

# Predictive Value of Neutrophil/Lymphocyte Ratios in the Diagnosis of Acute Appendicitis

# Akut Apandisit Tanısında Nötrofil/Lenfosit Oranlarının Prediktif Değeri

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#### ABSTRACT

**Objective:** The debate on the value of laboratory tests in the diagnosis of acute appendicitis (AA) continues. In this study, we aimed to evaluate the blood count parameters and the diagnostic value of neutrophil/lymphocyte ratio in the diagnosis of acute appendicitis. **Method:** 851 patients who underwent appendectomy under emergency conditions were included in the study. Patients were divided into 2 groups; Group 1 was negative appendectomy and Group 2 was acute appendicitis. In addition, they were divided into subgroups as 18-39 years, and 60 years and older. Neutrophil, platelet, lymphocyte count and Neutrophil/lymphocyte ratio were compared in groups and subgroups.

**Results:** There were 146 patients (17.1%) in Group 1 (negative appendectomy group) and 705 patients (82.9%) in Group 2 (acute appendicitis group). Male sex was dominant in Group 2 (p=0.049). Neutrophil count and neutrophil / lymphocyte ratio (NLR) were higher in Group 2 (p<0.001, p<0.001, p<0.001, respectively), whereas in Group 1, lymphocyte count and platelet count were higher (p=0.008, p=0.002, respectively). The cutoff value for NLR was found to be 5.29 in the ROC curve analysis. In this value, NLR sensitivity was found as 57.3%, specificity as 69.9%, positive predictive value as 57,1%, negative predictive value as 69,2%. Multivariate analysis showed that the risk of acute appendicitis was 6.71 times higher in patients with NLR 15.29 (OR: 6.71+0.28; 95% CI: 6,150-7,276; p=0.024). In subgroups, the cut-off point for NLR was 5.10 for 18-39 years; 6.63 for 40-59 years; and 5.80 for 60 years and older. The highest sensitivity for these cut-off points was in the age group of 60 and over with 69%, while the highest specificity was in the 40-59 years age group with 58.2%.

**Conclusion:** Although the sensitivity and specificity of neutrophil /lymphocyte ratio (NLR) varies according to age groups, it is a useful and helpful parameter for physical examination and other diagnostic methods in the diagnosis of acute appendicitis.

Keywords: neutrophil-to-lymphocyte ratio, acute appendicitis, diagnosis

#### ÖZ

Amaç: Bu çalışmada akut apandisit tanısı koymada kan sayımı parametreleri ve nötrofil/lenfosit oranının tanısal değerini değerlendirmeyi amaçladık.

**Yöntem:** Acil şartlarda appendektomi yapılan 851 hasta çalışmaya dahil edildi. Postoperatif patoloji bulhusuna göre hastalar Grup 1 negatif appendektomi; Grup 2 akut apandisit olmak üzere iki gruba ayrıldı. Ayrıca 18-39, 40-59, 60 yaş ve üstü olmak üzere subgruplara ayrıldı. Nötrofil, platelet, lenfosit sayısı ve Nötrofil/lenfosit oranı gruplarda ve subgruplarda karşılaştırıldı. p<0,05 değeri istatistiksel olarak anlamlı kabul edildi.

**Bulgular:** Grup 1 negatif appendektomi grubunda de 146 hasta %17,1 Grup 2 akut apandisit grubunda 705 hasta %82,9 yer aliyordu. Grup 2 de erkek cinsiyet baskındı p=0,049. Grup 2'de nötrofil sayısı p<0,001 ve nötrofil/ lenfosit oranı (NLO) p<0,001 daha yüksek iken Grup 1'de lenfosit sayısı p=0,008 ve platelet sayısı p=0,002 daha yükkek bulundu. NLOiçin (ROC) eğrisi analizinde kesme noktası 5,29 bulundu. Bu değerde NLO sensitivesi %57.3, spesifitesi %69,9 pozitif prediktif değerini %57,1 negatif prediktif değeri %69,2 bulundu. Multivartant analizde NLO ≥5,29 olan olgularda akut apandisit riskinin 6,71 kat daha yüksek olduğu saptandı (OR: 6,71+0,28; 95% CI: 6, 150-7, 276; p=0,024). Sub gruplarda NLO için kesme noktası 18-39 için 5, 10; 40-59 için 6,63 ve 60 yaş ve üzeri için 5,80 bulundu. Bu kesme noktaları için en yüksek sensivite %58,2 ile 40-59 yaş grubunda bulundu.

