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RESEARCH ARTICLE

Does a Distal Surgical Margin Closer than 10 mm Increase the Risk of Recurrence in Locally Advanced Rectal Cancer in a Mid-Distal Location?

Orta-Distal Yerleşimli Lokal İleri Rektum Kanserinde 10 mm'den Yakın Distal Cerahi Sınır Nüks Riskini Artırır mı?

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ABSTRACT

Aim: Although many factors affecting recurrence, including surgical margin involvement, have been considered in rectum cancer surgery, there is no consensus on the definition of a safe distal surgical margin (DSM).We aimed to investigate the oncological safety of a DSM closer than 10 mm and the factors affecting relapse in mid-distal located rectum tumours.

Method: Patients who underwent sphincter-preserving rectal curative resection following neoadjuvant chemoradiotheraphy between February 2006 and June 2019 for mid-distal lying rectum tumours were investigated retrospectively. Patients with radial or distal surgical margin involvement, having a complete pathologic response, or being lost to follow-up were excluded from the study. Patients and tumour characteristics, clinical and pathological disease stages, and recurrence and disease-free survival rates were compared between groups created along a cut-off value of 10 mm in DSM (DSM <10 and DSM ≥10).

Results: The study group consisted of 23 patients (DSM <10, n=11; DSM ≥10, n=12). Most of the tumours were located distally (70% , n=16). Handsewn anastomosis was performed in 81.8% of patients in the DSM <10 group (Turnbull-Cutait, n=5; coloanal anastomosis, n=4) and in 33% of patients in the DSM ≥10 group (Turnbull-Cutait, n=2; coloanal anastomosis, n=2). During a median follow-up time of 72 (6-158) months, three cases of systemic recurrence developed while no local recurrence was faced. The recurrence rates and disease-free survival rates were similar (p=0.17 and p=0.184, respectively). Younger age, bulkier tumour, presence of perineural invasion, ypN stage, and number of metastatic lymph nodes were associated with recurrence (p=0.017, p=0.00, p=0.014, p=0.030, and p=0.024, respectively).

Conclusion: Our study supports the view that obtaining a DSM closer than 10 mm but without tumour can be sufficient in terms of oncological safety, allowing permanent colostomy to be avoided. Young age, large tumour size, presence of perineural invasion and increased number of metastatic lymph nodes stand out as risk factors for recurrence.

Keywords: Distal surgical margin, rectum cancer, recurrence, risk factor

ÖZ

Amaç: Rektum kanseri cerrahisinde sınır tutulumu dahil nükse etki eden birçok faktör tanımlanmışsa da güvenli distal cerrahi sınır (DCS) tanımı üzerinde fikir birliğine varılamamıştır. DCS'nin 10 mm'den yakın olmasının onkolojik güvenilirliğini ve nükse etki eden faktörleri incelemeyi amaçladık.

Yöntem: Şubat 2006-Haziran 2019 arasında orta-distal rektum yerleşimli malignitelerde neoadjuvan kemoradyoterapi sonrası küratif sfinkter koruyucu rezeksiyon yapılan olgular retrospektif olarak incelendi. Radyal ve DCS pozitifliği olan, takip yapılamayan veya patolojik tam yanıt gelişen olgular çalışma dışı bırakıldı. Distal cerrahi sınır 10 mm eşik değerine göre oluşturulan gruplar arasında (DCS <10 ve DCS ≥10) hasta ve tümör biyolojik özellikleri, klinik ve patolojik evreler ile nüks gelişimi, hastalıksız sağkalım oranları karşılaştırıldı.

