# PROGNOSTIC IMPORTANCE OF THE LYMPH NODE RATIO IN STAGE III COLORECTAL CANCERS

## EVRE III KOLOREKTAL KANSERLERDE LENF NODU POZİTİFLİK ORANININ PROGNOSTİK ÖNEMİ

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## Öz

### Amaç

Kolorektal kanserler, tüm dünyada sık görülen ve mortalitesi yüksek kanserlerdendir. Bu kanserler ile ilgili birçok prognostik faktör tanımlanmıştır. Bunlardan bir tanesi de lenf nodu pozitiflik oranıdır. Bu çalışmanın amacı, Evre III kolorektal kanserlerde lenf nodu pozitiflik oranının prognostik önemini ortaya koymaktır.

### Gereç ve Yöntem

Ocak 1998 ile Mayıs 2014 tarihleri arasında kolorektal kanser tanısı ile opere edilip adjuvan kemoterapi alan, evre III hastaların kayıtları retrospektif olarak incelendi. Hastalar literatüre benzer şekilde lenf nodu pozitiflik oranına göre 0-0,20 arası olanlar 1. grup, 0,21-0,50 arası olanlar 2. grup ve 0,51-1 arası olanlar 3. grup şeklinde üç gruba ayrıldı. Hastaların demografik özellikleri, çıkarılan pozitif ve toplam lenf nodu sayısı, lenf nodu pozitiflik oranı, serbest tümör nodülü varlığı ve sağ kalım verileri incelendi.

### Bulgular

Çalışmaya 263 hasta dâhil edildi. Hastaların 163'ü (%61,9) erkek iken, yaş ortanca değeri 62 (min: 25-max:85) idi. Ortalama çıkarılan lenf nodu sayısı 17.46 (±11.55) ve ortalama pozitif lenf nodu sayısı 3.48 (±5.13) idi. Hastalıksız sağkalım süresi ortalama 65,2(±46,07) ay (min=6, max=223) idi. Genel sağkalım süresi ortalama 70,9 (±44,4) ay (min=6, max=223) idi. Hastalıksız sağkalım ve genel sağkalım ile lenf nodu grupları arasındaki ilişki tek değişkenli analizde incelendiğinde; lenf nodu pozitiflik oranını arttıkça nüksün ve mortalitenin istatistiksel olarak anlamlı şekilde arttığı gözlendi (p<0,001). Çok değişkenli analiz sonuçlarına göre de hastalıksız sağkalım ve genel sağkalım ile lenf nodu pozitiflik oranını grupları arasındaki ilişki [sırasıyla (p=0,030), (p=0,019)] istatistiksel olarak anlamlı bulundu.

### Sonuç

Opere evre III kolorektal kanserlerde lenf nodu pozitiflik oranın hastalıksız sağ kalım ve genel sağ kalım üzerine, etkili bir prognostik faktördür.

**Anahtar Kelimeler:** Adjuvan kemoterapi, Kolorektal kanser, Lenf nodu oranı, Prognoz

## Abstract

### Objective

Colorectal cancers (CRCs) are among the most com-

mon cancers all over the world with a high mortality rate. Many prognostic factors have been identified for these cancers, one of which is the lymph node ratio (LNR). The purpose of this study was to reveal the prognostic importance of the LNR in stage III CRCs.

**Material and Method**
The records of stage III colorectal patients who received adjuvant chemotherapy between January 1998 and May 2014 were examined retrospectively. Similar to the literature, the patients were divided into three groups according to their LNRs. Those with a ratio of 0–0.20 were in the 1st group, with 0.21–0.50 were in the 2nd group, and with 0.51–1 were in the 3rd group. Demographic characteristics of the patients, number of positive and total lymph nodes removed, lymph node positivity rate, presence of free tumor nodules, and survival were evaluated.

