RESEARCH ARTICLE / ARAŞTIRMA MAKALESI

# *Associated Factors of The Metastatic Lymph Node Involvement in Colorectal Cancers*

## Kolorektal Kanserlerde Metastatik Lenf Nodu Tutulumu ile İlişkili Faktörler

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### *Abstract*

***Introduction*** The number of metastatic lymph nodes is the most important prognostic factor that affects disease-free and overall survival in many cancer types. In the study, the factors associated with metastatic lymph node involvement were investigated in colorectal cancers.

***Materials and Methods*** A total of 192 colorectal cancer patients who underwent curative surgery between 2016 and 2021 were included in the study. Patients who had a diagnosis other than adenocarcinoma, whose data could not be obtained and emergency cases were excluded from the study. According to these 4 groups, patients were compared in terms of parameters such as age, gender, tumor stage, histopathological grade, tumor localization, lymphovascular invasion, perineural invasion, neutrophil/lymphocyte ratio, lymphocyte/monocyte ratio, monocyte count, and the total number of lymph nodes.

***Results*** Among the 192 patients included in the study, 75 (39.06%) were female, and 117 (60.94%) were male. The mean age was 67 (23: 89), and the mean follow-up time was 20 (2: 63) months. According to metastatic lymph node involvement, the number of N0, N1, N2a, and N2b patients was 101, 57, 20, 14, respectively. No significant relations were detected between metastatic lymph node involvement and age, gender, neutrophil/lymphocyte ratio, and lymphocyte/monocyte ratio. As the number of metastatic lymph nodes increased, survival rates decreased (p=0.002). Histopathological grade, T stage, lymphovascular invasion, perineural invasion, increased tumor diameter, the total number of lymph nodes removed and increased monocytes were found to be significantly associated with metastatic lymph node involvement (p<0,001; p<0,001; p<0,001; p<0,001; p=0,036; p<0,001; p=0,035).

***Conclusion*** In the present study, except for standard prognostic factors, increased monocytes were associated with lymph node enlargement. High monocyte count in colorectal cancer patients undergoing surgical treatment requires careful evaluation in terms of lymph node involvement.

***Keywords*** Colorectal cancer, lymph node involvement, prognostic factors

### *Özet*

***Amaç*** Metastatik lenf nodu sayısı birçok kanserde hastalıksız ve genel sağkalımı etkileyen en önemli prognostik faktördür. Çalışmamızda kolorektal kanserler hastalarında metastatik lenf nodu tutulumu ile ilişkili faktörler idelendi.

***Gereç ve Yöntemle*** Çalışmaya 2016-2021 yılları arasında küratif cerrahi uygulanan 192 kolorektal kanser hastası dahil edildi. Adenokanser dışı tanı alan, verilerine ulaşılmayan ve acil olgular çalışma dışı bırakıldı. Olgular lenf nodu tutulumuna göre dört gruba ayrıldı. Buna göre hastalar yaş, cinsiyet, tümör evresi, histopatolojik grade, tümör lokalizasyonu, lenfovasküler invazyon, perinöral invazyon, nötrofil/lenfosit ile lenfosit/monosit oranı, monosit sayısı, toplam lenf nodu sayısı gibi parametreler açısından karşılaştırıldı.

***Bulgular*** Çalışmaya dahil edilen 192 hastanın 75'i (%39.06) kadın, 117'si (%60,94) erkekti. Ortalama yaş 67 (23: 89) ve takip süresi 20 (2: 63) aydı. Metastatik lenf nodu tutulumuna göre N0, N1, N2a ve N2b hasta sayısı, sırasıyla 101, 57, 20 ve 14'tü. Metastatik lenf nodu tutulumu ile yaş, cinsiyet nötrofil / lenfosit oranı, lenfosit / monosit oranı arasında anlamlı bir ilişki bulunmadı. Metastatik lenf nodu sayısı ile sağ kalım arasında ters ilişki saptandı ( p=0.002). Histopatolojik grade, tümör evresi, lenfovasküler ile perinöral invazyon, artmış tümör çapı, çıkartılan total lenf nodu sayısı ve artmış monosit sayısı metastatik lenf nodu tutulumu ile anlamlı ilişkili bulundu (p<0,001, p<0,001, p<0,001, p<0,001, p=0,036, p<0,001, p=0,035).

