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Original Article

Rectum cancer: The effects of perioperative outcomes of patients as long-term prognostic factor

Refik Bademci[1], Ozlem Ondes Bayar[2], Selvi Tabak Dincer[3], Arzu Akan[4], Cemalettin Camci[4], M. Yavuz Eryavuz[4]

[1]Istanbul Medipol University, Clinic of General Surgery, Istanbul, Turkey
[2]Siirt State Hospital, Clinic of General Surgery, Siirt, Turkey
[3]Okmeydani Training and Research Hospital, Department of Radiation Oncology, Istanbul, Turkey
[4]Okmeydani Training and Research Hospital, Clinic of General Surgery, Istanbul, Turkey

Abstract

Aim: After cancer treatment, patients and clinicians expect accurate prediction of long-term prognosis. The aim of this study was to determine which perioperative factors that may also be useful in determining long-term prognosis.

Material and Methods: The data of rectum cancer patients operated on between 1998 and 2006 were retrospectively compared in respect of clinicopathological and operative results, and long-term survival. Survival was calculated using a Kaplan-Meier method. Data thought to be associated with survival were subjected to univariate analysis followed by Cox proportion regression.

Results: A total of 348 patients were included in the study. The mean age was 56 (±12) years in patients and 195 (56%) were male patients. After retrospective evaluation of the database, the mean duration of disease-free survival was 54 (±50) months and the mean duration of life was 60 (±48) months. There was no statistically significant correlation between gender, surgical procedure, histopathologic type of tumor, T level of the tumor, stage of the patient, ca 19-9 and mean life span. Grade, lymph node status and CEA were statistically correlated with survival time.

Conclusion: We have demonstrated that grade, lymph node status and CEA are associated with long-term survival. These clinical factors are suitable to provide a good clinical guide to prognosis.

Keywords: Rectum cancer; prognosis; long term survival.

INTRODUCTION

Colorectal cancer is ranked as 3rd in men and 2nd in women in the frequency of cancers. Similar to the data related to other tumors, mortality and morbidity decrease in early stages (1). Rectum cancer is also treated with abdominoperineal resection and with low anterior resection surgical procedures as well as with chemo-radiotherapy (2, 3). Rectum cancers also have prognostic factors that determine survival rates (4). Generally, initial clinical staging of rectal cancer patients determines the adjuvant chemotherapy regimen and follow-up schedule according to guidelines and pathological staging of patients using determinants of cancer-related survival (5). Patients' survival in Rectum cancer varies, and the reasons for this may be due to tumor histopathology or other causes, and these factors still remain unclear even today.

The objective of our study is to determine the factors that may be useful in determining long-term prognosis by examining preoperative, operative and postoperative values after curative surgery in rectal cancer.

MATERIAL and METHODS

The preoperative, operative and postoperative data of the patients, who underwent curative surgery with the diagnosis of rectum cancer between 1998 and 2006 at Okmeydani Training and Research Hospital were retrospectively analyzed. The patients who had undergone elective surgery and had surgery for rectal cancer without any disease affecting the surgical technique were included in the study. The overall survival time was defined as the time from the initial diagnosis to the date of death. The duration of the disease-free survival was defined as the

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Corresponding Author: Refik Bademci, Istanbul Medipol University, Clinic of General Surgery, Istanbul, Turkey
E-mail: refikbademci@gmail.com

time from the date of diagnosis until the date of the first recurrence.

Patients who undergo rectosigmoidoscopic examination and who have tumors in the first 15 cm in the rectum can be considered as having rectal cancer. We operated our patients with two different surgical procedures (low anterior resection and abdominoperineal resection). Patients were evaluated pre-operatively with thoraco-abdominal computed tomography (CT), tumor markers CEA (carcinoembryonic antigen) and ca19-9 (cancer antigen 19-9) and upper abdominal MRI if necessary. Neoadjuvant long-term chemoradiotherapy was applied to patients with stage 2 and above according to the stage of the patients.

Clinical, radiological and pathological results of the patients were evaluated. The anatomicopathological features and lymph node status of the specimen were evaluated according to the 6th edition of the American Cancer Classification Committee (6).