**Results**
A total of 263 patients were included in the study. Whi-

le 163 (61.9%) of the patients were male, the median age was 62 (min: 25–max: 85). The mean number of lymph nodes removed was 17.46 (±11.55), and the mean number of positive lymph nodes was 3.48 (±5.13). The mean duration of disease-free survival (DFS) was 65.2 (±46.07) months (min = 6, max = 223). The mean overall survival time (OS) was 70.9 (±44.4) months (min = 6, max = 223). In univariate analysis, it was observed that as the LNR increased, recurrence and mortality increased statistically significantly (P < 0.001). According to the results of multivariate analysis, the relationship of DFS and OS with the LNR groups was statistically significant (P = 0.030 and P = 0.019, respectively).

**Conclusion**
The LNR in operated stage III CRC is an effective prognostic factor on DFS and OS.

**Keywords:** Adjuvant chemotherapy, Colorectal cancer, Lymph node ratio, Prognosis

## Introduction

Colorectal cancers (CRCs) have become a global problem worldwide, with the increasing population and aging in developed and developing countries, as well as the increase in the number of cases and related deaths. It is the third most common cancer in men and the second in women worldwide (1). CRCs can be detected in the asymptomatic period as a result of the examinations for the patient's symptom or through screening programs (2).

Primary treatment in stage I–III CRCs is surgery. The pathological stage of the tumor is the most important prognostic factor. In addition, lymph node involvement and the number of involved lymph nodes are also important prognostic factors. Patients with lymph node involvement are candidates for adjuvant chemotherapy (3). Removal of 12 or more lymph nodes has been shown to be associated with survival (4).

Recently, it was reported that the lymph node ratio (LNR) (metastatic lymph node count/total lymph node count) is a prognostic factor in addition to the positive lymph node count and total lymph node count. In a study that included stage III CRCs, the LNR was shown to be an independent predictor of disease-free survival (DFS) and overall survival (OS), and a better prognostic factor than the number of metastatic lymph nodes (5).

The purpose of this study was to reveal the prognostic importance of the LNR in stage III CRCs.

## Material and Method

In this study, the records of stage III patients according to the American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) classification, who were operated with the diagnosis of CRC and received adjuvant chemotherapy in the Training and Research Hospital, between January 1998 and May 2014, were analyzed retrospectively. A total of 263 patients were included in this study. Similar to the literature, the patients were divided into three groups according to their LNR. Those with a ratio of 0–0.20 were in the 1st group, with 0.21–0.50 were in the 2nd group, and with 0.51–1 were in the 3rd group. Demographic characteristics of the patients, number of positive and total lymph nodes removed, lymph node positivity rate, presence of free tumor nodules, and survival were evaluated. Approval was obtained from the Ankara Numune Training and Research Hospital Clinical Research Ethics Committee (2017-1329 Date: 29.03.2017).

The inclusion criteria for the study were defined as being >18 years of age, having a pathologically confirmed diagnosis of adenocarcinoma, and having received at least one cycle of adjuvant chemotherapy. Patients with insufficient file data, who dropped out of

the follow-up, and who received neoadjuvant therapy were excluded from the study.

**Statistical Analysis**

In the evaluation of the data, the mean ± standard deviation, median, quartiles, minimum and maximum values were used for numerical measurements from descriptive statistics. For the qualitative measurements, numbers and percentages were used. Kaplan-Meier Survival analysis was used to carry out a univariate examination of factors affecting OS rates and DFS rates. DFS was determined as the time from operation to recurrence. In patients who died before the recurrence assessment, the date of death was considered the date of recurrence. The last date of disease evaluation was used in patients who were alive and did not show recurrence until the end of the study. OS was determined as the time from operation to death. In patients who were still alive at the end of the study, the last date the patient was seen was taken as a basis.

The survival curves of the groups were compared according to the log-rank test, and bilateral comparisons were made according to the log-rank Mantel-Cox statistic for cases in which the difference between the survival curves was significant. Univariate Cox regression analysis was used to examine the effects on the survival rates for the numerical values. Variables that were found to be significant as a result of univariate analyses were then analyzed with the multivariate Cox regression model. Hazard ratios, 95% confidence intervals, and P-values were obtained in the Cox regression analysis. For the statistical analysis, $P < 0.05$ was considered significant and IBM SPSS Statistics for Windows 21.0 (IBM Corp., Armonk, NY, USA) was used in all analyses.