***Sonuç*** Çalışmamızda standart prognostik faktörler haricinde artmış monosit sayısı lenf nodu tulumu ile ilişkili bulundu. Cerrahi açıdan tedavi planı yapılan kolorektal kanser hastalarında, monosit sayısının yüksek olması, lenf nodu tutulumu açısından dikkatli değerlendirme yapılmasını gerektirmektedir

***Anahtar Kelimeler*** Kolorektal kanser, lenf nodu tutulumu, prognostik faktörler

## INTRODUCTION

Colorectal Cancers (CRC) are among the most common causes of cancer-related morbidity and mortality in the world and our country. It is the 3rd most common cancer on a global scale (1-3). However, it is seen with the 2nd frequency in young age (25-49 years old) with an increasing frequency in this age group. In our country, it ranks 2nd in cancer-related mortality. According to the 2017 cancer data of the Ministry of Health, it is the most common cancer in men who are aged 25-49 years (4). The lifetime risk of developing CRC is around 5% (1). The fact that CRCs, which occur with the effect of genetic and environmental factors, can be detected at earlier stages will reveal positive results in terms of their treatment and prognosis. Although many factors guide the treatment choice, there are still many uncertainties in terms of treatment modalities. Tumors with different biological characteristics have different responses to treatment, and patients at the same stage may show different clinical outcomes (5,6). It is still a matter of debate to which patient group adjuvant chemotherapy should be administered in stage II CRC (6) . With the advancement of minimally invasive surgery in recent years, more limited organ-sparing surgeries have gained popularity. EMR (Endoscopic mucosal resection) and ESD (Endoscopic submucosal dissection) are now applied with increasing frequency for suitable colorectal cancers. In some cases, imaging methods are insufficient to demonstrate metastatic lymph node involvement, which is the most important decision-making point for radical surgery in early-stage tumors. For this reason, there are hesitations in patient selection.

The definitive staging of colorectal cancers is made with pathological examination. Lymph node involvement is the most important step in pathological staging and is the most important factor in giving adjuvant chemotherapy. However, some stage II patients who need to receive adjuvant chemotherapy as a result of insufficient lymph node examination that originates from the surgeon or pathologist are deprived of this right and their survival decreases.

In the present study, the purpose was to examine the factors associated with metastatic lymph node involvement, to determine the risk factors for minimally invasive surgery, and to identify stage II colorectal cancers that would benefit from adjuvant chemotherapy

## MATERIAL and METHODS

### i- Ethical Approval

This study was approved by Tekirdağ Namık Kemal University Health Research Ethics Committee [Protocol No: 2021.124.04.19] in line with the ethical standards of the institutional/national research committee and the 1964 Helsinki Declaration. All patients who agreed to participate in the study were informed about the contents and informed consents were obtained.

### ii- Data Sources

The present study was conducted in Tekirdağ Namık Kemal University, Department of General Surgery. In this study, the data of 256 patients who underwent curative surgical resection for CRC between 2016-2021 were analyzed retrospectively. The data of the patients [pathological, clinical, and survival data] were obtained from the archives of Tekirdağ Namık Kemal University.

### iii- Patient population

The following parameters were used as the prognostic indicators; age, gender, localization, tumor size, perineural invasion, lymphatic invasion, histopathological grade, tumor stage, number of lymph nodes with metastases, total lymph node count, neutrophil, lymphocyte, monocytes count, etc. along with various hematological parameters. Patients who had the following characteristics were excluded from the study;those diagnosed with non-adenocarcinoma CRC, patients dying in 1 month, patients who underwent emergency surgery, patients whose demographic and clinicopathological data could not be obtained, patients with inflammatory conditions such as inflammatory bowel disease or rheumatoid arthritis. As a result, we obtained a population of 192 patients. Demographic characteristics are shown in table-1.

### iv- Hematological Examination

The blood samples that were taken before the surgery were

collected in standard tubes containing ethylenediaminetetraacetic acid (EDTA). The numbers of platelets [x103/μL], lymphocytes [x109/L], and other blood parameters were analyzed by using an automated hematology analyzer [Beckman Coulter, CA, the USA], and were then evaluated by an experienced biochemist. neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte ratio (LMR), and platelet-lymphocyte ratio (PLR) were also calculated. In addition, systemic inflammation score (SIS), modified glasgow prognostic score albumin-NLR score, and prognostic nutritional index (PNindex) calculations were made.