**Sonuç:** Nötrofil/lenfosit oranının (NLO) sensivitesi ve spesivitesi yaş gruplarına bağlı olarak değişmekle birlikte; akut apandisit tanısı koymada fizik muayene ve diğer tanısal yöntemlere yardımcı ve kullanışlı bir parametredir.

Anahtar kelimeler: nötrofil/Lenfosit oranı, akut apandisit, teşhis

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# INTRODUCTION

The most common cause of acute abdomen requiring surgical intervention is acute appendicitis (AA) globally <sup>(1)</sup>. Approximately 8% of the general population in Western countries undergo appendectomy during their lifetime <sup>(2)</sup>. The overall incidence of perforated appendicitis in cases with acute appendicitis is 4-39%, and the rate of negative appendectomy in patients operated for acute appendicitis is reported to be 9-15% in the literature <sup>(3-6)</sup>.

The diagnosis of acute appendicitis is still difficult when it's only based on clinical and laboratory data. Pathologies of gastrointestinal, urological or gynecological origin mimicking acute appendicitis make diagnosis even more difficult in adult patients. There is no laboratory marker which can distinguish AA by itself, from various other etiologies of abdominal pain <sup>(7)</sup>.

Delay in diagnosis leads to perforation and thus increased morbidity rates, while negative appendectomy rates increase with premature decisions to perform surgery <sup>(8)</sup>. To increase early detection of acute appendicitis and reduce misdiagnosis rates, researchers have used many parameters. Erythrocyte sedimentation rate (ESR), white blood cell (WBC) count, C-reactive protein (CRP) and bilirubin levels, immature granulocyte ratio and neutrophil / lymphocyte ratio (NLR) are some of them <sup>(2,9,10)</sup>.

The physiological response of leukocytes to inflammation increases neutrophil and decreases lymphocyte counts Therefore, the ratios of these leukocyte subsets (neutrophil / lymphocyte ratio) can be used as an important marker of inflammation <sup>(7,11)</sup>.

Goodman et al. demonstrated neutrophil-lymphocyte ratio (NLR) as a diagnostic tool for the first time, and when this ratio was greater than 3.5, they found that it was significant in diagnosing acute appendicitis <sup>(12)</sup>. In the following years, many authors have reported that the neutrophil / lymphocyte ratio (NLR) is a marker of inflammation and found it to have a preoperative diagnostic parameter in AA <sup>(13-15)</sup>.

Kahramanca et al. associated a 4.68 NLR value with acute appendicitis (p<0.001). The sensitivity, specifi-

city, negative (NPV), and positive predictive values (PPV) of this cut-off value were 65.3%-54.7%, 23.0%, and 88.4% respectively <sup>(13)</sup>.

With this study, we aimed to determine the diagnostic value of NLR in the diagnosis of acute appendicitis.

# **MATERIAL and METHOD**

The study included 851 patients who were surgically treated for acute appendicitis between January 2013 and January 2019 at Erciyes University Faculty of Medicine General Surgery Clinic. 12.06.2019 dated and numbered Approval was received from the local Ethics Committee. (date: 06. 12. 2019 decision no. 2019/431) Patient files and records of the hospital information system were reviewed and a database was created. Using this database, cases were analyzed retrospectively. The diagnosis of acute appendicitis was made based on physical examination, medical history, and supporting laboratory values and radiological findings. Patients who underwent appendectomy with the diagnosis of acute appendicitis and their pathology reports were included in the study. Patients under 18 years of age, pregnants, patients with a chronic inflammatory disease (tuberculosis, sarcoidosis), an autoimmune disease, hematologic disease, patients using steroids, pathological tumors and those whose records couldn't be reached were excluded from the study.