In order to investigate the prognostic factors affecting survival in patients; Patients' gender, age, stage of the tumor (TNM classification), histological type (WHO classification), degree of differentiation (good, moderate, bad), number of removed lymph nodes, lymph node involvement (how many lymph node involvement), preoperative CEA (ng / ml) levels, preoperative ca19-9 (ng / ml) levels of the operation procedure (miles, low anterior resection), operation times, death times and death data were analyzed and recorded.
As per the stage of the disease for every patient, every 4 to 6 months Serum CEA and CA 19.9 levels were measured, chest and abdominopelvic CT were conducted and colonoscopy was performed with 1 year intervals. Adjuvant treatments were applied according to the disease stage. Adjuvant therapy was performed in stage II patients with high recurrence risk, except for stage III patients and medical contraindications. Patients were evaluated for overall survival as well as for local and distant recurrence.

Mean, standard deviation, frequency and ratio values were used in descriptive statistics of the data. Survival analysis utilized the life table and the Kaplan-Meier analysis. Log-rank ((mantel .cox) was used for the differences between the groups and SPSS 19.0 program was utilized for the analysis.

RESULTS

After the analysis of the data, we included 348 patients to our study. The mean age of the patients was 56 (± 12), and 195 (56%) patients were male. As a surgical procedure, 208 (59.7%) patients underwent low anterior resection and 140 (40.3%) patients underwent miles operation. In the postoperative pathology results, 288 (82.8%) patients had adenocarcinoma and 60 (17.2%) had mucinous adenocarcinoma, and 89 (25.6%) patients were differentiated as being in a good condition, 221 (63.5%) patients were considered as average condition and 38 (10.9%) patients were poorly differentiated. When lymph node positivity was evaluated, it was observed that in 97 patients (27.1%), no invasion was detected in the lymph nodes, n1 in 171 (49.1%) patients, n2 in 60 (17.2%) patients, and n3 in 20 (5.9%) patients. In the evaluation of T levels of the patients, 15 (0.3%) patients were T1, 66 (18.9%) were T2, 257 (73.8%) were T3, 10 (0.2%) were T4. When looking at the stages of patients; 4.3% patients were observed to be at stage 1, 30.1% patients were stage 2, and 65.6% patients were at stage 3. When CEA levels of the patients were evaluated, 178 (51.2%) patients were found to have normal levels and 170 (48.8%) patients were found to have high levels. When the ca19-9 levels of the patients were examined, 325 (94.4%) of the patients were observed to have normal levels and 23 (6.6%) of the patients were found to have high levels. The mean number of lymph nodes removed was 9.7±7.2 and the mean number of invasive lymph nodes detected was found to be 1.7 ± 3.7. 205 (58.9%) of the patients died during their follow-up (Table 1).

Table 1. Clinicopathological data of patients operated for rectal cancer

		n: 348
Age (mean + - ss)		56±12
gender n (%)		
	Male	195 (56)
	Female	153 (44)
Surgical Technique n (%)		
	low anterior	208 (59.7)
	Miles	140 (40.3)
Histology (%)		
	Adenocarcinoma	288(82.8)
	Mucinous adenocarcinoma	60(17.2)
Grade n (%)		
	Good	89 (25.6)
	Medium	221 (63.5)
	Bad	38 (10.9)
N n (%)		
	0	97 (27.8)
	1	171 (49.1)
	2	60 (17.2)
	3	20 (5.9)
T n (%)		
	1	15 (0.3)
	2	66 (18.9)
	3	257 (73.8)
	4	10 (0.2)
Stage n(%)		
	Stage 1	15 (4.3)
	Stage2	105(30.1)
	Stage 3	228 (65.6)
CEA n(%)		
	normal	178 (51.2)
	High	170 (48.8)
Ca 19-9 n(%)		
	normal	325 (94.4)
	High	23 (6.6)
removed lymph node (mean +- ss)		9.7 ±12 7.2
metastatic lymph node (mean +- ss)		1.7 ±12 3.7