**v- Histopathologic Evaluation**

The slides and paraffin blocks were re-evaluated by experienced pathologists by using a conventional light microscope [Nikon Eclipse E600, Nikon AG Instruments, Switzerland] and x10-x20 objective. The grade, presence of lymphovascular invasion[LVI], and presence of perineural invasion [PNI] were confirmed. Tumor sizes and metastatic lymph node ratios were scanned retrospectively.

**vi- Optimal cutoff value**

It is extremely important to determine the optimal cut-off value in studies for diagnostic tests. As a definition, this value has the highest true positive and lowest false negative rates. Also, the Area Under the ROC Curve [AUC] is very helpful in demonstrating the benefit of a test, and a larger area [AUC → 1] indicates the better utility of the test. In our study, the optimal cut-off value was determined with the Receiver Operating Characteristic [ROC] Test.

**vii- Statistical evaluation**

The Shapiro Wilk Test was used to assess whether the variables followeda normal distribution or not. The continuous variables were presented as median[minimum:maximum] values. The categorical variables were reported as n [%]. The Pearson Chi-Square or FisherFreeman-Halton Test was used for comparing categorical variables. The SPSS [IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY: IBM Corp.] was used for statistical analysis, and a p value <0.05 was considered statistically significant.

## RESULTS

Among the 192 patients, 117 [60.94%] were male, and 75 [39.06%] were female. The mean age was found to be 67 (23-89). No significant differenceswere detected in terms of age and gender.However, males were numerically more in all 4 groups. The mean tumor diameter was found to be 5 [2-17]. As the tumor diameter increased the number of metastatic lymph nodes increased[p<0.036]. Approximately 70% of the cancers were localized in the descending colon, sigmoid colon, and rectum. Less metastatic lymph node involvement was observed in the cecum and sigmoid colon cancers. The mean total number of lymph nodes removed was 10[3-46]. It was found that the number of metastatic lymph nodes increased as the number of removed lymph nodes increased [p<0.001] Statistically significant differences were detected between the tumor wall invasion [T stage] and the number of MLN [p:0.029 for T1, p:0.019 for T2, p: 0.012]. The number of MLNs was significantly lower in T1 and T2 tumors than in T4 tumors, and MLN involvement was less common in well-differentiated tumors. MLN involvement was more common in poorly differentiated tumors [p<0.001]. Statistically significant differenceswere detected between LVI, PNI, and MLN counts [P<0.001]. Metastatic lymph node involvement was significantly less in cases without LVI and PNI. No significant differenceswere detected in terms of nutritional scores [mGPS, SIS, alb/NLR, PNindex] and hematological parameters [NLR, LMO, PLO, etc.]. However, statistically significant differenceswere found between the number of monocytes and the number of MLN [p:0.035]. Table -2 summarizes the relations between metastatic lymph node involvement and other variables.

## DISCUSSION

The most important independent prognostic factors that are still valid for colorectal cancer are; tumor stage, histopathological features, surgical treatment, and surgeon factor7. The factors listed here are related directly to the number of metastatic lymph nodes. In the present study, significant relationswere detected between tumor wall in-