## Results

Of the patients, 163 (61.9%) were male and 100 (38.1%) were female. The median age was 62, and the age range was between 25 and 85. Moreover, 22 (8.4%) of the patients had a history of CRC, and 69 (26.2%) had a history of some type of cancer. Considering the tumor localizations, 128 (48.7%) were in the rectum, 58 (22.1%) in the sigmoid colon, 40 (15.2%) in the right colon, 24 (9.1%) in the left colon, 8 (3%) in the transverse colon, and 5 (1.9%) in the cecum. When the operations performed on the patients were examined, it was observed that segmental colectomy was performed in 131 (49.8%) patients, low anterior resection in 90 (34.2%) patients, abdominoperineal resection in 36 (13.7%) patients, and total colectomy in 6 (2.3%) patients. Of the patients, 23 (8.7%) were operated on due to obstruction and 4 (1.5%) were operated on for perforation.

When the pathology subtype was examined, non-mucinous adeno ca was found in 231 (87.8%) patients, and adeno ca with a mucinous component was found in 32 (12.2%) patients. In terms of the pathological grade, 112 (42.6%) patients were good, 113 (43%) moderate, and 38 (14.4%) poor. There was lymphatic invasion in 41 (20.2%) patients, while 162 (79.8%) patients did not have lymphatic invasion. Vascular invasion was present in 78 (33.5%) patients, and 8 (3%) patients had positive surgical margins. It was found that 61 (48%) patients had free tumor nodules.

When the tumor staging of the patients according to the cancer staging atlas published by the American Joint Committee on Cancer (AJCC) in 2017 was carried out, it was observed that 15 (5.7%) patients were T2, 211 (80.2%) patients were T3, 37 (14.1%) patients were T4. 187 (71.1%) patients were N1, and 76 (29.9%) were N2. When the TNM stages were examined, it was seen that 11 (4.2%) patients were Stage IIIA, 214 (81.4%) were Stage IIIB, and 38 (14.4%) were Stage IIIC.

When the number of removed lymph nodes was examined, it was seen that an average of 17.46 (±11.55) (min: 2–max: 85) lymph nodes were removed from the patients. The mean number of positive lymph nodes was 3.48 (±5.13) (min: 0–max: 57). The mean LNR was 0.24 (±0.24) (min: 0.0 and max: 1.0).

**Table 1** Grouping of study patients according to the LNR (N: 263)

| LNR | Number | Percentage (%) |
|---|---|---|
| 1st Group (0–0.20) | 163 | 62 |
| 2nd Group (0.21–0.50) | 66 | 25.1 |
| 3rd Group (0.51–1.00) | 34 | 12.9 |

LNR: Lymph Node Ratio

The 1st group consisted of 163 (62%) patients, the 2nd group consisted of 66 (25.1%) patients, and the 3rd group consisted of 34 (12.9%) patients (Table 1). Moreover, 60 (22.8%) of the patients received FU-FA and 203 (77.2%) received FOLFOX regimens. A total of 134 (51%) patients received radiotherapy.

When the survival of the patients was examined, it was seen that 169 (64.3%) patients survived and 94 (35.7%) patients died. The mean DFS was 65.2 (±46.07) months, with a minimum of 6 months and a maximum of 223 months. The mean OS was 70.9 (±44.4) months, with a minimum of 6 months and a maximum of 223 months. When the presence of recurrence was examined, it was found that 109 (41.4%) patients had recurrence and 154 (58.6%) patients did not have recurrence. Of the 109 patients that had recurrence, 54 (49.5%) had local recurrence and 55 (50.5%) had distant recurrence.

