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RESEARCH ARTICLE

Evaluation of Factors Associated with Anastomotic Leakage in Colorectal Surgery

Kolorektal Cerrahide Anastomoz Kaçağı ile İlişkili Faktörlerin Değerlendirilmesi

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ABSTRACT

Aim: One of the most feared complications after surgical treatment of colorectal diseases is anastomotic leaks. Regarding this issue, we aimed to determine factors that may cause anastomotic leaks by analyzing cases of colorectal disease in which we created anastomoses in our center.

Method: The study included patients who underwent surgery including creation of anastomosis due to colorectal disease between January 2012 and December 2016 in the general surgery unit of a public hospital in İzmir. The patients' data were evaluated retrospectively as two groups: those with anastomotic leakage (group 1) and without anastomotic leakage (group 2). The groups were evaluated in terms of factors such as age, gender, performance of bowel preparation, anastomosis configuration, anastomosis technique, etc.

Results: A total of 94 patients were included in the study, 10 (10.5%) in group 1 and 84 (89.5%) in group 2. Mean age of the patients was 70.3+12.2 years in group 1 and 62.5±12.6 years in group 2 (p=0.049). Length of hospital stay was significantly longer in group 1 (p<0.0001). The mortality rate was 40% in group 1 and 2% in group 2 (p=0.001). There was no significant difference when the groups were compared based on gender, presence of protective ostomy, anastomosis configuration (end-to-end, end-to-side, side-to-side), anastomosis technique [manual or mechanical (linear cutter, circular stapler)], or anastomosis type (colocolonic, ileocolonic, etc.) (p>0.05).

Conclusion: The results of this study suggest that more caution regarding anastomotic leak is warranted in elderly patients. Studying larger patient samples is recommended for more productive research.

Keywords: Anastomosis, colorectal surgery, complication

ÖZ

Amaç: Kolorektal hastalıklarda cerrahi tedaviden sonra en korkulan komplikasyonlarından birisi anastomoz kaçaklarıdır. Ciddi bir sorun haline gelen bu konuyla ilgili olarak çalışmamızda kolorektal hastalıklarda anastomoz uyguladığımız olguları inceleyerek anastomoz kaçağına neden olabilecek ilişkili faktörleri belirlemeyi amaçladık.

Yöntem: Çalışmaya İzmir ilinde bir kamu hastanesinin genel cerrahi kliniğinde Ocak 2012-Aralık 2016 tarihleri arasında kolorektal hastalıklar nedeniyle ameliyat edilen ve anastomoz uygulanan olgular dahil edildi. Araştırmanın verileri retrospektif olarak değerlendirildi. Anastomoz uygulanan olguların verileri, anastomoz kaçağı görülen (grup 1) ve anastomoz kaçağı görülmeyen (grup 2) olmak üzere iki gruba ayrıldı. Gruplar; yaş, cinsiyet, barsak hazırlığı yapılıp/yapılmama durumu, anastomoz şekli, anastomoz tekniği vb. faktörler yönünden değerlendirildi.

Bulgular: Çalışmaya kolorektal cerrahi geçiren 94 olgu dahil edildi. Grup 1; 10 olgu (%10,5) ve grup 2 ise; 84 (%89,5) olgudan oluştu. Grup 1'deki olguların yaş ortalaması 70,3+12,2, grup 2'deki olguların ise 62,5±12,61 yıl olarak belirlendi. İki grubun da yaş ortalamaları arasında anlamlı fark vardı (p=0,049). Grup 1'deki olguların hastanede kalış süresi anlamlı olarak yüksekti (p<0,0001). Grup 1'de mortalite oranı %40, grup 2'de ise %2 olarak belirlendi ve gruplar arasında anlamlı fark saptandı (p=0,001). Gruplar arasında cinsiyet, koruyucu ostomi olup olmaması, anastomoz şekli (uç-uca, uç-yan, yan-yana olması), anastomozun elle ya da teknolojik yöntemlerle (lineer-cutter, sirküler stapler) yapılması, anastomoz uçlarının kolo-kolonik, ileo-kolonik yapılması gibi değişkenler karşılaştırıldığında anlamlı fark saptanmadı (p>0,05).

Sonuç: Çalışmanın sonucu ileri yaş gruplarında anastomoz kaçağı yönünden daha dikkatli olunması gerektiğini göstermektedir. Araştırmanın verimliliği açısından daha büyük bir grupla çalışılması önerilmektedir.