Based on histopathological evaluation, the patients were divided into 2 groups as Group 1 (negative appendectomy patients), and Group 2 (acute appendicitis patients). The basic demographic data (age, sex) and preoperative laboratory findings (lymphocyte count/mm<sup>3</sup>, neutrophil count/mm<sup>3</sup>, platelet count/mm<sup>3</sup>, and neutrophil/lymphocyte ratio (NLR)) were compared between Groups 1 and 2. Additionally, Groups 1 and 2 were divided into 3 subgroups by age; as subgroups of patients aged 18-39, 40-59, and  $\geq$  60 years. The same parameters were compared between the age subgroups.

The total blood count was measured using an automated hematology analyzer (Roche Hitachi Cobas<sup>®</sup> 8000 Roche Diagnostics, Indianapolis, IN, USA). The NLR was calculated for each patient by dividing neutrophil counts by lymphocyte counts

#### **Statistical Analysis**

The data were analyzed using the IBM SPSS Statistics for Windows, version 24 package program (IBM Corp., Armonk, N.Y., USA). Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) as well as the Student's t test were used to compare quantitative data, and the Mann Whitney U test was used for the evaluation of the non-normally distributed neutrophil / lymphocyte ratios. For the comparison of gualitative data, Pearson's chi-square test and Fisher's exact test were used. Multivariate logistic regression tanalysis was also employed. The diagnostic accuracy was evaluated and examined using receiver operating characteristic (ROC) curve analysis. The appropriate cut-off values were identified, and the specificity, sensitivity, positive, and negative predictive values, positive, and negative likelihood ratios were calculated for the parameters with an area under the curve (AUC) value of above 0.600. p<0.05 value was considered statistically significant.

## RESULTS

A total of 851 patients were included in the study. The negative appendectomy group (Group 1) consisted of 146 and the acute appendicitis group (Group 2) consisted of 705 patients. The mean age of the patients was 33.6±13.7 years in Group 1; and 35.4±15.1 in Group 2 (p=0.184). Sex distribution was equal in Group 1, while male patients constituted 57.9% of the patient population in Group 2. In univariate analyses, neutrophil, lymphocyte, platelet counts and NLR values were found to be significantly different between the two groups. These parameters were determined to be independent variables in the diagnosis of acute appendicitis in multivariate logistic regression analysis. The comparison between Groups 1 and 2 is detailed in Table 1. In the ROC curve analyses of these independent variables, AUC was above 0.600 for the neutrophil count and NLR (Figure 1). The proposed cut-off values and the performance characteristics of these variables are detailed in Table 2. When the patients were subgrouped by

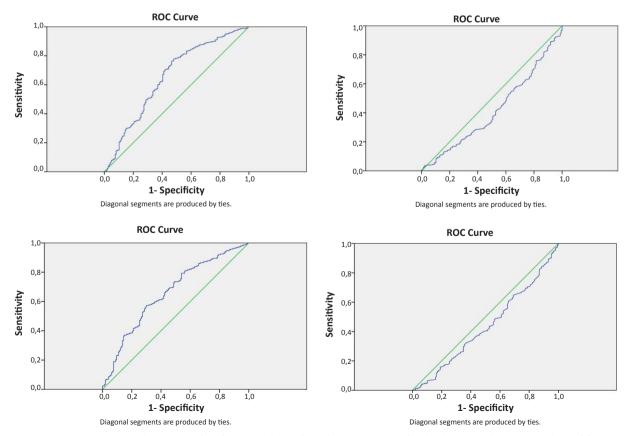


Figure 1. Receiver operating characteristic (ROC) curve analyses of significant parameters for the diagnosis of acute appendicitis: (a) Neutrophil count (b) Lymphocyte count (c) Neutrophil/lymphocyte ratio (NLR), (d) Platelet count.