When the univariate analyses of the data on DFS were examined, the following results were obtained: sex (P = 0.571), presence of tumor in the family (P = 0.383), tumor localization (P = 0.569), type of operation (P = 0.259) and presence of obstruction (P = 0.105) and perforation (P = 0.605) before surgery, lymphatic invasion (P = 0.126), presence of vascular invasion (P = 0.914) surgical margin positivity (P = 0.102) and free tumor nodule (P = 0.254), chemotherapy regimen (P = 0.067), radiotherapy status (P = 0.321), age (P = 0.434), and number of lymph nodes removed (P = 0.455) were not statistically correlated with DFS. However, for those with a family history of colon tumor (P = 0.022), mucinous component (P = 0.004) as the grade of the tumor (P = 0.003), the T stage (P = 0.017), N stage (P = 0.001), TNM stage (P = 0.001), LNR (P = 0.001), and positive lymph node number (P = 0.001) increased, and recurrence increased statistically significantly.

When the relationship between DFS and lymph node groups was examined in the univariate analysis, there was a statistically significant difference between the groups in terms of recurrence (P =0.001). The mean expected DFS of the 1st group was 144.6 (10.38) months, it was 191.7 (8.31) months for the 2nd group, and 52.6 (8.84) months for the 3rd group (Table 2).

**Table 2** Correlation between DFS and lymph node groups

| Groups | Total | Had recurrence | No reccurence | P-value |
|---|---|---|---|---|
| 1st Group (LNR:0–0.20) | 163 | 52 (31.9%) | 111 (68.1%) | 0.001 |
| 2nd Group (LNR: 0.21–0.50) | 66 | 33 (50%) | 33 (50%) | |
| 3rd Group (LNR: 0.51–1.00) | 34 | 24 (70.6%) | 10 (29.4%) | |

| | Mean | | | | Median | | | |
|---|---|---|---|---|---|---|---|---|
| | Estimate | Standard deviaton | 95% confidence interval | | Estimate | Standard deviaton | 95% confidence interval | |
| | | | Lower limit | Upper limit | | | Lower limit | Upper limit |
| 1st group | 144.6 | 10.38 | 124.2 | 164.9 | 156 | | | . |
| 2nd group | 91.7 | 8.31 | 75.3 | 108.0 | 109 | 10.56 | 88.29 | 129.7 |
| 3rd group | 52.6 | 8.84 | 35.2 | 69.9 | 25 | 5.09 | 15.01 | 34.98 |
| Overall | 123.1 | 8.49 | 106.5 | 139.8 | 134 | 15.01 | 104.58 | 163.4 |

LNR: Lymph Node Ratio, DFS: disease-free survival   P < 0.05 was statistically significant.

**Table 3**  Multivariate analysis results for DFS

| | B | SE | Wald | df | Sig. | Exp(B) | 95% CI for Exp(B) Lower | 95% CI for Exp(B) Upper |
|---|---|---|---|---|---|---|---|---|
| ECOG | 0.414 | 0.143 | 8.441 | 1 | 0.004 | 1.513 | 1.144 | 2.002 |
| History of Colon Tumors in the Family | 0.513 | 0.309 | 2.745 | 1 | 0.098 | 1.670 | 0.910 | 3.062 |
| Pathology Subtype | 0.047 | 0.385 | 0.015 | 1 | 0.903 | 1.048 | 0.493 | 2.230 |
| Grade | | | 1.663 | 2 | 0.435 | | | |
| Grade 1 | 0.013 | 0.229 | 0.003 | 1 | 0.956 | 1.013 | 0.646 | 1.587 |
| Grade 2 | 0.482 | 0.392 | 1.507 | 1 | 0.220 | 1.619 | 0.750 | 3.492 |
| T | | | 2.614 | 2 | 0.271 | | | |
| T 1 | 0.474 | 0.516 | ,843 | 1 | 0.359 | 1.606 | 0.584 | 4.418 |
| T 2 | 0.808 | 0.562 | 2.068 | 1 | 0.150 | 2.244 | 0.746 | 6.751 |
| N | 0.131 | 0.304 | 0.186 | 1 | 0.666 | 1.140 | 0.629 | 2.068 |
| Lymph Node Group | | | 7.046 | 2 | 0.030 | | | |
| Lymph Node Group 1 | 0.328 | 0.274 | 1.425 | 1 | 0.233 | 1.388 | 0.810 | 2.376 |
| Lymph Node Group 2 | 0.943 | 0.357 | 6.976 | 1 | 0.008 | 2.568 | 1.275 | 5.171 |
| Positive Lymph Node Number | 0.013 | 0.023 | 0.346 | 1 | 0.556 | 1.014 | 0.969 | 1.060 |

