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The Association of Systemic Inflammatory Indices with Alvarado Score-based Risk Stratification in Acute Appendicitis: A Retrospective Study

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Abstract

Aim: This study aimed to evaluate the association between systemic inflammatory indices, including the systemic immune-inflammation index (SII), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR), and the Alvarado score for risk stratification in patients presenting to the emergency department with a diagnosis of acute appendicitis (AA).

Materials and Methods: This retrospective descriptive study was approved by the Tekirdağ Namık Kemal University Faculty of Medicine Ethic Committee (approval number: 2025.70.04.06, date: 30.07.2025). A total of 69 adult patients who met inclusion criteria and presented with abdominal pain to the emergency department between January 1, 2023, and January 1, 2024 were enrolled. Among the patients, 53.6% were female and 46.4% male, with a mean age of 41.25±17.46 years. No significant age difference was observed between genders (p=0.8). The diagnosis of AA was confirmed by contrast-enhanced abdominal computed tomography in all cases. **Results:** ROC curve analysis was performed to assess the ability of inflammatory indices to discriminate among Alvarado score-defined risk categories. According to these analyses, NLR showed significant discriminatory performance across Alvarado score-defined high-risk categories with p=0.004 and [area under the curve (AUC)=0.81 95% confidence interval (CI): 0.71-0.91], and SII did so with p=0.009 and AUC=0.78 (95% CI: 0.66-0.90), whereas PLR was less predictive (p=0.16, AUC=0.65).

Conclusion: Our findings suggest that SII shows meaningful association with Alvarado score-based risk stratification and should not be interpreted as a standalone diagnostic marker. However, these markers should be used in conjunction with clinical assessment, and larger, multicenter prospective studies are needed to confirm their usefulness.

Keywords: Acute appendicitis, emergency department, neutrophil-to-lymphocyte ratio, systemic immune-inflammation index, platelet-to-lymphocyte ratio

Introduction

The appendix is a finger-shaped sac 5 to 10 cm long and 3 to 6 mm in diameter that extends from the cecum. Acute appendicitis (AA) is inflammation of the appendix, which is located in the abdominal cavity. AA is one of the most common surgical emergencies encountered among patients presenting to the emergency department. If it is not diagnosed promptly, it can lead to serious complications such as perforation, peritonitis, and sepsis. The lifetime risk of developing AA in the general population is reported to be approximately 7-8%, and the symptoms and clinical findings of the disease can vary from patient to patient. While AA usually presents with symptoms such as right lower quadrant pain, loss of appetite, nausea, and vomiting, these symptoms are non-specific,

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and a significant proportion of patients present with atypical features. This complicates diagnosis and can lead to unnecessary imaging tests or overlooking false-negative cases.

While physical examination and clinical evaluation are crucial in the diagnosis of AA, they alone do not provide sufficient diagnostic certainty. Laboratory tests [white blood cell (WBC) count, C-reactive protein (CRP) level, etc.] and imaging methods (ultrasound, computed tomography) are widely used to support the diagnosis. However, when access to imaging is limited or when radiation exposure is undesirable (e.g., in pregnant women), alternative diagnostic approaches are needed. In recent years, the potential role of inflammatory markers in the diagnosis of AA has been increasingly investigated.

Systemic inflammation indices are biochemical parameters that assess the inflammatory process in the body and are increasingly used in the diagnosis of acute and chronic inflammatory diseases. Among these parameters, the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) stand out as promising biomarkers, particularly in the differential diagnosis of surgical and infectious diseases. Many studies have reported significant changes in NLR and PLR during acute inflammation, while SII has been reported to demonstrate stronger associations with inflammatory burden in diagnostic studies.