*Table-1 Demographic characteristics*

| | n=192 |
|---|---|
| **Metastatic lymph node involvement** | |
| N0 | 101(52.60%) |
| N1 (1-3) | 57(29.69%) |
| N2a (4-6) | 20(10.42%) |
| N2b (≥7) | 14(7.29%) |
| Gender | |
| Female | 75(39.06%) |
| Male | 117(60.94%) |
| **Age** | 67(23:89) |
| **Clinical Stage** | |
| 1 | 37(19.27%) |
| 2 | 64(33.33%) |
| 3A | 14(7.29%) |
| 3B | 36(18.75%) |
| 3C | 22(11.45%) |
| 4 | 19(9.89%) |
| **T Stage** | |
| 1 | 10(5.21%) |
| 2 | 40(20.83%) |
| 3 | 118(61.46%) |
| 4 | 24(12.50%) |
| **Localization** | |
| Caecum | 24(12.50%) |
| Ascending colon | 24(12.50%) |
| Hepatic flexure | 9(4.69%) |
| Descending colon | 8(4.17%) |
| Rectosigmoid | 29(15.10%) |
| Rectum | 40(20.83%) |
| Splenic flexure | 11(5.73%) |
| Sigmoid colon | 41(21.35%) |
| Transverse colon | 6(3.12%) |
| **Grade** | |
| 1 | 48(25%) |
| 2 | 133(69.27%) |
| 3 | 11(5.73%) |
| **LVI** | |
| No | 83(43.23%) |
| Yes | 109(56.77%) |
| **PNI** | |
| NO | 132(68.75%) |
| Yes | 60(31.25%) |
| **MGPS** | |
| 0 | 70(36.46%) |
| 1 | 98(51.04%) |
| 2 | 24(12.50%) |
| **SIS** | |
| 0 | 31(16.15%) |
| 1 | 91(47.40%) |
| 2 | 70(36.46%) |
| **Albumin/NLR** | |
| 0 | 50(26.04%) |
| 1 | 88(45.83%) |
| 2 | 54(28.12%) |
| **Tumor diameter** | 5(2:17) |
| **Total lymph node count** | 10(3:46) |
| **CRP** | 15(0:271) |
| **Albumin** | 4(2:4.90) |
| **MPV** | 8.70(6.88:11) |
| **PDW** | 14.50(0:21) |
| **Monocyte** | 0.60(0.02:7) |
| **Neutrophil** | 5(1.49:23) |
| **Lymph**ocyte | 1.71(0.32:12) |
| **PLT** | 294(140:790) |
| **PLR** | 169(29.30:1100) |
| **LMR** | 3(0.30:44) |
| **NLR** | 2.80(0.40:51) |
| **PN index** | 40.05(20.05:430.40) |

*Data areexpressed as n(%)andmedian(minimum:maximum).*

vasion degree [T stage], LVI, PNI, histopathological grade, tumor diameter, the total number of lymph nodes removed, and the number of metastatic lymph nodes, which is consistent with the literature data. It was also shown that the number of MLNs increased at significant levels when the number of monocytes increased.

Lymph node metastasis is the most important factor that guidesthe treatment of Colorectal Cancers (8,9). Today, the factors considered in patient selection for minimally invasive surgery include the depth of invasion of the colon and rectum wall of the tumor, lymph node status, tumor diameter, lymphovascular invasion, and histopathological grade10. Knowing the factors listed before and after the surgery will affect the radical surgery decision and the adjuvant chemotherapy decision. Lymph node metastasis is around 10% in tumors without submucosa invasion. If the tumor characteristics of these patients are known, 90% of them will be spared from unnecessary radical surgeries and adjuvant chemotherapyn (11,12). There is no consensus on which patients should be given adjuvant chemotherapy in stageII CRC. Adjuvant chemotherapy is recommended for stage II CRCs in cases witha poor histopathological grade, LVI, T4 tumor, perforation or obstruction, and removal of less than 12 lymph nodes (8,9).

*Table-2. Associated factors of the metastatic lymph node involvement in colorectal cancers*