Bulgular: DCS <10 grubunda 11, DCS ≥10 grubunda 12 olmak üzere 23 olgu ile çalışma grubu oluşturuldu. Olguların yaklaşık %70'de (n=16) distal yerleşim mevcuttu. DCS <1cm grubunda 9 (%81,8) olguda anastomozlar el ile (Turnbull-Cutait; n=5, koloanal anastomoz; n=4) yapılırken

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DCS ≥1cm olan grupta 4 (%33) olguda (Turnbull-Cutait, n=2; koloanal anastomoz, n=2) el ile rekonstruksiyon yapıldı. Median 72 (6-158) ay takip süresinde lokal nüks saptanmazken 3 olguda sistemik nüks gelişti. Gruplar arasında nüks ve hastalıksız sağkalım açısından istatiksel olarak anlamlı fark saptanmadı (p=0,217, p=0,184). Genç yaş (p=0,017), büyük tümör çapı (p=0,004), perinöral invazyon (p=0,014), ypN evresi (p=0,030), metastatik lenf nodu sayısı (p=0,024) ile nüks arasında negatif yönde anlamlı ilişki saptandı.

Sonuç: Çalışmamız 1 cm'den yakın ancak tümörsüz DCS elde edilmesinin onkolojik açıdan yeterli olabileceğini ve kalıcı kolostomiden kaçınılabileceği görüşünü destekler niteliktedir. Genç yaş, perinöral invazyon varlığı, metastatik LN sayısı ile büyük tümör çapı rekürrensle ilişkili risk faktörleri olarak öne çıkmaktadır.

Anahtar Kelimeler: Distal cerrahi sınır, rektum kanseri, nüks, risk faktör

Introduction

Significant improvement was achieved in local recurrence and survival rates for distally located rectal cancer surgery through neoadjuvant chemoradiotherapy (CRT) and the total mesorectal excision technique (TME) defined by Heald et al.[1] The development of stapler devices made it possible to perform even more sphincter-sparing surgery.

Despite these developments, it has been proven that there is microscopic involvement in up to 33% of resection margins and that the radial surgical margin (RSM) involvement adversely affects overall survival (OS) and disease-free survival (DFS).[2] Although the correlation of the distal surgical margin (DSM) with oncological outcomes has been examined in many publications, there is no exact distance accepted.[3] It is known that tumours can spread intramurally to a distance of 1 cm from the macroscopic margin.[4] In distal rectum cancer, surgeons try to achieve a minimum of a 2-cm DSM. While patients quality of life improves without stoma, it is not always possible to obtain a DSM of minimum 1 cm.

In our study, we aimed primarily to investigate the oncological reliability of DSM < 10 mm in patients with mid-distal rectal cancer who underwent sphincter-sparing curative surgery after neoadjuvant CRT. Secondarily, we investigated factors affecting recurrence in this group of patients.

Materials and Methods

Patient Selection and Parameters

After approval was obtained from the ethics committee of Acıbadem University (date: 12.03.2020; number: ATADEK 2020-04/39), patients who were clinically diagnosed with rectal cancer and underwent curative resection between February 2006 and June 2019 were retrospectively scanned from the digital data system of Bursa Acıbadem Hospital. One hundred and six cases were detected. The following cases were excluded from the study: patients with disease in TNM stages I and IV, upper rectum tumours, or synchronous tumours; patients who underwent abdominoperineal resection (APR) or received adjuvant or short-term radiotherapy; patients who were unable to receive radiotherapy due to morbidity or refusal of treatment; patients with complete pathological response, with DSM involvement (0 mm), or with RSM involvement (1 mm); and patients with incomplete follow-up. The final study group consisted of 23 patients who had a rectum tumour located in the middle or distal part of the rectum, had locally advanced disease, and underwent curative sphincter-sparing surgery (low anterior, very low anterior, coloanal anastomosis, or Turnbull-Cutait) after neoadjuvant CRT (Figure 1).