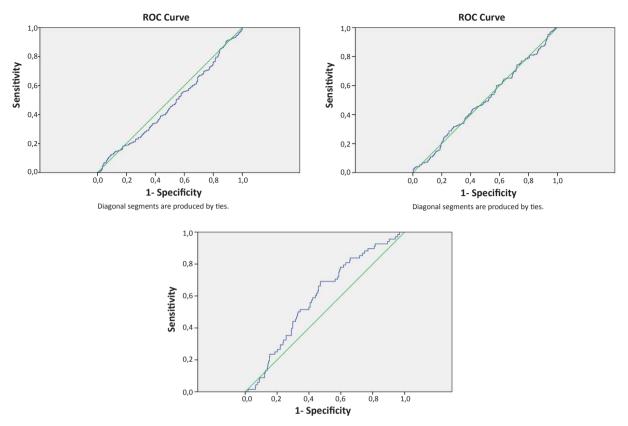


Figure 2. Receiver operating characteristic (ROC) curve analyses of NLR for the diagnosis of acute appendicitis in the age subgroups.

|                       | Univariate analysis      |                          |       | Multi       | Roc curve analysis  |       |       |                    |       |
|-----------------------|--------------------------|--------------------------|-------|-------------|---------------------|-------|-------|--------------------|-------|
| Parameters            | Negative<br>appendectomy | Acute<br>appendicitis    | р     | OR          | 95% Cl<br>(min-max) | р     | AUC   | 95%Cl<br>(min-max) | р     |
| Patient number        | 146                      | 705                      |       |             |                     |       |       |                    |       |
| Age                   | 33,6+13,7<br>(18-85)     | 35,4+15,1<br>(18-87)     | 0,184 |             |                     |       |       |                    |       |
| Sex<br>Male<br>Female | 73 (50,0)<br>73 (50,0)   | 408 (57,9)<br>297 (42,1) | 0,049 |             |                     |       |       |                    |       |
| Neutrophil (x10³/mm³) | 8,2+4,5<br>(1,31-29,16)  | 10,1+3,9<br>(1,75-23,83) | 0,000 | 9,21+0,18   | 8,850-9,570         | 0,033 | 0,654 | 0,602-0,706        | 0,000 |
| Lymphocyte (x10³/mm³) | 1,95+0,8<br>(0,51-4,81)  | 1,74+0,8<br>(0,26-7,29)  | 0,008 | 1,84+0,04   | 1,771-1,927         | 0,008 | 0,419 | 0,36-0,469         | 0,002 |
| NLR                   | 5,39+4,7<br>(0,52-26,08) | 8,03+6,5<br>(0,72-48,46) | 0,000 | 6,71+0,28   | 6,150-7,276         | 0,024 | 0,660 | 0,611-0,709        | 0,000 |
| PLT (x10³/mm³)        | 267,2+94,7<br>(92-810)   | 245,5+73,4<br>(64-758)   | 0,002 | 256,38+3,52 | 249,46-263,29       | 0,011 | 0,436 | 0,386-0,487        | 0,016 |