ECOG :Eastern Cooperative Oncology Group, DFS: disease-free survival, T:Tumor, N:Node  $P < 0.05$ was statistically significant.

**Table 4**  Correlation between OS and the lymph node groups

| | Total | Deceased | Alive | P-value |
|---|---|---|---|---|
| Groups | | | | |
| 1st Group (LNR: 0–0.20) | 163 | 42 (25.6%) | 121 (%74.2%) | 0.001 |
| 2nd Group (LNR: 0.21–0.50) | 66 | 32 (48.5%) | 34 (51.5%) | 0.001 |
| 3rd Group (LNR: 0.51–1.00) | 34 | 20 (58.8%) | 14 (41.2%) | 0.001 |

| | Mean | | | | Median | | | |
|---|---|---|---|---|---|---|---|---|
| | Estimate | Standard deviaton | 95% confidence interval Lower limit | 95% confidence interval Upper limit | Estimate | Standard deviaton | 95% confidence interval Lower limit | 95% confidence interval Upper limit |
| 1st group | 163.6 | 7.95 | 148.0 | 179.2 | . | . | . | . |
| 2nd group | 102.0 | 9.65 | 83.1 | 120.9 | 109 | 13.75 | 82.05 | 135.9 |
| 3rd group | 71.5 | 10.00 | 51.9 | 91.1 | 55 | 7.045 | 41.19 | 68.8 |
| Overall | 140.5 | 7.44 | 125.9 | 155.1 | 157 | . | . | . |

OS:overall survival , LNR: Lymph Node Ratio,  $P < 0.05$ was statistically significant.

**Table 5**    Multivariate analysis results for OS

| | B | SE | Wald | df | Sig. | Exp(B) | 95% CI for Exp(B) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Upper |
| History of Colon Tumors in the Family | 1.165 | 0.362 | 10.363 | 1 | 0.001 | 3.206 | 1.577 | 6.516 |
| ECOG | 0.652 | 0.169 | 14.925 | 1 | 0.001 | 1.919 | 1.379 | 2.671 |
| Pathology Subtype | –0.357 | 0.425 | 0.706 | 1 | 0.401 | 0.700 | 0.304 | 1.609 |
| Grade | | | 13.902 | 2 | 0.001 | | | |
| Grade 1 | –0.759 | 0.275 | 7.632 | 1 | 0.006 | 0.468 | 0.273 | 0.802 |
| Grade 2 | 0.555 | 0.400 | 1.920 | 1 | 0.166 | 1.742 | 0.795 | 3.817 |
| N | 0.191 | 0.326 | 0.342 | 1 | 0.558 | 1.210 | 0.639 | 2.293 |
| Lymph Node Group | | | 7.915 | 2 | 0.019 | | | |
| Lymph Node Group 1 | 0.637 | 0.293 | 4.728 | 1 | 0.030 | 1.890 | 1.065 | 3.355 |
| Lymph Node Group 2 | 1.136 | 0.423 | 7.208 | 1 | 0.007 | 3.115 | 1.359 | 7.142 |
| TNM Stage | | | 3.863 | 2 | 0.145 | | | |
| TNM Stage 1 | 0.170 | 1.052 | 0.026 | 1 | 0.872 | 1.185 | 0.151 | 9.322 |
| TNM Stage 2 | –0.574 | 1.109 | 0.268 | 1 | 0.605 | 0.563 | 0.064 | 4.955 |
| Chemotherapy Regimen | 1.628 | 0.340 | 22.965 | 1 | 0.001 | 5.095 | 2.618 | 9.915 |
| Positive Lymph Node Number | 0.016 | 0.026 | 0.397 | 1 | 0.528 | 1.016 | 0.967 | 1.069 |
| Presence of Recurrence | 13.845 | 52.687 | 0.069 | 1 | 0.793 | 1030013.4 | 0.000 | 7.252 |