Demographic characteristics of the patients, biological characteristics of the tumours (perineural, venous, lymphatic, extranodal invasions, differentiation degree), DSM, RSM, total and metastatic lymph node (LN) numbers, tumour size, clinical T stage (cT), clinical N stage (cN), clinical TNM stage (cTNM), pathological T stage (ypT), pathological N stage (ypN), pathological TNM stage (ypTNM), relapse (local & systemic), and disease-free (DFS) and OS times were examined. DFS was accepted as the time until the first detection of systemic or local recurrence after

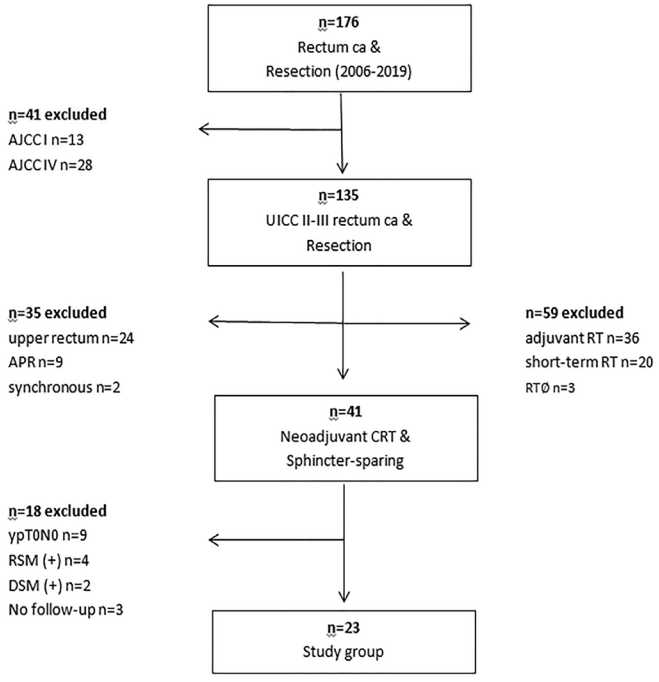

Figure 1. Patient selection flowchart

AJCC: AJCC Cancer Staging Manual. 8th ed (TNM Classification)
RTØ: Not given radiotherapy, ypT0N0: Complete pathological response, CRT: Chemoradiotherapy, APR: Abdominoperineal resection, DSM: Distal surgical margin, RSM: Radial surgical margin

curative resection, and OS was accepted as total survival. The patients were divided into two groups according to the threshold value of 10 mm DSM: patients with DSM <10 mm and patients with DSM ≥10 mm.

Staging, Neoadjuvant Therapy

Clinical staging was done using abdominal ultrasonography, thorax/abdominal computed tomography (CT) and pelvic magnetic resonance (MR) imaging techniques in patients with histopathologically proven adenocarcinoma. Neoadjuvant CRT was recommended for patients with cT3 and cT4 stage disease and/or nodal metastasis. In the protocol, 5-Fluorouracil/leucovorin or oral capecitabine and/or intravenous oxaliplatin were administered to the pelvic area simultaneously with radiotherapy at a total dose of 50.0 Gy (2 Gy/day, 5 days a week for 5 weeks). Surgical intervention was performed 10 weeks after the completion of radiotherapy.

Surgery

Intestinal cleansing was performed in all patients before surgery. Antibiotic prophylaxis was started 30 minutes before the operation and continued for 2 days postoperatively. Resection was performed in accordance with TME principles by surgeons experienced in colorectal surgery. The anastomoses were performed manually or with a stapler device according to the proximity of the tumour, the findings observed in the surgery and the surgeon's preferences. Routine protective ileostomy was performed. A 2-stage Turnbull-Cutait procedure without ileostomy was used in some patients.

Pathology and Surgical Margin

The resected specimen was sent to pathologist immediately after pinning. DSM was defined in pinned fresh specimen as the closest distance between the distal edge of the resection edge and the closest tumour cell. RSM was defined as the distance between the mesorectal radial edge and the closest tumour cell. The stapler donut was examined pathologically, but was not included in the surgical margin. Pathological staging was made on the basis of the American Joint Committee on Cancer-TNM staging system, version 8 (AJCC-8th) and expressed as "yp".[5]