### Table 1. Comparison of the two groups.

Neutrophil-to lymphocyte ratio (NLR), PLT: Platelet count, AUC: Area under the curve, OR: Odds ratio

|   | Cut-off value | Sensitivity (%) | Specificity (%) | PPV  | NPV  | OR   | pLLR | nLRR | AUC   |
|---|---------------|-----------------|-----------------|------|------|------|------|------|-------|
| Neutrophil (x10 <sup>3</sup> /mm <sup>3</sup> ) | 8,04          | 70,1            | 58,2            | 69,1 | 58,1 | 6,14 | 1,24 | 0,38 | 0,654 |
| Lymphocyte (x10 <sup>3</sup> /mm <sup>3</sup> ) | 1,57          | 52,3            | 38,4            | 51,2 | 38,3 | 1,25 | 0,93 | 1,37 | 0,419 |
| NLR   | 5,29          | 57,3            | 69,9            | 57,1 | 69,2 | 4,55 | 1,20 | 0,39 | 0,660 |
| PLT (x10³/mm³)                                  | 238,5         | 48,2            | 43,8            | 47,3 | 55,4 | 1,21 | 0,94 | 1,29 | 0,436 |

#### Table 2. Proposed cut-off values for significant parameters in the diagnosis of acute appendicitis.

Neutrophil-to-lymphocyte ratio (NLR), PLT: Platelet count, AUC: Area under the curve, PPV: Positive predictive value; NPV: Negative predictive value; OR: Odds ratio; pLLR: Positive likelihood ratio; nLLR: Negative likelihood ratio

### Table 3. Comparison of the subgroups.

|                          |                          | Univariate a            | nalysis                 |       | Mul       | tivariate analys    | is    | Roc curve analysis |   |       |  |
|--------------------------|--------------------------|-------------------------|-------------------------|-------|-----------|---------------------|-------|--------------------|---|-------|--|
| Parameters               | 18-39                    | 40-59                   | 60 and older            | р     | OR        | 95% Cl<br>(min-max) | р     | AUC                | 95%Cl<br>(min-max)                        | р     |  |
| Patient number           | 588                      | 195                     | 68                      |       |           |                     |       |                    |   |       |  |
| Age                      |                          |                         |                         |       |           |                     |       |                    |   |       |  |
| Sex<br>Male<br>Female    | 332 (56,5)<br>256 (43,5) | 113 (57,9)<br>82 (42,1) | 36 (52,9)<br>32 (47,1)  | 0,772 |           |                     |       |                    |   |       |  |
| Neutrophil<br>(x10³/mm³) | 10,1+4,1<br>(1,31-29,16) | 9,2+3,9<br>(1,59-23,07) | 9,2+3,6<br>(2,38-16,29) | 0,024 | 9,5+0,2   | 9,173-9,958         | 0,009 | 0,445              | 0,519-0,600<br>0,400-0,490<br>0,391-0,529 |       |  |
| Lymphocyte<br>(x10³/mm³) | 1,85+0,8<br>(0,34-7,29)  | 1,69+0,8<br>(0,26-6,59) | 1,38+0,6<br>(0,35-3,56) | 0,000 | 1,64+0,04 | 1,562-1,729         | 0,023 | 0,464              | 0,540-0,622<br>0,418-0,510<br>0,288-0,415 | 0,12  |  |
| NLR                      | 7,4+6,2<br>(0,52-48,46)  | 7,7+7,1<br>(1,13-47,64) | 8,2+4,7<br>(1,34-26,78) | 0,568 | 7,8+3,1   | 7,203-8,429         | 0,001 | 0,498              | 0,428-0,511<br>0,452-0,544<br>0,530-0,658 | - / - |  |
| PLT (x10³/mm³)           | 248,0+70,8<br>(64-810)   | 254,8+90,6<br>(98-758)  | 243,5+95<br>(75,2-629)  | 0,464 | 248,8+3,8 | 241,33-256,29       | 0,002 | 0,509              | 0,466-0,553<br>0,462-0,556<br>0,371-0,532 | 0,70  |  |

Neutrophil-to-lymphocyte ratio (NLR), PLT: Platelet count,AUC: Area under the curve,OR: Odds ratio