Anahtar Kelimeler: Anastomoz, kolorektal cerrahi, komplikasyon

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Introduction

Anastomotic leaks are among the most dreaded complications of colorectal surgery. Leakage from the created anastomosis results in prolonged hospital stays, increased costs, and higher morbidity and mortality rates. Although it is argued that leaks may occur at a rate of 3-6% in procedures performed by experienced colorectal surgeons, rates reported in the literature vary from 1 to 30% globally.[1] Anastomotic leaks are responsible for one third of deaths occurring after colorectal surgery.[2] It has been reported that anastomotic leaks after rectal cancer surgery reduce both early and long-term survival.[3] Choice of anastomotic technique following colectomy depends on the location of the resected colon segment, the bowel diameter, and the personal experience of the surgeon.[4] Many different techniques have been and continue to be investigated to reduce the rate of anastomotic leakage.[1] The most prominent of these methods is the creation of a protective stoma proximal to the anastomosis. Although this may prevent anastomotic leak in the short-term when practiced routinely, it is not preferred for all patients due to a number of long-term problems, such as stoma reclosure and the development of stomal stricture, stoma retraction, necrosis, and parastomal hernias. Therefore, protective stomas are generally used only in patients with advanced age and comorbid illnesses.[1] A consensus has yet to be reached regarding the optimal management of anastomotic leaks.[5] In this study, we aimed to investigate the factors that may lead to leakage from the anastomoses created to treat colorectal disease in our center and to compare them with the literature.

Materials and Methods

The data of patients who underwent surgery involving anastomosis due to colorectal pathologies in our center between January 2012 and December 2016 were retrieved from the hospital information management software (Probel) and analyzed retrospectively. All surgeries were performed by general surgeons experienced in the field of colorectal surgery at a tertiary training and research hospital in the province of İzmir. Conventional long-term neoadjuvant radiotherapy was applied to stage T3 lymph node-positive middle and lower rectal tumors. Total mesorectal excision + colorectal anastomosis was performed within 6-8 weeks after neoadjuvant therapy. Ileostomy was not performed routinely, but was done in selected cases based on the clinical condition of the patient, level of anastomosis, and technical problems encountered during anastomosis, etc. For colon cancer patients, surgery was performed according to oncologic principles. The data of patients who underwent anastomosis were divided into those with anastomotic leak (group 1) and those without anastomotic leak (group 2). The groups were compared on the basis of age, sex, emergency or elective surgery, benign or malignant pathology, presence of a protective ostomy, American Society of Anesthesiologists (ASA) score, whether bowel preparation was done, type of anastomosis (end-to-end, end-to-side, side-to-side), and anastomosis technique (manual, circular stapler, linear cutter). We also investigated whether neoadjuvant therapy was administered to patients with malignant disease and its relationship with oncological outcomes. The study was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments. Ethics committee approval was not sought due to the retrospective nature of the study. SPSS version 22.0 (IBM Corparation, Armonk, New York, USA) software was used for data analysis. Independent Samples t-tests and Mann-Whitney U tests were used for comparisons of two independent groups. Pearson chi-square and Fisher exact tests were used to compare categorical variables. Variables were analyzed with a 95% confidence interval and $p<0.05$ was regarded as significant.

Results

Ninety-four patients who underwent colorectal surgery were included in the study. There were 10 patients (10.5%) in group 1 and 84 patients (89.5%) in group 2. The groups did not differ significantly in terms of sex, emergency/elective surgery, absence/presence of protective ostomy, or having performed bowel preparation ($p>0.05$). When patients were examined based on the presence of benign or malignant disease, we found that 10 of the 80 malignant patients (50 cases of colon cancer and 30 cases of rectal cancer) had anastomotic leaks. There were no leaks in the anastomoses created due to benign causes. There was no significant difference between surgeries performed due to malignant or benign causes in terms of anastomotic leak rate ($p>0.05$). The mortality rate was 40% in group 1 and 2% in group 2 ($p=0.001$). Comparison of the groups based on clinical features is shown in detail in Table 1. Mean age was 70.3±12.2 years in group 1 and 62.5±12.6 years in group 2 ($p=0.049$). The average hospital stay was significantly longer in group 1 ($p<0.0001$). There was no difference between the groups in terms of ASA score (Table 2). Anastomotic leak was not significantly correlated with anastomosis configuration (end-to-end, end-to-side, side-to-side), whether the anastomosis was created manually or using a device (linear cutter, circular stapler), or anastomosis type (colocolic, ileocolic, etc.) ($p>0.05$). Detailed analysis of these parameters is shown in Table 3. Evaluation of tumor (T), node (N), and TN-metastasis (TNM) stages and history of neoadjuvant therapy in patients with and without

