# New inflammatory markers in diagnosing acute appendicitis

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## Abstract

**Aim:** Acute appendicitis (AA) is the most common cause of abdominal pain, acute abdomen and emergency abdominal operation. The diagnosis of AA is usually based on clinical history and physical examination. Assessment of the systemic inflammatory response of the neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR), which can be achieved through a simple blood count such as a complete blood count, is shown as a new biomarker. The aim of our study is to examine whether readily available markers such as NLR, PLR, RDW, and MPV can be used to distinguish AA whether complicated and uncomplicated appendicitis cases.

**Materials and Methods:** We retrospectively reviewed the patients who had been admitted to the Erzurum Regional Education and Research Hospital between January 2016 and June 2016 with abdominal pain complaints and applied appendectomy. Preoperative and postoperative CRP, leukocyte, RDW, neutrophil, platelet values were recorded. The NLO and PLO values were manually calculated from the complete blood count.

**Results:** Preop NLR was found 5.58 ± 4.44 in the appendicitis group and 4.65 ± 4.93 in the complicated appendicitis group. Post op NLO values were 2.87 ± 1.76 and post op NLR in the appendicitis group. Postop NLO and CRP values significantly decreased compared to Preop values. ( p<0.04 and p< 0.00, respectively). In ROC analysis, NLO ≥1.6 had 90% sensitivity and 90% specificity and CRP 1.01 had 86% sensitivity and 80% specificity inpredicting acute appendicitis.

**Conclusion:** Postop NLR and CRP values significantly decreased compared to preop values. As a result, NLR value calculated from a simple hemogram test, which can be obtained in almost every health care facility, which can be obtained more easily than CRP, which has better sensitivity and specificity in the diagnosis of acute appendicitis, can be used to diagnose appendicitis.

**Keywords:** Appendicitis; biomarkers; inflammation

## INTRODUCTION

Acute appendicitis (AA) is the most common cause of abdominal pain, acute abdomen and emergency abdominal operation. The increased permeability of the mucosal barrier due to lumen obstruction causes the inflammatory response. Thus, intestinal luminal neutrophil sequestration occurs and the proinflammatory cytokines (IL-1, IL-6), tumor necrosis factor α (TNFα), interferon gamma (INF- γ) and antiinflammatory cytokines (IL-4, IL-10) are released to create the systemic inflammation response (1,2).

The diagnosis of AA is usually based on clinical history and physical examination (3). In some cases imaging methods are also used. In addition, laboratory parameters such as whole blood count and C-reactive protein (CRP) are also used in AA (4,5). However, it is still very difficult to diagnose cases where classical history and clinical findings are absent. A delayed diagnosis of AA increases perforation and complication rates. Besides all these data, negative laparotomy rate in AA cases is still around 20% (2).

In addition to all these biological markers, recently, new, easily accessible, reproducible biological inflammatory markers have been introduced in AA. Leukocyte count and subtypes are some of the determinants of chronic inflammation. Neutrophils and leukocytes play an important role in inflammatory processes. Assessment of the systemic inflammatory response of the neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR), which can be achieved through a simple blood count such as a complete blood count, is shown as a new biomarker (6,7).

Red cell distribution width (RDW) is the size of red blood cells. In addition to being used in differential diagnosis of the anemia, there are also studies showing that can

be used as a mortality indicator for acute heart failure, pulmonary embolism, acute myocardial infarction (AMI), peripheral arterial disease and acute renal failure in the general population (8-10).

Mean platelet volume (MPV) indicates platelet volume and platelet volume is a potential indication of platelet activity (11). Increased MPV is associated with increased thrombotic activity, such as platelet aggregation, thromboxane synthesis, and release of adhesion molecules. Elevated MPV values have been demonstrated in patients with chronic obstructive pulmonary disease, MI and diabetes. There are also studies showing increased MPV value in relation to inflammation (12).