Table 2. Long-term survival rates of patients operated for rectal cancer

		survival (60.months)	survival (36.months)	survival (60.months)
Gender n(%)				
	Male	78 (40)	146 (75)	78 (40)
	Female	65 (42.4)	111 (72)	65 (42)
Age n(%)				
	< 40	22(43.1)	40 (78)	22 (43)
	40	121 (40.7)	117 (73)	121 (41)
Surgical procedure n(%)				
	Low anterior	84 (40.3)	157 (75)	84 (40)
	Miles	59 (42.1)	98 (70)	59 (42)
Grade n(%)				
	Good	27 (56.25)	37 (78)	27 (56)
	Medium	110 (49.3)	166 (74)	110 (49)
	Bad	6 (15.7)	23 (57)	6 (15)
Histology n(%)				
	Adenocarcinoma	118 (40.9)	168 (74)	118 (41)
	Mucinous adenocarcinoma	25 (41.6)	41 (68)	25 (41)
N n(%)				
	0	56 (57.7)	80 (83)	56 (58)
	1	73 (42)	132 (76)	73 (42)
	2	11 (18.3)	91 (56)	11 (18)
	3	3 (15)	7 (33)	3 (15)
T n(%)				
	1	9 (60)	9 (60)	9 (60)
	2	33 (50)	53 (81)	33 (50)
	3	98 (38.1)	183 (71)	98 (38)
	4	3 (30)	7 (70)	3 (30)
Stage n(%)				
	Stage 1	8 (53.3)	16 (100)	8 (50)
	Stage 2	54 (51.4)	84 (80)	54 (51)
	Stage 3	81 (35.5)	162 (70)	81 (35)
CEA n(%)				
	Normal	91 (51.1)	142 (80)	91 (51)
	High	52 (30.5)	114 (66)	52 (30)
Ca 19-9				
	Normal	137(42.1)	241 (74)	137(42)
	High	6 (26)	14 (63)	6 (26)

Table 3. Rectum cancer long-term life expectancy

		Average lifeterm	P
gender (month)*			0.227
	male	72.3 (±4.5)	
	female	81.6 (±5.4)	
age (month)*			0.344
	< 40	85.8(±11)	
	40	75.3(±3.7)	
Surgical technique (month)*			0.797
	low anterior	76.6 (±4.6)	
	miles	74.8 (±5.5)	
grade (month)*			0.001
	good	98.4 (±7.4)	
	medium	72.3 (±4.1)	
	Bad	44.4 (±7.3)	
Histology(month) *			0.618
	adenocarcinoma	74.6 (±3.7)	
	mucinous adenocarcinoma	81 (±8.9)	
N (month)*			0.001
	0	82 (±8.1)	
	1	72.2 (±6)	
	2	46.7 (±9.1)	
	3	25 (±7.8)	
T (month)*			0.724
	1	103.2 (±33.3)	
	2	86.8 (±8)	
	3	73.4 (±4)	
	4	52(±13.9)	
stage (month)*			0.076
	Stage 1	82.2 (±21.4)	
	Stage 2	78.8 (±7.8)	
	Stage 3	65.4 (±5.1)	
CEA (month)*			0.001
	normal	87.4 (±4.9)	
	high	64.9 (±4.8)	
ca 19-9			0.1
	normal	78.1 (±3.6)	
	high	54.9 (±12.9)	
Number of patients who died n(%)		205(58.9)	
Death due to disease		179(87.5)	
Patients who died without disease		26 (12.5)	

* mean ± sd

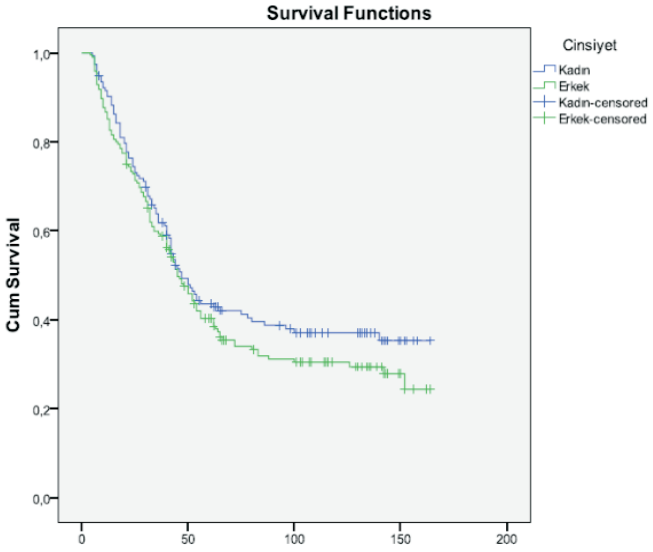

Figure 1. Survival according to rectum cancer gender. Green line: men; blue line: women.