| | Metastasis Lymph Node Involvement | | | | p-value |
|---|---|---|---|---|---|
| | N0 | N1 (1-3) | N2a (4-6) | N2b (≥7) | |
| **Gender** | | | | | |
| Male | 59(50.43%) | 32(27.35%) | 15(12.82%) | 11(9.40%) | 0.230a |
| Female | 42(56.00%) | 25(33.33%) | 5(6.67%) | 3(4%) | |
| **Age** | 67(33:89) | 67(31:89) | 70(23:88) | 66(41:88) | 0.573b |
| **Survival** | | | | | |
| Alive | 82(61.19%) | 35(26.12%) | 10(7.46%) | 7(5.22%) | 0.002a |
| Ex | 19(32.76%) | 22(37.93%) | 10(17.24%) | 7(12.07%) | |
| **Follow-up time** | 24(0:62) | 22(1:63) | 12.50(0:60) | 4.50(0:41) | 0.008b |
| **Clinical stage** | | | | | |
| 1 | 37(100%) | 0 | 0 | 0 | <0.001c |
| 2 | 64(100%) | 0 | 0 | 0 | <0.001a |
| 3A | 0 | 14(100%) | 0 | 0 | <0.001c |
| 3B | 0 | 35(97.2%) | 1(2.8%) | 0 | <0.001c |
| 3C | 0 | 2(9.09%) | 11(50%) | 9(40.09%) | <0.001c |
| 4 | 0 | 6(31.57%) | 8(42.10%) | 5(26.31%) | <0.001c |
| **T Stage** | | | | | |
| 1 | 10(100%) | 0 | 0 | 0 | 0.029c |
| 2 | 29(72.50%) | 9(22.50%) | 2(5.00%) | 0 | 0.019c |
| 3 | 55(46.61%) | 40(33.90%) | 14(11.86%) | 9(7.63%) | 0.208a |
| 4 | 7(29.17%) | 8(33.33%) | 4(16.67%) | 5(20.83%) | 0.012c |
| **Localization** | | | | | |
| Cecum | 10(41.67%) | 6(25%) | 2(8.33%) | 6(25%) | 0.018c |
| Ascendin colon | 12(50%) | 8(33.33%) | 3(12.50%) | 1(4.17%) | 0.893c |
| Hepatic flexure | 4(44.44%) | 2(22.22%) | 2(22.22%) | 1(11.11%) | 0.416c |
| Descending colon | 5(62.50%) | 2(25%) | 1(12.50%) | 0 | >0.99c |
| Rectosigmoid | 14(48.28%) | 10(34.48%) | 4(13.79%) | 1(3.45%) | 0.706c |
| Rectum | 26(65%) | 8(20%) | 2(5%) | 4(10%) | 0.173c |
| Splenic flexure | 7(63.64%) | 2(18.18%) | 2(18.18%) | 0 | 0.523c |
| Sigmoid | 21(51.21%) | 18(43.9%) | 2(4.87%) | 0 | 0.043c |
| Transverse colon | 2(33.33%) | 1(16.67%) | 2(33.33%) | 1(16.67%) | 0.121c |
| **Grade** | | | | | |
| 1 | 35(72.92%) | 10(20.83%) | 3(6.25%) | 0 | <0.001c |
| 2 | 63(47.37%) | 45(33.83%) | 16(12.03%) | 9(6.77%) | |
| 3 | 3(27.27%) | 2(18.18%) | 1(9.09%) | 5(45.45%) | |
| **LVI** | | | | | |
| - | 69(83.13%) | 8(9.64%) | 5(6.02%) | 1(1.20%) | <0.001a |
| + | 32(29.36%) | 49(44.95%) | 15(13.76%) | 13(11.93%) | |
| **PNI** | | | | | |
| - | 82(62.12%) | 36(27.27%) | 11(8.33%) | 3(2.27%) | <0.001a |
| + | 19(31.67%) | 21(35%) | 9(15%) | 11(18.33%) | |
| **MGPS** | | | | | |
| 0 | 33(47.14%) | 25(35.71%) | 7(10%) | 5(7.14%) | 0.263a |
| 1 | 56(57.14%) | 28(28.57%) | 9(9.18%) | 5(5.10%) | |
| 2 | 12(50%) | 4(16.67%) | 4(16.67%) | 4(16.67%) | |
| **SIS** | | | | | |
| 0 | 19(61.29%) | 7(22.58%) | 3(9.68%) | 2(6.45%) | 0.383a |
| 1 | 50(54.95%) | 30(32.97%) | 6(6.59%) | 5(5.49%) | |
| 2 | 32(45.71%) | 20(28.57%) | 11(15.71%) | 7(10%) | |
| **Albumin/NLR** | | | | | |
| 0 | 31(62%) | 11(22%) | 3(6%) | 5(10%) | 0.152a |
| 1 | 44(50%) | 32(36.36%) | 7(7.95%) | 5(5.68%) | |
| 2 | 26(48.15%) | 14(25.93%) | 10(18.52%) | 4(7.41%) | |
| **PLT** | | | | | |
| <260 | 35(50.72%) | 24(34.78%) | 5(7.25%) | 5(7.25%) | 0.561a |
| ≥260 | 66(53.66%) | 33(26.83%) | 15(12.20%) | 9(7.32%) | |
| **PLR** | | | | | |
| <150 | 39(52%) | 22(29.33%) | 7(9.33%) | 7(9.33%) | 0.839a |
| ≥150 | 61(52.59%) | 35(30.17%) | 13(11.21%) | 7(6.03%) | |
| **LMR** | | | | | |
| <3.8 | 60(47.24%) | 41(32.28%) | 15(11.81%) | 11(8.66%) | 0.239a |
| ≥3.8 | 40(62.50%) | 16(25%) | 5(7.81%) | 3(4.69%) | |
| **NLR** | | | | | |
| <2.8 | 54(56.84%) | 25(26.32%) | 8(8.42%) | 8(8.42%) | 0.530a |
| ≥2.8 | 47(48.96%) | 31(32.29%) | 12(12.50%) | 6(6.25%) | |
| **PN index** | | | | | |
| <40 | 44(51.16%) | 23(26.74%) | 12(13.95%) | 7(8.14%) | 0.468a |
| ≥40 | 57(53.77%) | 34(32.08%) | 8(7.55%) | 7(6.60%) | |
| **Tumor diameter** | 4.25(0:17) | 4(2:12) | 4.50(2:10) | 6(3:12) | 0.036b |
| **Total lymph node count** | 8(0:25) | 9(0:46) | 10.50(5:33) | 13.50(10:22) | <0.001b |
| **CRP** | 15(0:271) | 14.40(0:88) | 21.50(1.83:229) | 19.70(1.20:125) | 0.861b |
| **ALBUMIN** | 4(2.40:4.90) | 4.10(2:4.80) | 3.59(2.25:4.60) | 3.98(2.50:4.40) | 0.350b |
| **MPV** | 8.70(6.90:11) | 8.80(6.88:11) | 8.60(6.88:10) | 8.70(7.30:11) | 0.715b |
| **PDW** | 14.50(0:21) | 14.80(0:20.50) | 14(0:18) | 14.25(0:21) | 0.755b |
| **Monocyte** | 0.59(0.03:4) | 0.59(0.02:1.05) | 0.66(0.23:2.20) | 0.70(0.49:7) | 0.035b |
| **Neutrophil** | 4.70(1.49:23) | 4.56(2:11.30) | 5.78(1.86:16) | 5(2:18) | 0.287b |
| **Lymphocyte** | 1.80(0.32:4) | 1.70(0.44:10) | 1.71(0.44:12) | 1.72(0.76:3) | 0.810b |