The aim of our study is to examine whether readily available markers such as NLR, PLR, RDW, and MPV can be used to distinguish AA whether complicated and uncomplicated appendicitis cases.

## MATERIALS and METHODS

We retrospectively reviewed the patients who had been admitted to the Erzurum Regional Education and Research Hospital between January 2016 and June 2016 with abdominal pain complaints and applied appendectomy. Patients older than 18 years were included in the study. Acute cerebrovascular disease, MI, pregnancy, heart failure, COPD, peripheral vascular disease, cancer, severe liver diseases, diabetes and hematologic diseases has been defined as the exclusion criteria. In addition, patients who use anticoagulants, nonsteroidal anti-inflammatory drugs, steroids and other drugs that may affect blood counts and patients without preoperative and postoperative blood values were not included in the

study. Patients were divided into 3 groups as normal appendix (patients who were operated with a pre-diagnosis of acute appendicitis, but a normal appendix was found as a result of pathology), uncomplicated appendicitis and complicated appendicitis (perforation, plastrone, necrotizing appendicitis, peritonitis) according to pathology results. Preoperative and postoperative CRP, leukocyte, RDW, neutrophil, platelet values were recorded. The NLR and PLR values was manually calculated from the complete blood count. A BeckmanCoulter LH 750 (Impedance Method) analyzer was used for the complete blood count.

We performed all statistical analyses using SPSS for Windows, version 17.0. Unless otherwise stated, results were expressed as mean ± SD. We used the Mann–Whitney U test or independent sample t test between two subject groups, and used the Pearson correlation test or Spearman correlation test, as appropriate. Categorical data were analyzed by Chi-square test The receiver operating characteristic (ROC) curve analysis assessed the cut-off of preoperatively NLR, PLR, CRP, RDW, and MPV with the best diagnostic accuracy for detecting scute appendicitis. We considered $p < 0.05$ as statistically significant.

## RESULTS

According to pathology results, 54 acute appendicitis; 30 complicated appendicitis and 30 normal appendicitis were included. 52 patients were identified as control group. The characteristics of the study groups are presented in Table 1. No statistically significant difference was found in terms of hemoglobin, hematocrit, AST and ALT values.

| Table 1. The characteristics of the study groups | | | | |
|---|---|---|---|---|
| | **Normal Appendix** | **Appendicitis** | **Complicated Appendicitis** | **Control** |
| Age | 34.00 ± 13.48 | 28.93 ± 12.84 | 33.53 ± 15.31 | 28.04 ± 11.45 |
| Gender (F/M) | 16/14 | 28/26 | 13/17 | 28/24 |
| Preop Lymphocytes | 2.22 ± 0.85 | 2.22 ± 0.88 | 1.91 ± 0.69 | 2.83 ± 1.77 |
| Postop lymphocytes* | 2.36 ± 0.76 | 2.43 ± 1.01 | 2.05 ± 0.71 | |
| Preop Neutrophils * | 9.44 ± 4.54 | 9.91 ± 5.15 | 9.10 ± 4.38 | 5.03 ± 2.48 |
| Postop Neutrophils | 5.60 ± 3.69 | 6.16 ± 3.38 | 7.14 ± 3.43 | |
| Preop Platelets | 259.05 ± 61.66 | 271.02 ± 63.94 | 261.76 ± 61.63 | 308.20 ± 95.93 |
| Postop Platelets | 324 ± 123.81 | 357.03 ± 426.5 | 285.25 ± 120.74 | |
| Preop RDW | 11.31 ± 0.76 | 11.22 ± 1.44 | 11.40 ± 0.95 | 10.59 ± 1.77 |
| Postop RDW | 12.01± 0.86 | 12.27 ± 1.68 | 12.53 ± 1.82 | |
| Preop MPV | 7.68 ± 1.41 | 7.68 ± 1.53 | 7.42 ± 1.33 | 7.03 ± 0.60 |
| Postop MPV* | 7.13 ±1.31 | 7.31 ± 1.29 | 8.15 ± 2.12 | |
| Preop CRP* | 6.56 ± 8.31* | 4.04 ± 4.52**,□ | 6.75 ± 5.68▲,□,○ | 0.87 ± 0.88*,**,○ |
| Postop CRP | 2.57 ± 2.63 | 1.62 ± 2.8 | 3.28 ± 4.59 | |
| Preop NLR* | 5.01 ± 3.4* | 5.58 ± 4.44** | 5.84 ± 4.55▲ | 2.37 ± 1.37*,**,▲ |
| Postop NLR | 2.83 ± 2.63 | 2.87 ±1.76 | 4.65 ± 4.93 | |
| Preop PLR | 133.58 ± 58* | 139.42 ± 57.97** | 158.43 ± 76.97▲ | 131.6 ± 58.79*,**,▲ |
| Postop PLR | 324 ±123.81 | 357.03 ± 426.5 | 288.25 ± 120.74 | |
| Preop WBC | 3562.96 ± 6637.39*,□ | 12473.5 ± 414.2** | 9266.28 ± 6846.6□ | 8339.3 ± 2495.67*,**,▲ |
| Postop WBC* | 7970 ± 3530 | 8590 ± 3690 | 9200 ± 3160 | |