Follow-up, Relapse and Adjuvant Therapy

Patients were followed up on by blood biochemistry, carcinoembryonic antigen, thoracoabdominal CT and colonoscopy at intervals (3-6-12 months) in accordance with the follow-up recommendations of the National Comprehensive Cancer Network (NCCN) guidelines.[3] In addition, cancer antigen 19-9 was measured at each control and annual pelvic MR was performed. Positron emission tomography was used optionally in cases of clinical suspicion. Digital and rectoscopic examinations were performed at every control. Locoregional recurrence was defined as clinical, radiological and/or pathological detection of the disease in the pelvis in the operation field, and systemic recurrence was defined as the detection of disease similar to the primary tumour outside the primary tumour area. Adjuvant treatment decisions were made in the multidisciplinary oncology council. 5-Fluorouracil/leucoverin (5-FUFA) or oxaliplatin/5-Fluorouracil/leucoverin (FOLFOX) regimens were used depending on the risk.

Statistical Analysis

All statistical analyses were performed using the IBM SPSS statistics program (ver. 26.0.0.0). Continuous (numerical) variables were expressed as median (lower-upper limit) and categorical variables were expressed as numbers and percentages unless otherwise specified. Differences between numerical variables were determined with the Mann-Whitney U test, and categorical comparisons were made using chi-square and Fisher's exact tests. The DFS curve was created by the Kaplan-Meier method. Overall and DFS results between groups were compared using the log rank (Mantel-Cox) test. The relationship between recurrence and parameters was analyzed using Spearman's rho correlation test. $P<0.05$ was considered significant in all statistical tests.

Results

A total of 23 patients (14 males and 9 females) were followed up on for a median of 72 (6-158) months. The median DSM in the whole study group was 10 mm (1-30). In 11 patients, DSM was found to be less than 10 mm (median 4 [1-5]), while in 12 patients, DSM was more than 10 mm (median 25 [10-30]). Tumours were in distal localization in approximately 70% (n=16) of the patients. While anastomoses were made manually (Turnbull-Cutait, n=5; coloanal anastomosis, n=4) in 9 (81.8%) patients in the DSM <10 mm group, manual reconstruction was performed in 4 (33%) patients in the DSM ≥10 mm group (Turnbull-Cutait, n=2; coloanal anastomosis, n=2). The demographic characteristics of the patients, tumour location, tumour diameter, and RSM and DSM distances are summarized in Table 1. In the DSM <10 mm group, it was observed that the number of females was significantly higher than males (n=7 vs n=2, p=0.036). There was no significant difference between other parameters. The biological properties of the tumours are detailed in Table 2. Extramural venous invasion was not detected in any of the patients. When lymphatic and venous invasion were combined as lymphovascular invasion (LVI), LVI was detected in three patients, and no relation was found between LVI and recurrence (r=0.150,

n=23, p=0.474; Spearman's rho correlation test). Tumour characteristics, LN numbers removed and metastatic LN numbers were similar between groups. The distribution of the clinical and pathological stages is summarized in Table 3. There was a significant difference between the groups only in terms of the ypN status (p=0.046).

While there was no local recurrence in any of the patients, three systemic relapses were detected in the group with DSM ≥10 mm. Liver and bone metastases developed in one patient after 8 months, and the patient died at the end of the 14th month. This patient was also the only patient who died in our study group. Lung metastasis developed at the end of the 43rd month in the second patient and liver metastasis at the 60th month in the third patient. During the median follow-up period of 72 (6-158) months, the systemic recurrence rate was 13.0% and the overall survival rate was 95.7%; there was no significant difference between the groups in terms of OS and DFS (Table 1). When the factors associated with recurrence were examined, there was a significant relationship between the presence of perineural invasion (PNI) (r=0.503, p=0.014), age (r= -0.492, p=0.017), large tumour diameter (r=0.575, p=0.004), pN stage (r=0.452, p=0.030), and metastatic LN number (r=0.469, p=0.024) (Tables 1, 2, 3).

Discussion

In our study, it was observed that obtaining a DSM of less than 10 mm in sphincter-preserving resections performed after neoadjuvant CRT in locally advanced rectal cancer did not pose an oncological risk, and the presence of large tumours, young age, metastatic LN count and PNI increased the risk of systemic recurrence.