The Alvarado score, defined by Dr. Alvarado in 1986, is based on clinical and laboratory findings for the diagnosis of AA. Its purpose is to support the diagnosis and reduce unnecessary laparotomies (1). Importantly, the Alvarado score is not a gold standard diagnostic test but a structured risk stratification system intended to guide clinical decision-making. Studies have reported that the SII demonstrates a statistically significant correlation with the Alvarado score and has been reported to show high specificity and sensitivity in previous diagnostic studies (2).

This study was designed to explore the association between systemic inflammatory indices and Alvarado score-based risk stratification in patients with computed tomography-confirmed AA, rather than assess diagnostic accuracy against a non-appendicitis population. The findings are anticipated to expedite risk management in emergency departments, reduce unnecessary imaging studies, and improve patient management.

Materials and Methods

Our retrospective descriptive study received approval from This retrospective descriptive study was approved by the Tekirdağ Namık Kemal University Faculty of Medicine Ethic Committee (approval number: 2025.70.04.06, date: 30.07.2025). Patients presenting to the emergency department of Tekirdağ Namık Kemal University Faculty of Medicine Hospital with abdominal pain between January 1, 2023, and January 1, 2024, and diagnosed with AA on imaging were included in this study.

All study expenses were covered by the study directors; no financial assistance was used. Sixty-nine patients who presented to the emergency department with abdominal pain between the specified dates and who met the inclusion criteria were included. Inclusion criteria for the study were age 18-80, presentation to the emergency department between January 1, 2023, and January 1, 2024, and a diagnosis of AA following examinations in the emergency department. Exclusion criteria for the study were the following: being under 18 or over 80 years of age; lack of access to required study data; personal or family history of FMF; and refusal of treatment, leaving the emergency department, or referral from the emergency department after diagnosis. Patients with documented active systemic infection, inflammatory bowel disease, malignancy, or autoimmune inflammatory conditions were excluded if identifiable on review of medical records.

The electronic files of patients included in the study were reviewed, and their complaints, vital signs, physical examination findings, and laboratory findings at presentation were recorded on a precreated case report form. The neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, systemic inflammation index, and Alvarado score were calculated. Platelet, neutrophil, and lymphocyte counts were recorded as cells/μL; therefore, SII values appear numerically higher than those reported in studies using $\times 10^9$/L units.

Statistical Analysis

All eligible cases within the specified dates were included in the retrospective analysis. Data were analyzed using SPSS version 18. Categorical variables were presented as counts and percentages and compared using chi-square tests. The Kolmogorov-Smirnov test assessed the normality of continuous variables. Normally distributed continuous variables were expressed as mean ± standard deviation and compared using Student's t-test, whereas non-normally distributed variables were presented as median (interquartile range) and compared using the Mann-Whitney U test. Fisher's exact test or chi-square test was applied for group comparisons, depending on the nature of the data. ROC curve analyses were conducted to evaluate the discriminatory ability of NLR, PLR, and SII across Alvarado score-defined risk categories. A p-value <0.05 was considered statistically significant.

Results

A total of 69 patients diagnosed with AA and admitted to the ward were included. Among them, 37 (53.6%) were female and 32

(46.4%) were male. The mean age was 41.25±17.46 years. There was no statistically significant age difference between females (40.78±16.73) and males (41.78±18.52) (p=0.8). The diagnosis of AA was confirmed by contrast-enhanced abdominal CT in all cases. All patients presented with abdominal pain. On abdominal examination, guarding and rebound tenderness were noted as overlapping clinical findings: guarding was present in 24 patients (34.8%), rebound tenderness was present in 23 patients (33.3%), and both signs were present in 12 patients (17.4%). Thirty-four patients (49.3%) had neither of these findings (Table 1).

Vital signs included a mean arterial pressure of 102.39 mmHg, an oxygen saturation of 98%, a temperature of 36.2 °C, and a pulse rate of 80 bpm (Table 2).