anastomotic leak revealed statistically significant differences in T and TNM stages between the groups (p<0.05). There was no difference in terms of N stage. Nine of the 72 patients who did not receive neoadjuvant therapy had anastomotic leaks. There was no statistically significant relationship between anastomotic leak and receiving or not receiving neoadjuvant therapy (p>0.05). Comparison of oncologic variables in the groups is shown in Table 4. In multiple regression analysis, none of the factors were significantly associated with anastomotic leak (Table 5).

Discussion

Anastomotic leaks are the most feared complication and a leading cause of significant morbidity and mortality after

Table 1. Distribution of patients with and without anastomotic leak according to gender and clinical characteristics

		Groups				Total		p*
	Group 1		Group 2					
		n	%	n	%	n	%	
Gender	Male	6	9.0	61	91.0	67	71.3	0.465
	Female	4	14.8	23	85.2	27	28.7	
Emergency/elective	Emergency	1	7.7	12	92.3	13	13.8	1.000
	Elective	9	11.1	72	88.9	81	86.2	
Benign/malignant	Malignant	10	12.5	70	87.5	80	85.1	0.349
	Benign	-	-	14	100.0	14	14.9	
Affected colon segment	Rectum	6	20.0	24	80.0	30	31.9	0.273
	Right colon	3	11.5	23	88.5	26	27.6	
	Left colon	-	-	1	100.0	1	1.1	
	Ostomy closure	-	-	12	100.0	12	12.7	
	Transverse colon	-	-	4	100.0	4	4.3	
	Sigmoid colon	1	4.7	20	95.3	21	22.3	
Protective ostomy	(+)	3	23.1	10	76.9	13	13.8	0.140
	(-)	7	8.6	74	91.4	81	86.2	
Mortality	(+)	4	66.7	2	33.3	6	6.4	**0.001**
	(-)	6	6.8	82	93.2	88	93.6	
Bowel preparation	(+)	6	15.4	33	84.6	39	41.5	0.310
	(-)	4	7.3	51	92.7	55	58.5	

*Fisher's Exact test

Table 2. Mean age, length of hospital stay, and American Society of Anesthesiologists (ASA) scores in patients with and without anastomotic leak

	Groups				p
	Group 1		Group 2		
	Mean ± SD	Min.-max.	Mean ± SD	Min.-max.	
Age (years)	70.3±12.24	44-83	62.56±12.61	21-84	**0.049**
Length of hospital stay (days)	28.8±18.23	15-57	9.99±5.82	0-42	**0.0001**
ASA score	2.4±0.52	2-3	2.31±0.66	1-5	0.524

Mann-Whitney U test, ASA: American Society of Anesthesiologists, SD: Standard deviation, Max.: Maximum, Min.: Minimum

Table 3. Distribution of anastomosis type, configuration, and technique among patients with and without anastomotic leak

		Groups						p*
		Group 1		Group 2		Total		
		n	%	n	%	n	%	
Anastomosis type	Ileorectal	1	25.0	3	75.0	4	4.3	0.252
	Ileotransverse	2	8.3	22	91.7	24	25.5	
	Colocolic	1	3.7	26	96.3	27	28.7	
	Colorectal	6	15.4	33	84.6	39	41.5	
Anastomosis configuration	End-to-end	6	15.4	33	84.6	39	41.5	0.400
	End-to-side	3	10.3	26	89.7	29	30.9	
	Side-to-side	1	3.8	25	96.2	26	27.7	
Anastomosis technique	Linear cutter	5	10.9	41	89.1	46	48.9	0.906
	Manual	2	13.3	13	86.7	15	16.0	
	Circular stapler	3	9.1	30	90.9	33	35.1	

*Fisher's exact test

Table 4. Distribution of tumor, node, and tumor, node, metastasis stages and neoadjuvant treatment rates in patients with and without anastomotic leak