After the application of the TME technique in rectal cancer, the 5-year local recurrence rate decreases to 4-6%, while systemic recurrence rates are around 20%.[6] Factors affecting relapse have been considered in many studies:

Table 1. Distribution of patient demographics, tumor localization and surgical margins by groups

	Total	<1 cm	1 cm	p	pδ
Gender, n(%)					
Male	14 (60.9)	4 (36.4)	10 (83.3)	0.036[1]	0.835
Female	9 (39.1)	7 (63.6)	2 (16.7)		
Age (years)*	53 (30-73)	51 (33-73)	55 (30-72)	0.378[2]	0.017
Localization, n(%)					
Middle	7 (30.4)	2 (18.2)	5 (41.7)	0.371[1]	0.912
Distal	16 (69.6)	9 (81.8)	7 (58.3)		
Tumor diameter (mm)*	20 (9-75)	20 (9-40)	22 (10-75)	0.773[2]	0.004
Radial surgical margin (mm)*	8 (2-20)	7 (2-15)	9 (2-20)	0.750[2]	0.979
Distal surgical margin (mm)*	10 (1-30)	4 (1-5)	25 (10-30)	0.000[2]	0.434
Recurrence*					
Yes	3 (13.0)	0 (0.0)	3 (25.0)	0.217[1]	na
No	20 (87.0)	11 (100.0)	9 (75.0)		
Overall survival*(months)	72 (6-158)	29 (6-158)	84 (8-128)	0.394[3]	na
Disease-free survival*(months)	60 (6-158)	29 (6-158)	78 (8-128)	0.184[3]	na

*Values are given as median (minimum-maximum)

[1]Fisher's exact test, [2]Mann-Whitney U, [3]Log Rank (Mantel-Cox)

[δ]Spearman's rho correlation test (Correlation with recurrence)

na: Not available, DSM: Distal surgical margin

Table 2. Distribution of biological features of tumors by groups and their relationship with recurrence

	Total	<1 cm	1 cm	p	p†
Lymph node total (n)*	29 (7-57)	26 (7-48)	30 (8-57)	0.387[1]	0.364
Lymph node metastatic (n)*	0 (0-17)	0 (0-3)	0 (0-17)	0.259[1]	0.024
Differentiation**					
Badly differentiated	5 (21.7)	2 (18.2)	3 (25.0)		
Moderately differentiated	13 (56.5)	7 (63.6)	6 (50.0)	0.805[2]	0.371
Well differentiated	5 (21.7)	2(18.2)	3 (25.0)		
Extranodal invasion**					
Yes	4 (17.4)	1 (9.1)	3 (25.0)	0.590[3]	0.458
No	19 (82.6)	10 (90.9)	9 (75.0)		
Lymphatic invasion**					
Yes	2 (8.7)	0 (0.0)	2 (16.7)	0.478[3]	0.587
No	21 (91.3)	11 (100.0)	10 (83.3)		
Venous invasion**					
Yes	2 (8.7)	1 (9.1)	1 (8.3)	0.949[3]	0.587
No	21 (91.3)	10 (90.9)	11 (91.7)		
Perineural invasion**					
Yes	4 (17.4)	1 (9.1)	3 (25.0)	0.590[3]	0.014
No	19 (82.6)	10 (90.9)	9 (75.0)		
Mucinous tumor**					
Yes	3 (13.0)	1 (9.1)	2 (16.7)	0.590[3]	0.284
No	20 (87.0)	10 (90.9)	10 (83.3)		
Signet ring cell tumor**					
Yes	2 (8.7)	0 (0.0)	2 (16.7)	0.478[3]	0.114
No	21 (91.3)	11 (100.0)	10 (83.3)		

* Values are given as median (minimum-maximum)

** Values are given as n (%)

[1]Mann-Whitney U [2]chi-square test, [3]Fisher's exact test

†Spearman's rho correlation test (Correlation with recurrence)

LVI, extramural venous invasion, metastatic LN number, PNI and especially RSM positivity have been considered as risk factors.[2,7,8,9,10,11,12] DSM stands out as another factor affecting the decision for sphincter-sparing surgery in patients without RSM involvement. In cases of involvement, the 5-year local recurrence rate increases to 24.1%, and the systemic recurrence rate increases to 35.5%.[13] Consensus has not been reached on the minimum safe distance. Repeated attempts at the treatment of local recurrence in rectal cancer have a low chance of success.[14] For this reason, surgeons

may prefer the APR technique, especially if DSM <10 mm is detected. However, life with a permanent stoma is not the first choice of any individual.