### Table 4. Proposed cut-off values for NLR in diagnosis of acute appendicitis to age groups.

| Age Groups   | Cut-off value | Sensitivity (%) | Specificity (%) | PPV  | NPV  | OR    | pLLR | nLRR | AUC   |
|--------------|---------------|-----------------|-----------------|------|------|-------|------|------|-------|
| 18-39        | 5,10          | 54,8            | 42,2            | 54,1 | 41,1 | 6,44  | 0,95 | 1,10 | 0,469 |
| 40-59        | 6,63          | 44,1            | 58,2            | 44,3 | 57,1 | 5,99  | 0,89 | 0,81 | 0,498 |
| 60 and older | 5,80          | 69,1            | 52,7            | 70,2 | 52,3 | 13,49 | 2,40 | 0,92 | 0,594 |

Neutrophil-to-lymphocyte ratio (NLR), AUC: Area under the curve, PPV: Positive predictive value; NPV: Negative predictive value; OR: Odds ratio; pLLR: Positive likelihood ratio; nLLR: Negative likelihood ratio

age, there were 588 patients aged 18-39, 195 patients aged 40-59, and 68 patients aged 60 years and older. Male sex dominance was present in all age subgroups. In univariate analyzes for age subgroups, lymphocyte and neutrophil counts were significantly different between groups. In multivariate logistic regression analysis, neutrophil, lymphocyte, platelet counts and NLR were independent variables in the diagnosis of acute appendicitis. The comparison between the subgroups by age is given in Table 4. In the ROC curve analyses of these independent variables in age subgroups, an AUC above 0.600 was not determined. The results of ROC curve analysis for NLR in age subgroups iare given in Figure 2. The proposed cut-off values and performance characteristics for NLR in age subgroups are shown in Table 4.

# DISCUSSION

Early diagnosis of acute appendicitis may not always be possible. Making the decision to observe a patient until a clear diagnosis can be made or to operate prematurely to prevent undesirable complications such as perforation and peritonitis represents a very serious dilemma for surgeons <sup>(13,16)</sup>.

In general, finding suitable, easily accessible and cost-effective diagnostic markers for early detection of diseases has always been the focus of interest of researchers. Many markers that can be used for early diagnosis were investigated because of morbidity and mortality caused by delayed diagnosis in patients followed up for acute abdominal pain in the emergency departments <sup>(9,10,13,17)</sup>.

The diagnosis of acute appendicitis, even in this modern era, is still a problem. A combination of physical examination, certain laboratory tests and a number of imaging studies are used for definitive diagnosis. There are several diagnostic tests which are used for appendicitis, including leukocyte count, percentage of neutrophils, C-reactive protein (CRP), procalcitonin and D-Dimer <sup>(18-20)</sup>.

Complete blood count is an easily accessible and rapidly evaluated test in the emergency department. Neutrophil, leukocyte, lymphocyte, and platelet counts, and neutrophil-lymphocyte ratio in complete blood counts have been investigated in various studies as markers of inflammation (7,9,10,13,14).

However, there is no single laboratory test or imaging method with 100% diagnostic sensitivity for acute appendicitis.

The mean age of the patients included in our study did not differ statistically between the groups. In accordance with the studies in the literature, male sex was dominant in the acute appendicitis group and male/female ratio was similar in the negative appendectomy group <sup>(9,13,17)</sup>. The negative appendectomy rate was 19.7% in female patients. We think that this rate is higher than male patients because of the gynecological causes of pelvic pain mimicking acute appendicitis symptoms.

In studies investigating the diagnostic value of NLR, for negative appendectomy was reported to be between 12.9-18.5% <sup>(8,9,13,17,21)</sup>. In our series, this rate was found to be 17.1%.

Complete blood count is an important component of diagnosis in patients with suspected acute appendicitis. Although leukocyte count generally increases in patients with acute appendicitis, it is not a specific marker for acute appendicitis and may increase in many diseases associated with other inflammatory conditions considered during differential diagnosis. In acute appendicitis, neutrophilia and a left shift in hemogram are often associated with lymphopenia (21,22). In a meta-analysis (neutrophil count> 6500 / mm<sup>3</sup>), Anderson reported a sensitivity of 71-89% and specificity of 48-80% <sup>(21)</sup>. In our study, the neutrophil count was found to be higher in the acute appendicitis group (p=0,000). The cut-off value determined according to the ROC curve analysis was found to have 70% specificity and 58% specificity (AUC: 0.654 (95% CI: 0.602-0.706) p=0.000)).