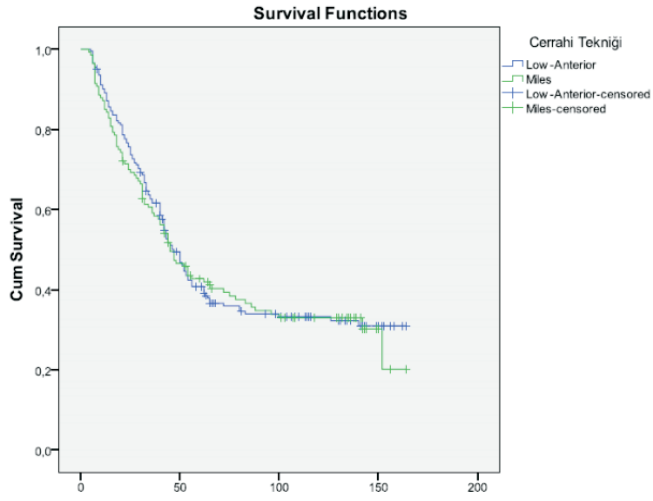

Figure 2. Survival according to rectum cancer surgical procedure. Green line: miles procedure; blue line: low anterior procedure

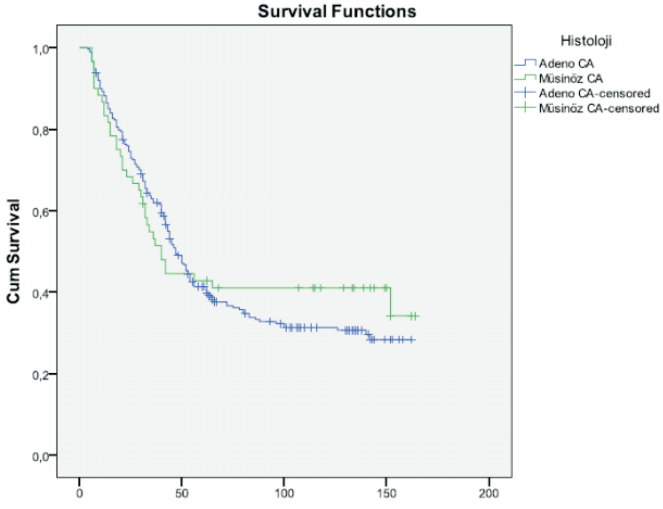

Figure 3. Survival according to rectum cancer histopathology. Green line: mucinous adenocarcinoma; blue line: adenocarcinoma

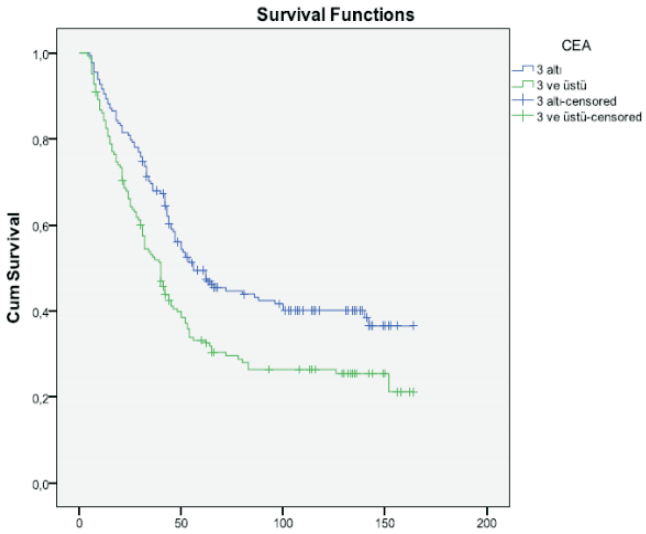

Figure 4. Survival according to rectum cancer CEA (carcinoembryonic antigen) level. Green line: CEA normal; blue line: CEA high level

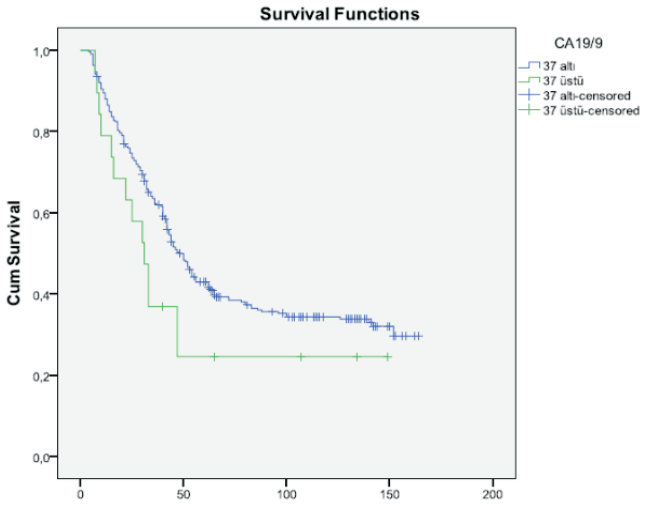

Figure 5. Survival according to rectum cancer ca19-9 (cancer antigen 19-9) level. Green line: ca 19-9 normal; blue line: ca19-high level