In the current NCCN rectal cancer guidelines, it is recommended to obtain a DSM of 5 cm for upper rectum tumours and 10-20 mm for sphincter-sparing surgery for middle and distal rectal tumours.[3] Sufficient DSM is associated with intramural and distal mesorectal lymphatic spread.[4] Distal intramural spread (DIS) rarely exceeds 2-3 cm.[10] Apart from its direct effect on mesorectal invasion, it has been found that there is a significant relationship between DIS, the number of metastatic LNs, T stage and tumour diameter.[9,15,16] LN metastasis plays a role in mesorectal tumour spread independent of DIS.[17] These results suggest that the risk of local recurrence may especially increase at a distance of <1 cm in patients with locally advanced disease.

No local recurrence was detected in any of the patients during a median follow-up period of 72 (6–158) months, while systemic recurrence was detected in 3 patients in the DSM ≥10 mm group. No statistically significant difference was found between the groups in terms of recurrence, DFS and OS (Table 1, Figure 2). However, considering that a minimum follow-up period of 5 years is required to detect 80% of local recurrences, the median follow-up period of 29 months for the group with DSM <10 mm may be misleading.[18] In a recent study of 88 patients with similar methodology, the local recurrence rate was 6.1% in the DSM <10 mm group and 5.5% in the DSM ≥10 mm group, which

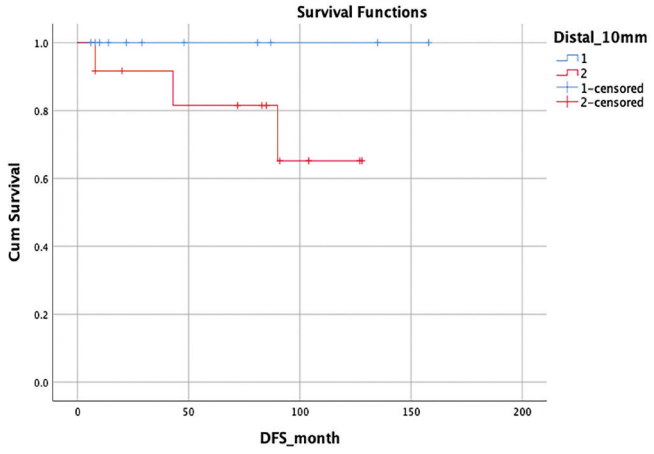

Figure 2. DFS (Disease-free survival); Log Rank (Mantel-Cox) p=0.184

Table 3. The distribution of clinical and pathological stages among the groups and their correlation with recurrence. All values are given as n (%)

A. Clinical stage		Total	DSM <1 cm	DSM ≥1 cm	p$^{\Phi}$	Recurrence p‡
	1	0 (0)	0 (0)	0 (0)		
cT	2	3 (13.0)	2 (18.2)	1 (8.3)	0.484	0.495
	3	20 (87.0)	9 (81.8)	11 (91.7)		
	0	5 (21.7)	3 (27.3)	2 (16.7)		
cN	1	6 (26.1)	4 (36.4)	2 (16.7)	0.339	0.950
	2	12 (52.2)	4 (36.4)	8 (66.7)		
	1	0 (0)	0 (0)	0 (0)		
cTNM	2	5 (21.7)	3 (27.3)	2 (16.7)	0.538	0.602
	3	18 (78.3)	8 (72.7)	10 (83.3)		
B. Pathological stage						
	1	4 (17.4)	3 (27.3)	1 (17.4)		
pT	2	7 (30.4)	4 (36.4)	3 (30.4)	0.343	0.120
	3	12 (52.2)	4 (36.4)	8 (66.7)		
	0	17 (73.9)	9 (81.8)	8 (66.7)		
pN	1	2 (8.7)	2 (18.2)	0 (0.0)	0.046	0.030
	2	4 (17.4)	0 (0.0)	4 (33.3)		
	1	8 (34.8)	6 (54.5)	2 (16.7)		
pTNM	2	9 (39.1)	3 (27.3)	6 (50.0)	0.163	0.077
	3	6 (26.1)	2 (18.2)	4 (33.3)		