N. Boshnak et al. found low lymphocyte count as a risk factor in both univariate and multivariate analyses. When they determined the lymphocyte count (OR: 0.0125; 95% CI: 0.0015-0.1031; p<.001) cut-off value as  $2.3 \times 10^9$ /L, they found the sensitivity (82.76%), specificity (63.64%), positive (85.7%), negative (58.3%) predictive values as indicated. In the same study, the mean platelet counts in the groups with acute appendicitis, and negative appendec-

tomy were found to be 109 / L 237.45±54.08 and 257.00±48.55, respectively (p=0.02). When the cutoff value for the platelet count was taken as 188x109  $\times$  / L, they found the sensitivity ( 31.03%), specificity (100%), positive (100%), and negative (35.5%) predictive values as indicated (23). In our study, the lymphocyte count was lower in the acute appendicitis group when compared to the negative appendectomy group (p=0.008). Multivariate analysis (OR: 1.84+0; 95% CI: 1.771-1.927; p=.008)x10<sup>3</sup>/mm<sup>3</sup> showed a sensitivity of 52.3%, a specificity of 38%, a positive predictive value of 51,2% and a negative predictive value of 38,3% when the cut-off value was taken as 1,57 x10<sup>3</sup>/mm<sup>3</sup>. Platelet counts were higher in the negative appendectomy group (p=0.002). Multivariate analysis (OR: 256.38+3.52; 95% CI: 249.46-263.29; p=0.011) showed a sensitivity of 48.2%, a specificity of 43.8%, a positive predictive value of 47.3% and a negative predictive value of 55.4% when the cut-off value was taken as  $1.57 \times 10^3$ / mm<sup>3</sup>. Although there are contradictory views regarding platelet counts in acute appendicitis and complicated appendicitis, our series were similar to that of N. Boshnak et al<sup>(24-26)</sup>.

The physiological response of leukocytes to stress is manifested as increased neutrophil, but decreased lymphocyte counts. Therefore, the ratio of these two parameters to each other is used as a marker of inflammation. During the inflammatory response, the ratio of leukocytes in the circulatory system changes. The increase in neutrophils is accompanied by relative lymphopenia. NLR can be claimed as a simple indicator of inflammatory response (27). The evaluation of NLR can give us information regarding two different immune pathways simultaneously and it is also indicative of the body's overall inflammatory state. First, neutrophils responsible for inflammation and second, lymphocytes has a regulatory function <sup>(28)</sup>. Previous studies have shown that NLR may be significant in a variety of clinical situations and is a robust diagnostic marker of acute appendicitis (12,13,27,29)

Goodman et al. first suggested NLR as a potential diagnostic tool and they found it to be significant for diagnosing acute appendicitis when this value was greater than 3.5 <sup>(15)</sup>. Many studies in the literature have reported preoperative NLR to be a useful para-

meter that helps diagnose acute appendicitis and differentiates between uncomplicated and complicated appendicitis <sup>(9,12,13,21)</sup>. In contrast, Aktimur et al. found that NLR did not differ significantly between patients with positive and negative appendectomy <sup>(26)</sup>.