		Groups						p*
		Group 1		Group 2		Total		
		n	%	n	%	n	%	
T stage	T0	-	-	2	100.0	2	2.5	0.013
	T1	3	75.0	1	25.0	4	5.0	
	T3	5	12.2	36	87.8	41	51.3	
	T4	2	6.1	31	93.9	33	41.3	
N stage	N0	5	11.6	38	88.4	43	53.8	1.000
	N1	3	14.3	18	85.7	21	26.3	
	N2	2	12.5	14	87.5	16	20.0	
TNM stage	1	4	66.7	2	33.3	6	7.5	0.001
	2	2	5.3	36	94.7	38	47.5	
	3	3	8.8	31	91.2	34	42.5	
	4	1	50.0	1	50.0	2	2.5	
Neoadjuvant TDV	Yes	1	12.5	7	87.5	8	10.0	1.000
	No	9	12.5	63	87.5	72	90.0	
	Group 1 Mean ± SD Min.-max.			**Group 2 Mean ± SD Min.-max.**				**p****
Number of lymph nodes removed	22.2±13.22		3-44	27.03±16.85		7-75		0.485
Number of metastatic lymph nodes	1.8±2.86		0-9	1.83±2.97		0-11		0.800

*Fisher's exact test **Mann Whitney U analysis, TNM: Tumor, node, metastasis, SD: Standard deviation, Max.: Maximum, Min.: Minimum

Table 5. Results of logistic regression analysis for the relationships between anastomotic leak and tumor stage, tumor-node-metastasis stage, and age

	B	SE	Wald	p	Exp (B)	95% CI for Exp (B)	
T stage	-0.045	0.430	0.011	0.917	0.956	0.412	2.220
TNM stage	-0.990	0.695	2.029	0.154	0.371	0.095	1.451
Age	-0.015	0.036	0.167	0.683	0.986	0.919	1.057
Constant	1.313	2.700	0.236	0.627	3.717		

TNM: Tumor, node, metastasis, CI: Confidence interval, SE: Standard error, Exp (B): Exponentiated logistic coefficients, B: Beta, Wald: Validity

colorectal surgery. Although rates of mortality associated with anastomotic leaks lower than 3% have been reported in some studies, the accepted mortality rate due to anastomotic complications varies between 6 and 22%.[2,3,6] The overall mortality rate in our study was 6%. However, 4 of the 10 patients with anastomotic leak died. We attribute the high mortality rate in our study to the fact that the anastomotic leak group consisted of patients who were older and had higher comorbidity. In a meta-analysis of 13 randomized controlled trials comparing stapled and manual anastomoses in colorectal surgery, MacRae and McLeod[7] found no difference in leak rates between the two techniques. In another Cochrane analysis, anastomoses were created with a stapler in 622 patients and manually in 611 patients, and no difference was found between them. At the end of the study, the need for randomized controlled trials was emphasized.[8] Similarly, we also observed no difference in leak rates between the stapled and manual anastomoses in our study. Brisinda et al.[9] investigated the relationship between leak rate and anastomosis configuration after bowel resection in patients with rectum cancer and found the rate of anastomotic leak to be higher among patients with end-to-end anastomoses compared to those with end-to-side anastomoses in a trial of 77 randomized cases. Another study in patients with right colon cancer showed no correlation between configuration and anastomotic leak.[10] The risks of anastomotic leak and postoperative mortality are known to be higher with anastomoses created during emergency surgery.[2,11] However, there was no difference between emergency and elective surgeries in our study. The presence of benign or malignant disease is another factor believed to be associated with anastomotic leak in colorectal surgery. In an analysis by Rencuzogullari et al.[12] involving 10.392 patients, no correlation was found between anastomotic leak and malignant or benign disease. In addition, similar to our study, the authors reported that length of hospital stay was significantly greater in the group of patients with anastomotic leak. There are different opinions in the literature regarding ASA score. It is argued that higher ASA score is associated with anastomotic leak.[13] In fact, Buchs et al.[14] stated that the risk of anastomotic leak increased 2.5 fold with every increment in ASA score. However, contrary to these reports, there are many other studies which demonstrated a lack of correlation between ASA score and anastomotic leak, as in our study.[1,3,12] Whether or not age plays a role in anastomotic leak also remains a subject of debate. Numerous investigators have reported no correlation between the two.[11,15,16] In fact, contrary to the notion that the elderly population is at greater risk, it has been reported that anastomotic leaks may be more common among the younger population.[3] Parthasarathy et al.[17] emphasized that young age was an independent risk factor for anastomotic leak. Unlike the literature, patients in the anastomotic leak group in our study had a significantly higher mean age. It is still unclear whether preoperative bowel preparation is necessary and if so, whether it should be mechanical only or combined with antibiotics. In their meta-analysis of 14 randomized controlled trials, Cao et al.[18] determined that bowel preparation did not impact the risk of postoperative complications or anastomotic leak. However, in a recent study involving elderly colorectal cancer patients, the authors argued that not performing bowel preparation increased anastomotic leak and morbidity rates. Moreover, they noted that morbidity and anastomosis leak rates were significantly lower when mechanical bowel preparation was combined with antibiotherapy.[19] Similarly, in a recent report of 8442 cases, Kiran et al.[20] compared patients with no bowel preparation, mechanical bowel preparation, and bowel preparation with antibiotics and found the risk of leakage and postoperative complications to be lowest in the group that received antibiotics. Patients that did not perform bowel preparation were found to have the worst outcomes and the authors concluded by emphasizing that mechanical bowel preparation decreases postoperative complication rates. In another study analyzing 32.359 cases, Koller et al.[21] found that complications such as anastomotic leak, prolonged hospitalization, and postoperative ileus were less common among patients who underwent bowel preparation with oral antibiotics. In addition, they observed that bowel preparation