$^{\Phi}$Chi-Square test, ‡Spearman's rho correlation test (Correlation with recurrence), DSM: Distal surgical margin

suggested that the results might change in the following period.[19] Another reason for the absence of local recurrence in our series might be performing APR in patients with worse pathological features (LVI, PNI, surgical margin positivity, poor differentiation).[17,20] In accordance with our methodology, there was no positive surgical margin and no extramural venous invasion in our study. The rates of LVI, PNI and poor differentiation were 13.4%, 17.4% and 21.7%, respectively.

It has been shown that tumour regression may occur in a scattered manner and small tumour deposits may remain after neoadjuvant CRT.[15,21,22] Mezhir et al.[16] calculated this rate as 55% and reported that DIS rarely exceeded 1 cm. Chiemelik et al.[23] found similar DIS (57%) rates and recommended a minimum DSM of 1 cm. Despite these findings, many clinical studies reported that DSM <1 cm did not increase the risk of recurrence.[4,9,11,17,18,19] Manegold et al.[19] reported that there was no difference between the groups in terms of recurrence when the 1 cm threshold was accepted for DSM following neoadjuvant CRT. Although similar results were reported in the Polish cohort study, it was a handicap to include patients with short- and long-term CRT without subgrouping in the study design.[24] It has been suggested to obtain 5 mm DSM by Kusters et al.[17] Han et al.[11] reported that DSM <1 cm did not increase local and systemic recurrence, even in patients not given RT. In another study sharing similar results, it was noted that the absence of neoadjuvant CRT increased the risk of local recurrence 2.2 times.[25] Andreola et al.[9] reported that DSM did not pose a risk for recurrence other than margin positivity,and Bujko et al.[4] reached the same result in a systematic review.

There are also authors who find DSM <1 cm risky.[12,13,26] Farhat et al.[26] reported that DSM increased recurrence. There were no homogeneous groups in that study because patients with stage 4 disease and patients who underwent APR and local excision were included. In another study, which reported that DSM < 8 mm increased the risk of recurrence, it was not possible to associate DSM with the results; this is because RSM positivity was included and patients with upper rectum tumours and stage 4 disease were included.[12] Zeng et al.[13] reported 12.4% local and 26.4% systemic recurrence in the median 61 month follow-up period in patients with a distal margin of 1-2 mm. Although 80% of the patients in the study group consisted of individuals with stage 2-3 disease, the neoadjuvant CRT ratio was 21.6%, leading to the results being questioned.

When the factors were examined that affected the recurrence of patients who underwent sphincter-sparing resection after neoadjuvant CRT, which was our secondary aim, a significant relationship was found between young age, large tumour size, number of LN metastases, presence of PNI and recurrence. The relationship between age and recurrence is a frequently studied parameter, and it is accepted that recurrence increases and survival is shortened under the age of 55 years.[27,28] In our series, the median ages of the patients with and without recurrence were found to be 37 (30-51) and 56 (33-73) years, respectively. It was observed that there was a significant negative correlation between age and recurrence (Table 1).

Although it is accepted that tumour size has an effect on the recurrence of colon tumours, the same relationship has not been generally accepted in rectal tumours. Few publications have reported that tumour diameter > 5 cm is a prognostic risk factor and is associated with the T stage.[29,30] In our series, tumour diameters in patients with and without recurrence were 4.4±2.2 and 2.0±0.8 cm, respectively (measured as mean ± standard deviation). A significant relationship was found between size and recurrence (Table 1). However, no relationship was found between the cT/pT stage and recurrence (Table 3).