OS:overall survival , P < 0.05 was statistically significant. TNM: Tumor, node, metastasis  ECOG: Eastern Cooperative Oncology Group, N:Node

For the 1st group, the 1st, 3rd, and 5th year DFS rates were 95%, 81%, and 76%, respectively. It was 87%, 63%, and 59% for the 2nd group and 76%, 44%, and 28% for the 3rd group, respectively. In Figure 1, the difference in the expected disease-free life expectancy between the three groups is shown.

The multivariate analysis evaluating the factors affecting DFS, it was found that the LNR groups were effective on DFS (Table 3).

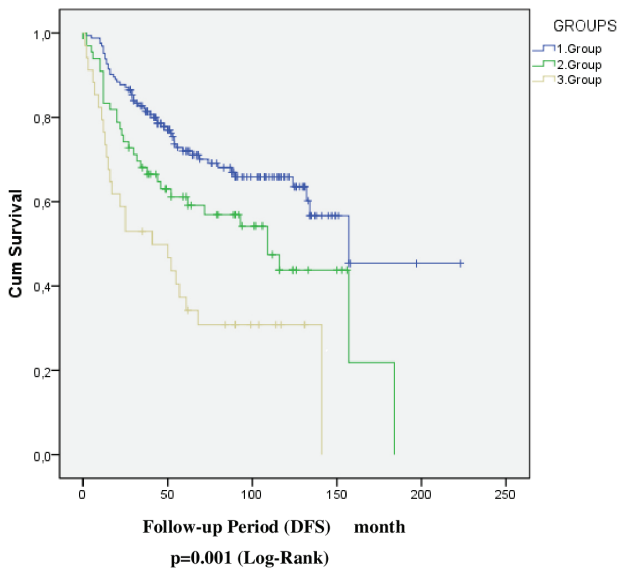When the univariate analyses of data on OS were examined, the following results were obtained: sex (P

**Figure 1**

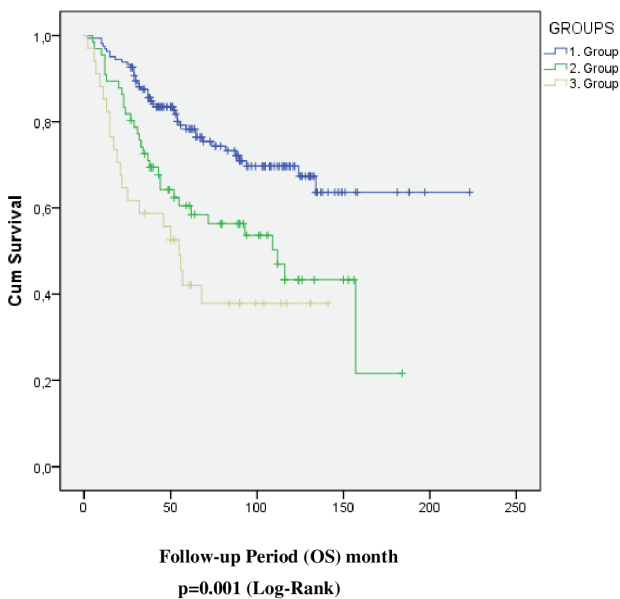Projection analysis between DFS and the lymph node groups