had no adverse effects on postoperative electrolyte imbalance or renal and cardiac complications.[17,21] In our study, only oral and rectal laxatives were administered to the group that underwent bowel preparation. Preoperative antibiotherapy was not administered and there was no difference in terms of anastomotic leak. These findings indicate that if bowel preparation is done prior to colorectal surgery, the addition of antibiotics can be considered. Creating a protective stoma is considered to reduce morbidity and mortality associated with anastomotic leaks, especially in rectal surgeries. Protective ileostomy is known to reduce leak and postoperative complication rates in rectal cancer.[22] A meta-analysis of 11 studies led to the conclusion that a protective stoma is necessary in patients undergoing lower anterior resection.[23] In our study, anastomotic leaks were detected in 20% of the patients who had surgery for rectal cancer. Forty percent of the rectal cancer patients had a protective ostomy. However, 2 patients developed an anastomotic leak despite having a protective ostomy. One patient underwent primary repair, while the other patient was followed with antibiotherapy. When we examined the risk of anastomotic leak based on oncological parameters, we found very high leak rates among T1 and TNM stage 1 patients. We observed no correlations with metastatic lymph node count, N stage, or neoadjuvant therapy. Unlike our study, Park et al.[3] found the risk of leak to be significant only in node-positive patients. Moreover, neoadjuvant therapy administered to patients with rectal cancer did not affect their anastomotic leak rate, consistent with the literature.[24] Studies involving larger patient series are needed in order to draw conclusions about the relationship between the oncological status and anastomotic leak. The management of patients presenting with anastomotic leak is critical. There are a variety of options available, including undoing the anastomosis and creating an end ostomy, creating a proximal deviation ileostomy/colostomy, undoing the anastomosis and performing redo surgery, placing a stent in the anastomosis, and endoscopic clipping. However, options involving ostomy are usually more prominent.[6,25] In our series, only one of the patients with leakage was followed without further intervention because they had a protective ileostomy. Another patient with a protective ileostomy underwent primary repair due to leakage. In 50% of the remaining patients with anastomotic leak, a protective ileostomy was made without intervention to the anastomosis itself, while in the other 50% of patients the anastomosis was undone and a Hartmann's colostomy was created. Limitations of the present study include the small sample size and retrospective study design. In addition, upper rectal tumors were not treated routinely with neoadjuvant radiotherapy in the early years of the time period encompassed in our study. Therefore, the protective ileostomy rate in our series is low. Currently, conventional long-term neoadjuvant radiotherapy is administered to all patients with T3 and lymph node-positive rectal cancers in our center. In conclusion, it was determined in this study that advanced age increases the risk of anastomotic leak after colorectal surgery, whereas leak rates were not affected by bowel preparation, manual or mechanical anastomosis technique, anastomosis configuration, and which bowel segments were joined in the anastomosis. Our findings show that more caution is needed in terms of anastomotic leak in older patient groups. Larger, prospective randomized studies of factors contributing to anastomotic leak are recommended to provide guidance to clinicians.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Consent form was filled out by all participants.

Peer-review: External and internal peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.Ü., S.B.A., Concept: O.Ü., E.İ., Design: O.Ü., U.G., Data Collection or Processing: E.D., D.A., Analysis or Interpretation: O.Ü., S.B.A., Literature Search: O.Ü., M.T.T., Writing: O.Ü., E.İ.

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