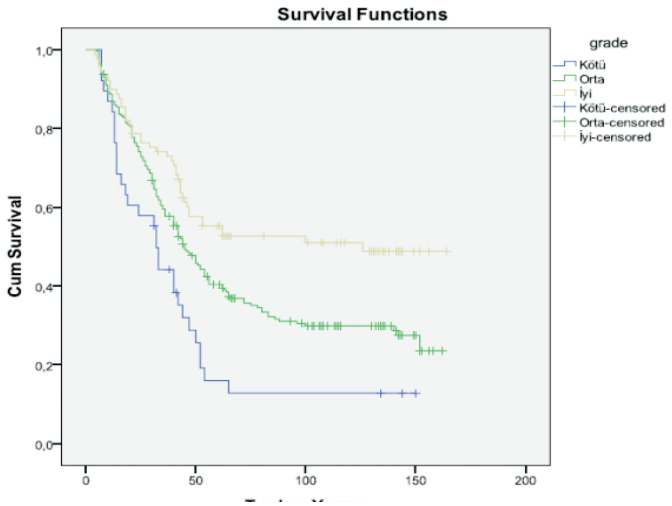

Figure 6. Survival according to rectum cancer grade. Yellow line: good, green line: Medium; blue line: bad

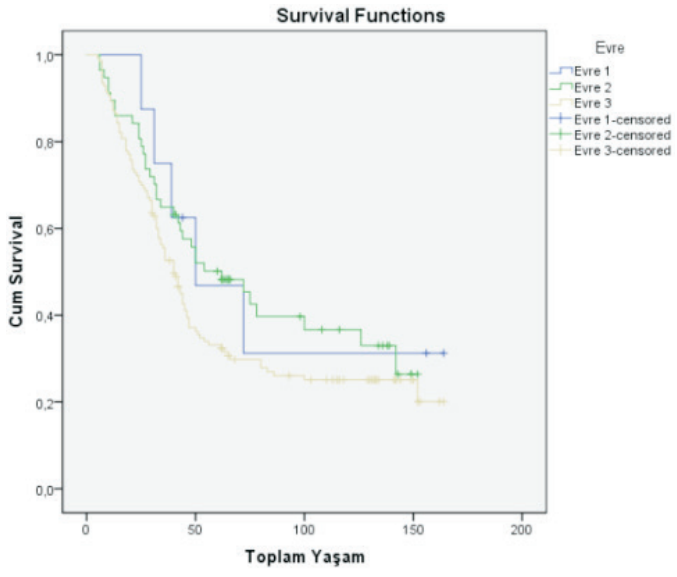

Figure 7. Survival according to rectum cancer stage.: Blue line: stage 1, green line: Stage 2; Yellow line: stage 3

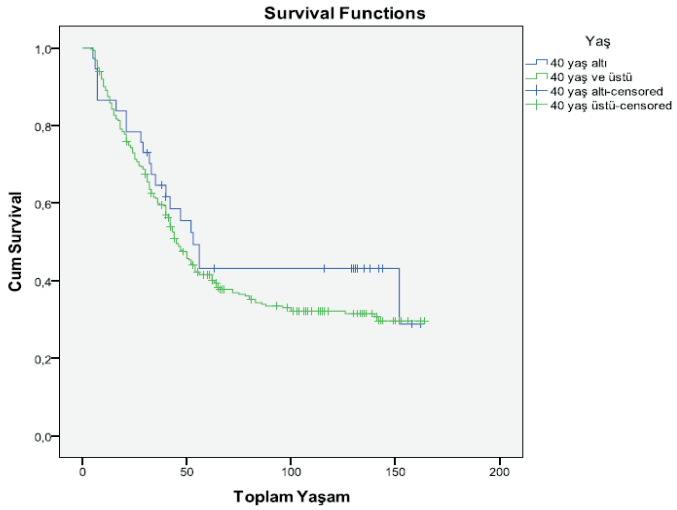

Figure 8. Survival according to rectum cancer age. Green line: 40; blue line: < 40.