*Data areexpressed as n(%)andmedian(minimum:maximum).* *a:PearsonChi-squared test, b: Kruskal-Wallis test, c:Fisher-Freeman Halton test*

No doubt, one of the factors that affect the number of metastatic lymph nodes is the width of the dissection. Two previous studies showed that the total number of lymph nodes removed in T2N0 and T3N0 tumors is associated with the prognosis (13,14). Prandi et al. reported in their study that stage II patients who had inadequate lymph node dissection should not be considered Stage II, and should be administered adjuvant chemotherapy(15). In the present study, it was found that the number of MLN increased as the total number of lymph nodes removed increased.

The depth of the invasion of the tumor in the colon wall [T stage] is one of the important factors that affect the number of MLN. The tumor begins to become lymphatic when the submucosa layer is involved. Although it is 5-20% in T1/T2, more than 50% lymph node involvement is detected in T3/T4 (16). In the present study, statistically significant differenceswere detected between the groups in terms of the T stage.

The effect of tumor location on lymph node involvement and prognosis is controversial. Wolmark et al. showed that survival in descending colon tumors is better than in other colon tumors(17). We associate this with the early detection of cancer because of the narrow lumen diameter of the colon at this level. With the large diameter of the right colon lumen, tumors are detected at later stages in this localization. In the present study, lymph node involvement was less common in sigmoid colon tumors, but less lymph node involvement was observed in cecum tumors, contrary to the literature data. No significant differenceswere detected in other localizations.

The effect of the tumor diameter is controversial on lymph node involvement. Tumor diameter is also a factor increasing the tumor wall invasion. There are contradictory data in the literature(18,19). Poorly differentiated aggressive tumors can metastasize to lymph nodes even in small diameters. In the present study, significant correlationswere detected between tumor diameter and MLN number.

Lymphovascular invasion and histopathological grade are among the most important factors that affect lymph node involvement in many other cancers as well as colorectal cancer(11,20-23). In their study in 1989, Minsky et al. defined LVI as an independent prognostic factor(24). Saclarides et al. reported that poor histopathological grade is an independent factor affecting the number of MLNs (25). In this study, it was found that the number of MLNs was lower at significant levels in patients without LVI and the number of MLN was increased in patients with LVI. It was also found that the number of MLNs in well-differentiated tumors was significantly lower than in poorly differentiated tumors.

Many studies in the literature show that PNI is a poor prognostic factor and is associated with lymph node involvement (26,27). In another study, PNI was defined as the invasion of nerves around the tumor and was defined as a poor prognostic factor in many cancer types such as colon and pancreatic cancer(28). In the present study, it was found that there was significantly less lymph node involvement in patients without perineural invasion. It was also found that lymph node involvement increased in patients with PNI.