Shimizu et al. recommends 5.0 as an cut-off value for NLR, with 44% sensitivity and 22% specificity for acute appendicitis.(30) Sevinc et al. reported an NLR cut-off value of 3.0 with a sensitivity of 81%, and specificity of 53% for the diagnosis of acute appendicitis and a cut-off value of 5.5 with a sensitivity of 78.4%, and a specificity of 4.1 % for the diagnosis of perforated appendicitis <sup>(9)</sup>. Kahramanca et al. reported in their series of 1067 cases that the preoperatively measured NLR cut-off value was 4.68 and it was statistically related with the detection of acute appendicitis. They found the sensitivity of NLR as 65.3%, specificity as 54.7%, a positive predictive value of 88.4%, and a negative predictive value of 23% (13). In our study, NLR was found to be statistically significant for diagnosing acute appendicitis in the univariate (p=0.000) and multivariate analyses (p=0.024). The sensitivity and specificity of NLR were calculated as 57.3% and 69.9%, respectively, and the positive predictive value was 57.1% while the negative predictive value was 69.2%. In our study, the risk of acute appendicitis was 6.71 times higher in cases with NLRs ≥5.29 (OR: 6.71+0.28; 95% CI: 6.150-7.276;p=0.024).

We explain these sensitivity and specificity values which are rather low, by the inclusion of only patients who were operated on, in this study, as previously mentioned in the literature. We believe that the data on other suspected cases that were not operated on, or medically treated were not known, which could be the source of this finding <sup>(13)</sup>.

It has been reported that as the severity of appendiceal inflammation increases, lymphocyte counts decrease greatly in addition to neutrophilia. Consequently, NLR increases as appendicitis progresses to appendiceal gangrene and subsequent perforation <sup>(21,31)</sup>. Sevinç et al. found the cut-off value as 3 for NLR. The rate of complicated appendicitis was 6.5% in their series <sup>(9)</sup>. In our series, we concluded that the cut-off value was higher than the series cited in the literature, which was related to the fact that the rate of complicated appendicitis in our acute appendicitis patients was higher than the literature. Indeed, in 10% of the patients had complicated appendicitis. Despite conflicting recommendations in the literature regarding cut-off values, we believe that NLR is an important diagnostic parameter.

There are limited number of studies in the literature regarding the diagnostic value of NLR in different age subgroups. Yavuz et al. found in their study that for the ROC curve for NLR; the sensitivity was 92.5% while the specificity was 59.3% when the cut-off value was taken as 3.93; the sensitivity was 87.5% and the specificity was 63% when the cut-off value was taken as 4.51; and the sensitivity was 85% while the specificity was found to be 64.2% when the cutoff value was taken as 4.64. They found that diagnostic values for diagnosing acute appendicitis were increased when the cut-off value decreased (32). Cigsar et al. found the cut-off value of NLR as 4.9 by the evaluation of ROC curve analysis in their series, the sensitivity and specificity were found to be 73% <sup>(33)</sup>. In our study, when the cut-off value was taken as 5.80 in the group of patients who were aged 60 years and older, the sensitivity was found to be 69.1%, specificity was 52.7%, the positive predictive value was 70.2% and the negative predictive value was calculated as 52.3%. The highest sensitivity for these cut-off values was detected in the age subgroup of 60 and over (69%), while the highest specificity was found in the 40-59 years age subgroup (58.2%).

The most important limitation of our study was that it was designed retrospectively. In addition, only appendectomy patients were included in the study; the patients who were suspected of acute appendicitis and followed up with medical treatment were excluded. However, our patient population was wider than the series in the literature. We believe that our study provides comprehensive data on the diagnostic accuracy of simple laboratory parameters in the suspicion of acute appendicitis, and this study contributes to the literature with useful and valuable reference data.

In conclusion, an NLR value of 5.29 seems to be a reliable parameter to help us diagnose acute appendicitis. Although sensitivity and specificity of NLR varies according to age subgroups, we have found the highest sensitivity in patients aged 60 years and older and the highest specificity in patients aged 40-59 years. However estimation of NLR value alone is not sufficient for the diagnosis of acute appendicitis, and normal NLR values alone cannot exclude acute appendicitis. The clinical evaluation of the surgeon should continue to be a priority in diagnosing acute appendicitis. In order to determine the diagnostic accuracy of NLR, further prospective randomized trials are needed.

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