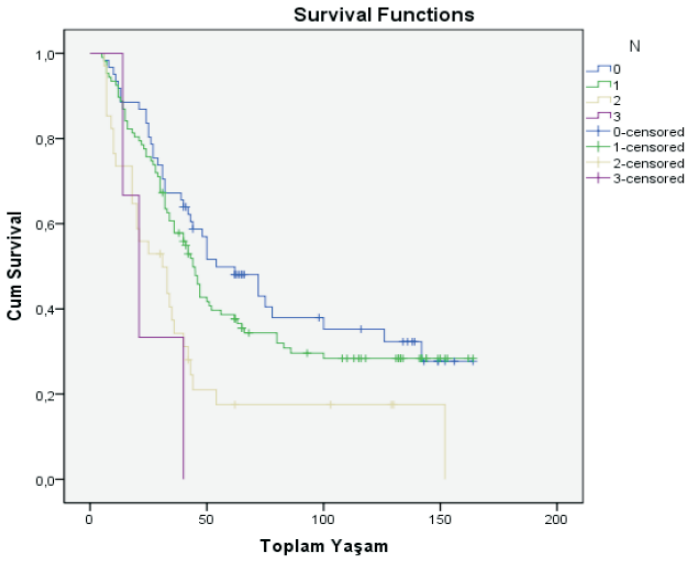

Figure 9. Survival according to rectum cancer n stage. Blue line: n 0, green line: n 1; Yellow line: n 2; purple line: n3

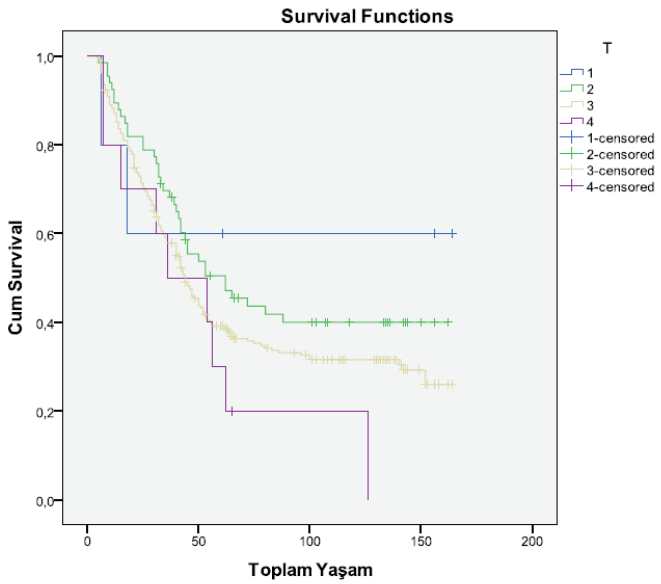

Figure 10. Survival according to rectum cancer T stage. Blue line: T1, green line: T2; Yellow line: T3; purple line: T4

The mean survival time of patients was 54 (± 50) months and the overall survival was 60 (± 48) months. In the follow-up, no statistically significant correlation was found between mean life expectancy and gender, surgical procedure, histopathological type of tumor, tumor's T level, patient's stage, and levels of ca 19-9. Grade, lymph node level and CEA level were found to be statistically correlated (p: 0.001). In general, 205 (58.9%) patients died and 26 (12.5%) of these patients died without disease (Table 2, 3, Figure 1-10).

DISCUSSION

Rectal carcinoma is a frequently occurring disease where the treatment and the follow-up should be performed by a specialized clinician. In patients with rectal cancer, factors that determine the long-term prognosis after surgical and oncological treatments are needed. Some factors have been identified in the literature related to this study (7-14). The aim of our study is to determine the factors that may be useful in determining long-term prognosis by examining preoperative, operative and postoperative values after curative surgery in rectal cancer.

The frequency of colorectal cancer is quite low between the ages of 20-39 and it starts to increase significantly between the ages of 40-50 and two thirds of the cases are diagnosed after 50 years of age (7-9). In some studies, it was stated that age was an important factor affecting prognosis (14), whereas in others it was deemed as not significant (7,10,11). Mehrkhani et al. (12) reported that age was a significant prognostic factor. However, Moghimi-Dehkordi et al. (14) reported that age was a significant prognostic factor. Mitry et al. (7) reported that young age was a poor prognostic factor, and they reported that this may be due to the more aggressive progression of hereditary cancers in young patients and also due to the fact that symptoms are observed at a more advanced

stage. In our study, it was observed that the age did not seem to be important factor in the prognosis.