It was shown in various studies on monocyte count that monocytes develop from myeloid cells together with neutrophils, and high monocyte counts in blood or tumor tissue are associated with poor prognosis(29). In another study in which advanced-stage oral cavity patients were analyzed, it was shown that the number of monocytes increased as the tumor volume increased (30). Monocytes cause a medium with a protumoral effect and allow the tumor to progress. It was observed in the present study that the number of metastatic lymph nodes increased as the number of monocytes increased.

This study had some limitations. Being retrospective may have caused it to be viewed with prejudice. If more homogeneous patient groups such as T1/T2 and T3/T4 or stage I/II had been studied, more satisfactory data would have been obtained. Also, the evaluation of tumor localization separately would provide more positive results. This study can be evaluated as a step for future studies, and a new study can be conducted in a more homogeneous pa-

tient group.

## CONCLUSION

Our study showed that the number of monocytes is associated with metastatic lymph node involvement, and the number of metastatic lymph nodes increases when the number of monocytes increases as well as the factors associated with known lymph node involvement. Further clarification of this will help in selecting patients who will be candidates for minimally invasive surgery and chemotherapy in the stage II CRC patient group.

***Ethical Declerations***

The approval for this study was obtained from Tekirdağ Namık Kemal University Health Research Ethics Committee (Protocol no: 2021.124.04.19).

***InformedConsent:***

Because the study was designed retrospectively, no written in formed consent form was obtained from patients.

***Conflict of Interest Statement:***

The authors have no conflicts of interest to declare.

***Financial Disclosure:***

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***Author Contributions:***

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Abbreviations

| | |
|---|---|
| PLR | : Platelet-Lymphocyte ratio, |
| NLR | : Neutrophil-Lymphocyte Ratio, |
| PDW | : Platelet distribution width, |
| PNI | : Perineural Invasion, |
| LVI | : Lymphovascular Invasion |
| H&E | : Hematoxylin and Eosin, |
| IHC | : Immunohistochemistry, |
| CRC | : Colorectal Cancer, |
| LMR | : Lymphocyte-monocyte ratio, |
| MGPS | : Modified Glasgow Prognostic Score, |
| SIS | : Systemic Inflammation Score, |
| PN index: | : Prognostic Nutritional Index |

## *References*

*1. Corman ML. Carcinoma of the Colon. In: Corman ML (Ed.) Colon & Rectal Surgery. 5th Ed. 767-903, Lippincot Williams & Wilkins, Philadelphia, 2005*

*2. U.S. Cancer Statistics Working Group. United States cancer statistics: 2002 Incidence and mortality web-based report version. Centers for Disease Control and Prevention, and National Cancer Institute, 2005. Available at http://www. cdc.gov/cancer/npcr/uscs, http://seer.cancer.gov/statistics, accessed January 18, 2006*

*3. Fry RD, Mahmoud N, Maron DJ, Ross HM. Colon and Rectum. In: Townsend CM, Beauchamp RD, Evers BM, Mattox KL (Eds.) Sabiston Textbook of Surgery. 18th Ed. 1348-1432, Saunders Elsevier, Philadelphia, 2008*

*4. TÜİK.Ölüm nedeni istatistikleri, 2017. tuikweb.tuik.gov.tr/PreHaberBultenleri.do.id=27592*

*5. Hari DM, Leung AM, Lee JH, et al. AJCC Cancer Staging Manual 7th edition criteria for colon cancer: do the complex modifications improve prognostic assessment? J Am Coll Surg 2013;217:181–90.*

*6. Benson AB, Schrag D, Somerfield MR, et al. American Society of Clinical Oncology recommendations on adjuvant chemotherapy for stage II colon cancer. J Clin Oncol 2004; 22: 3408-19.*

*7. Hermanek P. Prognostic factor research in oncology. J Clin Epidemiol 1999; 52:371-374*

*8. Sarli L, Bader G, Lusco D, et al. Number of lymph nodes examined and prognosis of TNM stage II colorectal cancer. Eur J Cancer 2005;41:272-279*

*9. Johnson PM, Poster GA, Ricciordi R and Baxter NN. Increasing negative lymph node count is independently associated with improved long term survival in stage IIIB and IIIC colon cancer. J Clin Oncol 2006;24:3570-3575*

*10. Wolff BG, Fleshman JW, Beck DE, Pemberton JH, Wexner SD. The ASCRS Textbook of Colon and Rectal Surgery. Bleday R, Garcia-Aguilar J, Surgical Treatment of Rectal Cancer. Springer, New York, 2007; 413-436*

