to have AS without significant significance (4, 17). In the present study, we showed that male sex is a significant risk factor for AL and the development of any complication after rectal cancer surgery. So, we say that no consensus has been reached about the impact of male sex on the development of postoperative complications. It is generally known that hand-sewn CAA is one of the most significant risk factors for the development of these complications in accordance with the present study (4). In this study, we also showed that there was a significant association between hand-sewn CAA and the diameter of the tumor with AL. Based on these results, it should be kept in mind that any hand-sewn CAA anastomosis in male patients can be regarded as a potential risk factor for future AL.

In studies evaluating the risk factors for AS, the authors found that ISR type anastomosis, smaller size staplers, male sex, preoperative radiotherapy, and previous AL were associated with the postoperative AS (4, 6, 9, 13). However, there was no significant association between AS and the patient- and tumor-related variables in the present study. There were two patients in whom both AL and AS occurred in this study, the other four cases were unrelated to AL. In addition, we could not show the impact of male sex and ISR-CAA on AS. Less number of AS in our small sample size may be an important issue for these controversial findings.

Preoperative radiotherapy has been shown as a significant risk factor permanent stoma due to anastomotic stenosis or stiffness and AL (3, 6). In Lee's study (4), postoperative radiotherapy and diverting ileostomy were shown to be independent risk factors for AS. We included all rectal cancer cases with preoperative radiotherapy and diverting ileostomy in the present study. Besides, due to the use of preoperative neoadjuvant radiotherapy as the inclusion criteria, postoperative radiotherapy was not necessitated in the study group. Therefore, we could not evaluate the impact of pre- and post-operative radiotherapy and diverting ileostomy on the anastomotic complications.

Rates of permanent stoma have been used as another variable to evaluate the impact of anastomotic complications (4). In the present study, there were several reasons to determine the reversal of ileostomy as a patient's desire and refusal to treatment, and the local and systematic progression of the disease. So, we did not try to compare our permanent stoma rate with that of other studies.

A single-center and retrospective character of the study and the relatively small sample size was the major limitations. We could not gather some medical information such as body mass index, operation time, and sizes of the circular staplers due to incomplete medical files. Besides, due to the absence of unstandardized approaches for the treatment of AL and AS, we could not analyze the outcomes. However, the analysis of a homogenous study group regarding neoadjuvant therapy and diverting ileostomy in patients only with middle and distal rectal tumors was the major strength of this study giving a detailed and complete profile of the complications. Besides, separately and together, the evaluation of both AL and AS in the same patient group was another strength.

CONCLUSION

In conclusion, among patients undergoing colorectal or coloanal anastomosis, male sex, type of anastomosis as ISR-CAA, and diameter of a tumor can be significant risk factors for the development of any anastomotic complication. A randomized controlled study with standardized inclusion criteria that control possible confounding factors may resolve the controversial issues for the development of anastomotic problems following rectal cancer surgery.

Conflict of interest : The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical approval: The study was approved by the local ethical committee (Karadeniz Technical University, 2020/137).

REFERENCES

1. Kim JC, Lee JL, Kim CW, et al. Mechanotechnical faults and particular issues of anastomotic complications following robot-assisted anterior resection in 968 rectal cancer patients. J Surg Oncol 2019;120:1436-45.
2. Lee S, Ahn B, Lee S. The relationship between the number of intersections of staple lines and anastomotic leakage after the use of a double stapling technique in laparoscopic colorectal surgery. Surg Laparosc Endosc Percutan Tech 2017;27:273-81.
3. Qin Q, Ma T, Deng Y, et al. Impact of preoperative radiotherapy on anastomotic leakage and stenosis after rectal cancer resection: post hoc analysis of a randomized controlled trial. Dis Colon Rectum 2016;59:934-42.
4. Lee SY, Kim CH, Kim YJ, et al. Anastomotic stricture after ultralow anterior resection or intersphincteric resection for very low-lying rectal cancer. Surg Endosc 2018;32:660-6.
5. Hiraki M, Tanaka T, Ikeda O, et al. Retrospective risk analysis for anastomotic leakage following laparoscopic rectal cancer surgery in a single institute. J Gastrointest Cancer 2020;51:908-13.

6. Zhu H, Bai B, Shan L, et al. Preoperative radiotherapy for patients with rectal cancer: a risk factor for non-reversal of ileostomy caused by stenosis or stiffness proximal to colorectal anastomosis. Oncotarget 2017;8:100746-53.
7. Wang XT, Li L, Kong FB, et al. Surgical-related risk factors associated with anastomotic leakage after resection for rectal cancer: a meta-analysis. Jpn J Clin Oncol 2020;50:20-8.
8. Olsen BC, Sakkestad ST, Pfeffer F, et al. Rate of Anastomotic Leakage After Rectal Anastomosis Depends on the Definition: Pelvic Abscesses are Significant. Scand J Surg 2019;108:241-9.
9. Zhang B, Zhuo GZ, Tian L, et al. Risk factors of coloanal anastomotic stricture after laparoscopic intersphincteric resection for low rectal cancer. Chinese J Gastrointestinal Surg 2019;22:755-61.
10. Park EJ, Kang J, Hur H, et al. Different clinical features according to the anastomotic leakage subtypes after rectal cancer surgeries: contained vs. free leakages PLoS One 2018;13:e0208572.
11. Rahbari NN, Weitz J, Hohenberger W, et al. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. Surgery 2010;147:339-51.
12. Sciuto A, Merola G, De Palma GD, et al. Predictive factors for anastomotic leakage after laparoscopic colorectal surgery. World J Gastroenterol 2018;24:2247-60.
13. Reif de Paula T, Simon H, Shah M, et al. Analysis of the impact of EEA stapler size on risk of anastomotic complications in colorectal anastomosis: does size matter? Tech Coloproctol 2020;24:283-90.
14. Eto K, Urashima M, Kosuge M, et al. Standardization of surgical procedures to reduce risk of anastomotic leakage, reoperation, and surgical site infection in colorectal cancer surgery: a retrospective cohort study of 1189 patients. Int J Colorectal Dis 2018;33:755-62.
15. Klose J, Tarantino I, von Fournier A, et al. A Nomogram to Predict Anastomotic Leakage in Open Rectal Surgery-Hope or Hype? J Gastrointest Surg 2018;22:1619-30.
16. Shinji S, Ueda Y, Yamada T, et al. Male sex and history of ischemic heart disease are major risk factors for anastomotic leakage after laparoscopic anterior resection in patients with rectal cancer. BMC Gastroenterol 2018;18:117.
17. Fukada M, Matsuhashi N, Takahashi T, et al. Risk and early predictive factors of anastomotic leakage in laparoscopic low anterior resection for rectal cancer. World J Surg Oncol 2019;17:178.
18. Zhou S, Zhou H, Zheng Z, et al. Predictive risk factors for anastomotic leakage after anterior resection of rectal cancer in elderly patients over 80 years old: an analysis of 288 consecutive patients. World J Surg Oncol 2019;17:112.
19. Zheng H, Wu Z, Wu Y, et al. Laparoscopic surgery may decrease the risk of clinical anastomotic leakage and a nomogram to predict anastomotic leakage after anterior resection for rectal cancer. Int J Colorectal Dis 2019;34:319-28.
20. Sparreboom CL, van Groningen JT, Lingsma HF, et al; Dutch ColoRectal Audit group. Different Risk Factors for Early and Late Colorectal Anastomotic Leakage in a Nationwide Audit. Dis Colon Rectum 2018;61:1258-66.