Rectal cancer is more common in men and there are studies showing that gender does not affect prognosis (3,9,16,17). In our study, it was determined that males had more rates of rectal cancer, but this did not affect the prognosis.

As the T stage in the tumor increases, it adversely affects the prognosis and it is one of the main prognostic factors (18,19). Hermanek (20) stated that T stage was an independent prognostic factor and stated that as the T phase increased, survival was worsening. Our study is consistent with the literature and the increase in T stage of the tumor is a factor that negatively affects prognosis.

As the number of metastatic lymph nodes increases, survival decreases (21,22). In the study, by Moran et al. it was stated that the lymph node involvement negatively affects prognosis (23). Chang et al. (24) reported that lymph node involvement was a negative prognostic factor and the number of retained lymph nodes was also important in survival. Moghimi-Dehkordi et al. (14) reported that lymph node involvement was not an independent prognostic factor in multivariate analysis despite a strong significance in univariate analysis. Park et al. (25) stated in their study that lymph node involvement is the main prognostic factor. In our study, it was seen that the duration of life was shorter in patients with lymph node involvement and the lymph node involvement affected the prognosis negatively in concordance with the literature.

In literature, many studies have indicated that the grade of the tumor is related to prognosis; as the grade increases, the patient's tumor aggression increases and the expected life time is shortened (26-29). In our study, the increase of the grade affected the prognosis negatively in accordance with the literature.

Whether histological features of the rectum tumor are important for prognosis is still a controversial issue. There are studies showing that mucinous component bearing tumors have a negative effect on prognosis as well as studies showing that there is no effect on the prognosis (3,28). Chen et al. (29) reported that the ring cell cancer was significantly lower than the other mucinous cancer and the mucinous cancer was significantly less than the other types. Han-Shiang et al. (30) reported that mucinous carcinomas were associated with a poorer prognosis than those without mucinous in a 2082 case study. In our study, there was no statistically significant difference between long-term prognosis of mucinous adenocarcinoma and rectum cancers diagnosed with adenocarcinoma.

In literature, it is stated that the high level of CEA seen in the preoperative period is a negative prognostic factor independent of the tumor stage (16,31-33). Park et al. (25) reported that patients with elevated serum CEA levels had a shorter survival than patients without lymph node involvement. In our study, it was observed that life expectancy was shorter in patients with CEA elevation at the time of initial diagnosis compared to normal patients and CEA level was determined as a negative prognostic factor.

Ca 19-9 has been shown to be a negative prognostic factor in many studies (31,33). In the study by Lavery et al. levels of many patients were not found to be high, they stated that it is important only in the follow-up (34). Nozoe et al. (32) reported that the high level of ca 19-9 and CEA levels were to be evaluated as a poor prognostic condition. In our study, patients with high levels of ca 19-9 had a relatively shorter life span, though no statistically significant difference was found.

Pathologic stage has been reported as an important prognostic factor in many studies. Newland et al. (35) stated that survival decreases as pathological stage increases. Moghimi-Dehkordi et al. (14) reported that the pathology did not have any meaning as an independent prognostic factor in multivariate analysis, although it showed a strong significance in univariate analysis. In our study, stage 4 patients were not included in the study and only stage 1-3 patients were examined and it was found that the universe was not related to prognosis. In our study, we believe that the distribution of the stages of the patients is irregular and this may have been the reason why it did not.

The retrospective nature of our study constitutes its limitations.

As a result, we think that if the preoperative CEA value is high in a patient who has been operated for rectal cancer, and if lymph node involvement is present and the patient's tumor grade becomes more aggressive, then the prognosis of the patient may be shorter and the use of these data will be useful in evaluating the adjuvant treatment of these patients and in evaluating their long-term prognosis.

Competing interests: The authors declare that they have no competing interest.

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Refik Bademci: ORCID:0000-0001-9378-4438
Ozlem Ondes Bayar: ORCID:0000-0003-2429-9310
Selvi Tabak Dincer: ORCID:0000-0002-7177-9539
Arzu Akan: ORCID:0000-0001-8435-9771
Cemalettin Camci: ORCID:0000-0002-0908-4971
M. Yavuz Eryavuz: ORCID:0000-0002-0021-7598

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