*11. Haggitt RC, Glotzbach RE, Soffer EE, Wruble LD. Prognostic factors in colorectal carcinoma arising in adenomas: implications for lesions removed by endoscopic polypectomy. Gastroenterology 1985;89: 328-36.*

*12. Haggitt RC. Management of the patients with Carcinomas in an adenoma. Prog Clin Biol Res 1988;279: 89-99.*

*13.Wang HS, Liang WY, Lin TC, et al. Curative resection of T1 colorectal carcinoma: risk of lymph node metastasis and long-term prognosis. Dis Colon Rectum 2005;48: 1182–1192.*

*14. Swanson RS, Compton CC, Stewart AK, Bland KI. The prognosis of of T3N0 colon cancer is dependent on the number of lymph nodes examined. Ann Surg Oncol 2003;10(1):65-71.*

*15. Prandi M, Lionetto R, Bini A, Francioni G, Accarpio G, Anfossi A, et al. Prognostic evalution of stage B colon cancer patients is improved by an adequate lymphadenectomy: results of secondary analysis of a large scale adjuvant trial. Ann Surg 2002;235(/4):458-63*

*16. Hermanek P, Gospodarowicz MK, Henson DE, et al. International Union Against Cancer (IUCC): Prognostic factors in cancer. Berlin. Springer New York, 1995.*

*17. Wolmark N, Wieand HS, Rockette HE, et al. The prognostic significance of tumor location and bowel obstruction in Dukes B and C colorectal cancer. Findings from the NSABP clinical trials. Ann Surg 1983;198:743-752.*

*18. Xu FY, Di MJ, Dong JK, et al. Influence of clinical and pathomorphological parameters on prognosis in colon carcinoma and rectal carcinoma. Zhejiang Da Xue Xue Bao Yi Xue Ban 2006;35: 303–310*

*19. Park YJ, Park KJ, Park JG, et al. Prognostic factors in 2230 Korean colorectal cancer patients: analysis of consecutively operated cases. World J Surg 1999;23: 721-726.*

*20. Minsky BD, Miles C, Rich TA, et al. Lymphatic vessel invasion as an independent prognostic factors for survival in colorectal cancer. Int Radiat Oncol Biol Phys 1989;17: 311-18.*

*21. Weiser MR, Landmann RG, Kattan MW, et al. Individualized prediction of colon cancer recurrence using nomogram. J Clin Oncol 2008;26:380-85.*

*22. Sökmen S. Kolorektal Kanserde Prognoz, Kolorektal Özel Sayısı. Türkiye Klinikleri Journal of Surgery 2004;9: 57-65.*

*23. Benek S, Tatar C, Kocakusak A, Ozer B, Kizilkaya MC, Aydin H. The effect of demographic, biochemical and patholojical parameters on survival in colorectal cancer. J Turgut Ozal Med Cent 2016;23(4):414-9.*

*24. Minsky BD, Mies C, Rich TA, Recht A. Lymphatic vessel invasion is an independent prognostic factor for survival in colorectal cancer. International Journal of Radiation Oncology* Biology* Physics. 1989; 17(2): 311-8*

*25. Saclarides TJ, Bhattacharyya AK, Britton-Kuzel C, Szeluga D, Economou SG. Predicting lymph node metastases in rectal cancer. Dis Colon Rectum 1994; 37: 2-57.*

*26. Shirouzu K, Isomoto H, Kakegawa T. Prognostic evaluation of perineurotic invasion in rectal cancer. AM J Surg. 1993;165:233-37*

*27. Fujita S, Shimoda T, Yoshimura K, et al. Prospective evaluation of prognostic factors in patients with colorectal cancer undergoing curative resection. J Surg Oncol 2003; 84: 127-31*

*28. Batsakis J. Nerves and neurotropic carcinomas. The Annals of otology, rhinology, and laryngology. 1985; 94(4 Pt 1):426.*

*29. Luo XL, He W, Huang H, et al. Design of a prognostic score model for nasopharyngeal carcinoma. Head Neck. In press. Head & Neck 2015; 37: 624-629*

*30. Tsai YD, Wang CP, Chen CY, et al. Pretreatment circulating monocyte count associated with poor prognosis in patients with oral cavity cancer. Head Neck 2014; 36: 947– 953.*