**Figure 2**

Projection analysis between OS and the lymph node groups

= 0.865), presence of tumor in the family (P = 0.641), presence of coronary artery disease (P = 0.290), tumor localization (P = 0.490), type of surgery performed (P = 0.524) and presence of preoperative obstruction (P = 0.484) and perforation (P = 0.407), presence of lymphatic invasion (P = 0.091), presence of vascular invasion (P = 0.409), positive surgical margins (P = 0.207), and presence of free tumor nodules (P = 0.127) ), T-stage increase (P = 0.132), number of cycles (P = 0.160) and radiotherapy status (P = 0.219), age (P = 0.531), number of lymph nodes removed (P = 0.471) were not in a statistically significantly correlated with OS. However, it was observed that for those with a family history of colon tumor (P = 0.012), those with mucinous component (P = 0.006), poor grade of the tumor (P = 0.001), as N stage (P = 0.001) and TNM stage (P = 0.001) increased, those with FOLFOX chemotherapy regimen (P = 0.024), those with recurrence (P = 0.001), as LNR (P = 0.001) and the number of positive lymph nodes (P = 0.001) increased, and mortality increased statistically significantly as well.

When the relationship between OS and lymph node groups was examined, it was determined that 42 (25.6%) patients in the 1st group, 32 (48.5%) patients in the 2nd group, and 20 (58.8%) patients in the 3rd group died. In the univariate analysis, there was a statistically significant difference between the groups in terms of survival. The mean expected survival time of the 1st group was 163.6 (±7.95) months. This was 102 (±9.65) months for the 2nd group and 71.5 (±10.0) months for the 3rd group (Table 4).

For the 1st group, the 1-year, 3-year, 5-year, and 10-year survival rates were 97%, 87%, 78%, and 69%, respectively. These rates were 95%, 83%, 60%, and 43% for the 2nd group and 85%, 58%, 42%, and 37% for the 3rd group, respectively. The difference in the expected OS time between the three groups is presented in Figure 2.

When the factors affecting OS were evaluated by multivariate analysis, it was determined that ECOG performance status, presence of colorectal tumor in the family, tumor grade, chemotherapy regimen, and LNR groups had an effect on OS (P < 0.05) (Table 5).

## Discussion

CRCs are the most common cancers of the gastrointestinal tract. For CRCs, which are very common and have a mortal course, screening programs have been developed (6). As a result of the screening programs for CRC, both mortality decreased and prognostic factors gained importance with the prolongation of the survival time, as the diagnosis could be made in young people. The most important prognostic factor in determining long-term survival is the stage at diagnosis (2, 7). In the present study, it was observed that 81.4% of the patients were stage IIIB, and DFS and OS decreased as the tumor stage increased. Apart from these, studies have been

conducted on many prognostic factors, such as the lymph node number, perineural invasion, vascular invasion, histological type, and age (8).

The number of positive lymph nodes is a strong prognostic factor in CRCs (3). In the present study, a significant correlation was found between the N stage, DFS, and OS, consistent with the literature. It was observed that mortality and recurrence increased as the N stage increased.

Removal of at least 12 lymph nodes is recommended for accurate staging (4, 7). In this study, mean number of removed lymph nodes was 17.46 (± 11.55).

The study of Chang et al., showed that the total number of removed lymph nodes has a positive effect on survival in stage II and stage III patients (9). In the present study, when the correlation between the total number of removed lymph nodes and OS was examined, it was observed that the total number of removed lymph nodes in the surviving patients was higher than in those who died. When the correlation between DFS and the number of removed lymph nodes was examined, it was seen that the total number of lymph nodes was higher in patients without recurrence, but this difference was not statistically significant. The possible reason for the positive effect of the total number of removed lymph nodes on OS and DFS may be that standard adequate surgery was performed in these patients and as a result, staging and correct treatment were possible.

In 2010, free tumor nodules began to be used in TNM staging. Thus, although the lymph node is negative, in the presence of a free tumor nodule, the N stage of the patients becomes N1c and shifts to TNM stages III A and III B, and consequently affects the prognosis (10). In the present study, 61 patients had positive free tumor nodules, of which 14 patients shifted from stage II to stage III, and these patients were given adjuvant chemotherapy.