It is known that LN metastasis increases recurrence in rectal cancer.[2,8,9,10,11,12,17,25,31] In our study, it was observed that the ypN stage was significantly higher in the DSM ≥10 mm group (p=0.046) and was significantly associated with recurrence (Table 3). The mean ± standard deviation numbers of metastatic LN in patients with and without recurrence were found to be 8.0±7.2 and 1.4±4.0, respectively. The relationship between the number of metastatic LNs and recurrence was confirmed in the analysis performed on the numerical parameters (Table 2). Our findings supported the negative role of LN metastases in recurrence.

Another independent prognostic factor that is accepted in colorectal malignancies is the presence of PNI.[8,13,25] In a recent study, it was observed that many structures, including lymph nodes, were shrunk or disappeared with neoadjuvant CRT, while the presence of PNI did not change.[31] Based on this, the author suggested that the presence of PNI might be associated with radioresistant cells and a poor prognosis. In our series, 3 (75%) of 4 patients with PNI had LN metastasis and a strong correlation was observed between PNI and recurrence (Table 2).

"Should the stapler doughnuts be part of the surgical margin?" is a common topic of discussion. Stapler doughnut involvement is an independent determinant of OS in proximal gastrointestinal malignancy surgery.[32] However, its role in rectal surgery is being discussed with increasing frequency after Pullyblank et al.[33] suggested that histological examination of the stapler doughnut has no effect on treatment. Many researchers have reported similar results, and it has even been suggested that this investigation causes a waste of time and resources.[34,35,36] Technically, the stapler doughnut cannot fully reflect the surgical margin

as it cannot surround the entire rectal stump. Therefore, it is recommended to consider the surgical margin as positive in patients with margin involvement but without stapler doughnut involvement.[37] Apart from these considerations, the fact that there is not enough tissue left to use for the stapler in distally located tumours is another technical difficulty. In our study, reconstruction was performed manually in approximately 82% of patients with DSM <10 mm.

Study Limitations

The limitations of our study were the 29-month median follow-up period of the target group, retrospective and single-centre study design, and the low number of patients. It should be kept in mind that the absence of extramural venous invasion and low number of patients with LVI (n=3), which are among the factors known to be effective on recurrence, in our study group may have affected our recurrence results.

The decision about surgical method in locally advanced rectal cancers is multi-factorial and complex. Oncologically safe DSM distance is controversial in mid-distal rectal cancer surgery. Controversial results may arise from differences in surgical experience, patient density, and treatment protocols as well as methodological differences. Considering the functional results, the remaining distance is more important than the removed one. Intersphincteric or partial sphincteric resections can reduce quality of life while enabling life without stoma. For a comfortable life, surgeons sometimes prefer to approach the tumour. As the evidence for safe DSM becomes more sufficient, there will be changes in our surgical practice. Before making a decision about APR, the involvement of the sphincter, the presence of poor prognostic factors, the presence of negative surgical margins and patient preferences should be evaluated in detail.

Conclusion

In this study, it was observed that DSM <10 mm did not pose an oncological risk, provided that all surgical boundaries were clean. Young age, presence of perineural invasion, metastatic LN number and large tumour diameter were identified as risk factors associated with recurrence.

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Ethics

Ethics Committee Approval: All of the procedures in our study complied with the institutional or national research committee ethical standards and the 1964 Helsinki Declaration or similar subsequent amendments/ethical standards.

Informed Consent: Informed consent was obtained from all patients participating in the study at the time of admission.

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Authorship Contributions

Surgical and Medical Practices: A.Z, L.V.T., O.S.G., Concept: L.V.T., Design: L.V.T., O.S.G., Data Collection or Processing: L.V.T., Analysis or Interpretation: L.V.T., A.Z Literature Search: L.V.T., Writing: L.V.T.

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