*Comparison between normal appendix and control ** comparison between appendicitis and control ▲comparison between appendicitis and control Complicated appendicitis versus appendicitis ○ Complicated appendicitis versus normal appendix □ Comparison between normal appendix and complicated appendicitis □□ normal Comparison of appendicitis with appendicitis

At the end of the study, preop and post op values were compared. Preop NLR was found 5.58 ± 4.44 in the appendicitis group and 4.65 ± 4.93 in the complicated appendicitis group. Post op NLR values were 2.87 ± 1.76 in appendicitis group These values were statistically significantly higher in the preop group compared to the normal and control groups. When the relationship between inflammation indicators was examined, preop NLR was significantly associated with appendicitis existance, preop PLR, CRP. (P <0.05). There was a significant correlation between preop PLR and preop NLR, CRP, preop MPV and age (p <0.05), but no significant correlation with appendicitis was found. The findings are shown in Table 2. Postop NLR and CRP values significantly decreased compared to Preop values. ( p<0.04 and p< 0.00, respectively)

When ROC analysis was performed, AUC for preop MPV: 0.665 p = 0.089, AUC for preop RDW 0.524 p= 0.801, AUC for preop NLR 0.936 p= 0.00, AUC for preop PLR 0.672 p= 0.076 and AUC for CRP 0.872 p = 0.00 was found. Sensitivity was 90% and specificity was 90% for NLR 1.6. The results are shown in Figure 1.

NLR and CRP were also sensitive and specific in diagnosing acute appendicitis. AUC value of NLR was 0.936 (p = 0.000) and CRP was 0.872 (p = 0.000). In ROC analysis, NLR ≥1.6 had 90% sensitivity and 90% specificity and CRP 1,01 had 86% sensitivity and 80% specificity inpredicting acute appendicitis. (Figure 2).

**Table 2. Bivariate correlation between preop NLR, preop PLR, preop RDW, preop MPV parameters and other variables in appendicitis group**