Neoadjuvant chemotherapy has been widely used recently, and accordingly, the number of removed lymph nodes is decreasing. Therefore, the LNR, which is independent of the number of lymph nodes removed, gains importance in staging and prognosis (11-13).

Studies showing that LNR may be a prognostic factor were primarily performed on breast and stomach cancers, followed by studies on colorectal cancers (14-15).

The correlation between the LNR and survival in CRCs was first suggested by Berger et al. in their study, who received adjuvant fluorouracil-based chemotherapy, the patients were divided into four groups according to their LNR. The LNR was shown to be statistically significant for OS, DFS, and cancer-specific survival in patients with more than 10 lymph nodes removed (16). In the study of Klos et al., it was emphasized that despite a good surgery in patients receiving neoadjuvant chemoradiotherapy, the number of removed lymph nodes was less than 12 and the LNR was a better prognostic marker than the number of positive lymph nodes in these patients (17). In a study by Garcia et al., the effect of lymph node excision and LNR on survival and treatment plan was researched retrospectively. It was observed that the LNR had an effect on OS and cancer-specific survival in patients with sufficient lymph node removal (12 or more). It was shown that survival markedly reduced in cases with a LNR of 0.16 and above, and suggested that an aggressive treatment plan should be implemented (18).

In a study by Leonard et al., the cut-off value for the LNR was accepted as 0.2 and patients were divided into high and low risk groups. The LNR was observed to be an independent prognostic factor for OS and ORFS (overall recurrence-free survival) if technical requirements such as optimal surgery, and adequate and precise lymph node removal were met (19).

In the present study, the effects of the LNR on OS and DFS in patients with stage III CRCs were evaluated. In the univariate analysis, the 5-year DFS rate was 76% in the group with a LNR of 0–0.20, 59% in the group with a LNR of 0.21–0.50, and 28% in the group with a LNR of 0.51–1.0. There was a difference between the three groups in terms of DFS. When the relationship between OS and the LNR was examined, it was seen that the 5-year survival rate was 78% for the 1st group, 60% for the 2nd group, and 42% for the 3rd group. It was determined that there was a difference between the three groups in terms of the expected OS time. In these groups, OS and DFS decreased as the LNR increased. In the results of multivariate analysis, a statistically significant decrease was found in DFS and OS with the increase in the LNR. The results of the present study for patients who received lymph node-positive adjuvant therapy were congruent with the literature data.

Many factors determine the number of lymph nodes removed in CRCs, together with neoadjuvant chemoradiotherapy. Among these, the factors related to the patients are age, weight, and geographical

location, and the factors related to the tumor are the T stage and localization of the tumor. It also varies depending on the experience of the surgeon, the length of the removed specimen, and the experience of the pathologist (17, 20-21). While there are so many factors affecting the number of lymph nodes removed, it is thought that using the positive lymph node number as a prognostic factor together with the LNR, which is an easily calculated method, will provide a more effective result.

The fact that the present study was retrospective, and thus it was not possible to fully obtain some data, was one of the limiting factors of this study.

## Conclusion

In conclusion, CRCs are the most common cancers of the gastrointestinal tract. Prognostic factors for these cancers have also gained importance. The present study also revealed that the LNR is an effective prognostic factor on DFS and OS.

### Conflict of Interest Statement
The authors have no conflicts of interest to declare.

### Ethical Approval
This study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendment. The study was granted ethical approval by the Ankara Numune Training and Research Hospital Clinical Research Ethics Committee (2017-1329 Date: 29.03.2017).

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### Availability of Data and Materials
Data available on request from the authors.

### Authors Contributions
K.E: Conceptualization, Data curation; Methodology, Formal analysis and investigation, Writing - original draft, Resources

N.Y: Conceptualization, Writing - review and editing, Supervision

A.E: Methodology, Writing - original draft, Resources; Validation;

O.S: Formal analysis; Investigation; Visualization; Resources

O.Y: Formal analysis; Investigation; Writing - review and editing

N.Ö: Conceptualization, Writing - review and editing, Supervision

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