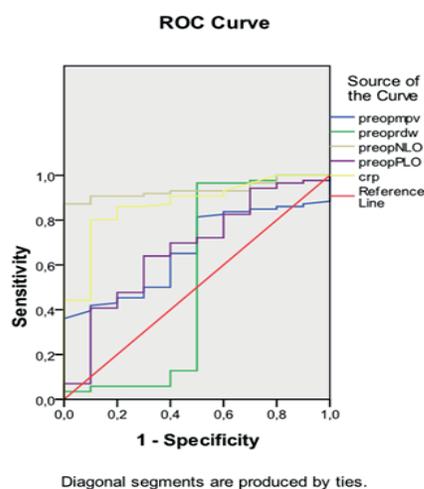| Variables | Preop NLR | | Preop PLR | | Preop RDW | | Preop MPV | |
|---|---|---|---|---|---|---|---|---|
| | r | p | r | p | r | p | r | p |
| Grup Appendicitis | 0.35 | 0.000* | 0.1 | 0.2 | 0.2 | 0.12 | 0.11 | 0.14 |
| Preop NLR | | | 0.57 | 0.000* | 0.05 | 0.48 | 0.12 | 0.12 |
| CRP | 0.45 | 0.000* | 0.33 | 0.001* | 0.15 | 0.12 | 0.15 | 0.11 |
| Preop PLR | 0.557 | 0.000* | | | 0.08 | 0.33 | -0.17 | 0.03* |
| Preop MPV | 0.12 | 0.12 | 0.17 | 0.03* | 0.19 | 0.01* | | |
| Preop RDW | 0.05 | 0.48 | 0.08 | 0.33 | | | 0.19 | 0.01* |
| Age | -0.039 | 0.63 | 0.13 | 0.09* | 0.19 | 0.02* | 0.01 | 0.19 |
| * p <0.05 | | | | | | | | |



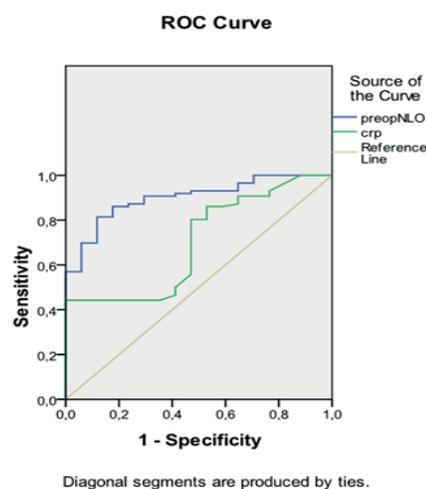**Figure 1.** ROC curve for MPV, RDW, NLR and PLR



**Figure 2.** ROC curve for NLR and CRP

## DISCUSSION

This study is the first study to examine the importance of simple serum markers for NLR, PLR, MPV and RDW in the diagnosis of acute complicated and noncomplicated appendicitis. Previous studies have shown that the number of leukocytes and neutrophils increases in cases of acute appendicitis (6,7). In addition, there are also studies showing that, CRP, a serum protein which increases in cases of inflammation, infection and injury with cytokine-

related inflammatory response, has sensitivities ranging from 76.5% to 95.6% and 26.1% and 77.7% specificity in the diagnosis of acute appendicitis (13).

In our study, preoperative neutrophil and NLR values were higher than the control group. In addition, there was a positive correlation between preop NLR, PLR and CRP values. Preop NLR value was more predictive of appendicitis group than preop CRP.

The association of activated platelets with inflammation is known. MPV is an indication of platelet size and increased MPV values are associated with platelet activation. In our study, preop MPV values were found to be higher than postop values in patients with pathologically diagnosed appendicitis, and MPV values after operation were regressed. In a study conducted by Bozkurt et al., It was observed that MPV value did not differ between appendicitis and control group (13). In our study, it was observed that preop values were higher in appendicitis group and postop MPV values were decreased according to preop values.

As a result, postop NLR and CRP values significantly decreased compared to preop values.

The value of simple laboratory tests in acute appendicitis is increasing. According to the results of ROC analysis in our study, preop NLR and CRP values were found to be important in the diagnosis. Sensitivity was 90%, specificity was 90%, for NLR value of 1.6 , and sensitivity was 86% and specificity was 80% for CRP value of 1.01. According to these findings, the value of NLR, which can be calculated manually in a simple blood count, is greater than CRP for the diagnosis of acute appendicitis.

## CONCLUSION

As a result, we think that the NLR value calculated from a simple hemogram test, which can be obtained in almost every health care facility, which can be obtained more easily than CRP, which has better sensitivity and specificity in the diagnosis of acute appendicitis, can be used to diagnose appendicitis.

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