Laboratory parameters showed mean CRP 59.5±82.3 mg/L, WBC 13.6±11.5 $\times 10^3$/µL, neutrophils 9.4±3.6 $\times 10^3$/µL, lymphocytes 3.2±10.7 $\times 10^3$/µL, and platelets 278±87 $\times 10^3$/µL. The mean NLR was 5.89±5.71, PLR 162.27±103.24, and SII 11,131±1,543 (Table 3).

According to standard Alvarado score classification, patients were stratified into three risk groups: low risk (≤4), intermediate risk (5-6), and high risk (≥7). The mean Alvarado score was 6.04±1.89.

ROC analysis in the high risk (≥7) group showed NLR with p=0.004 and AUC=0.81 (0.71-0.91), SII with p=0.009 and AUC=0.78 (0.66-0.90), and PLR with p=0.16 and AUC=0.65 (0.49-0.81).

In the intermediate-risk (5-6) group, NLR had p=0.002 and AUC=0.74 (0.62-0.86); SII had p<0.001 and AUC=0.78 (0.67-0.89); and PLR had p=0.07 and AUC=0.63 (0.48-0.78).

In the low risk (≤4) group, NLR showed p=0.013 and AUC=0.32 (0.19-0.45), SII p<0.023 and AUC=0.33 (0.20-0.46), and PLR p=0.35 and AUC=0.43 (0.29-0.57).

For patients with Alvarado scores ≥5, ROC analyses revealed NLR with p=0.004 and AUC=0.74 (0.60-0.88), SII with p<0.001 and AUC=0.80 (0.65-0.94), and PLR with p=0.05 and AUC=0.67 (0.50-0.84).

In the low-risk group (Alvarado score ≤4), all inflammatory indices exhibited limited discriminatory performance (AUC <0.50).

Within the study population, NLR demonstrated its highest discriminatory performance at a cut-off value of 4.34, while PLR and SII showed optimal discrimination at cut-off values of 0.118 and 1.235, respectively. These cut-off points were associated with greater specificity in the higher Alvarado score categories, indicating improved discriminative capacity as clinical risk increased. Logistic regression analysis evaluating the association of Alvarado score, SII, NLR, and PLR with higher-risk categories showed coefficients for NLR=0.1639 (p=0.184), PLR=-0.0088 (p=0.065), and SII=0.0016 (p=0.008). The distribution of Alvarado score categories with NLR, PLR, and SII data is detailed in Figure 1.

Table 1. Demographic data and physical examination findings of the cases

Data	n (%), mean ± SD
Age	41.25±17.46
Gender Female Male	 37 (53.6%) 32 (46.4%)
Guarding Rebound tenderness Both signs Neither findings	24 (34.8%) 23 (33.3%) 12 (17.4%) 34 (49.3%)

Percentages are calculated for overlapping binary clinical findings. Categories are not mutually exclusive; therefore, percentages do not sum to 100%. SD: Standard deviation

Table 2. Vital signs of the cases

Vital signs	n (%), mean ± SD
Mean arterial pressure	102.39±16.32 mmHg
Pulse	80±16/minutes
Saturation	98±2%
Temperature	36.2±0.18°C

SD: Standard deviation

Table 3. Laboratory data of the cases

Data	mean ± SD
CRP	59.5±82.3
WBC	13.6±11.5
Neutrophil	9.4±3.6
Lymphocyte	3.2±10.7
Platelet	278±87
Neutrophil-to-lymphocyte ratio	5.89±5.71
Platelet-to-lymphocyte ratio	162.27±103.24
Systemic inflammation index	11.13 ±1.54

SD: Standard deviation CRP: C-reactive protein, WBC: White blood cell

Discussion

This study demonstrates that systemic inflammatory indices are associated with Alvarado score-based risk stratification and do not provide independent diagnostic accuracy for AA. By analyzing the contribution of SII to the diagnostic process, we aimed to obtain data to better understand the role of laboratory markers in diagnosing AA. We anticipate that our study findings may expedite the diagnostic process, reduce unnecessary imaging studies, and improve patient management. We believe, based on the literature, that stating that gender is not significant

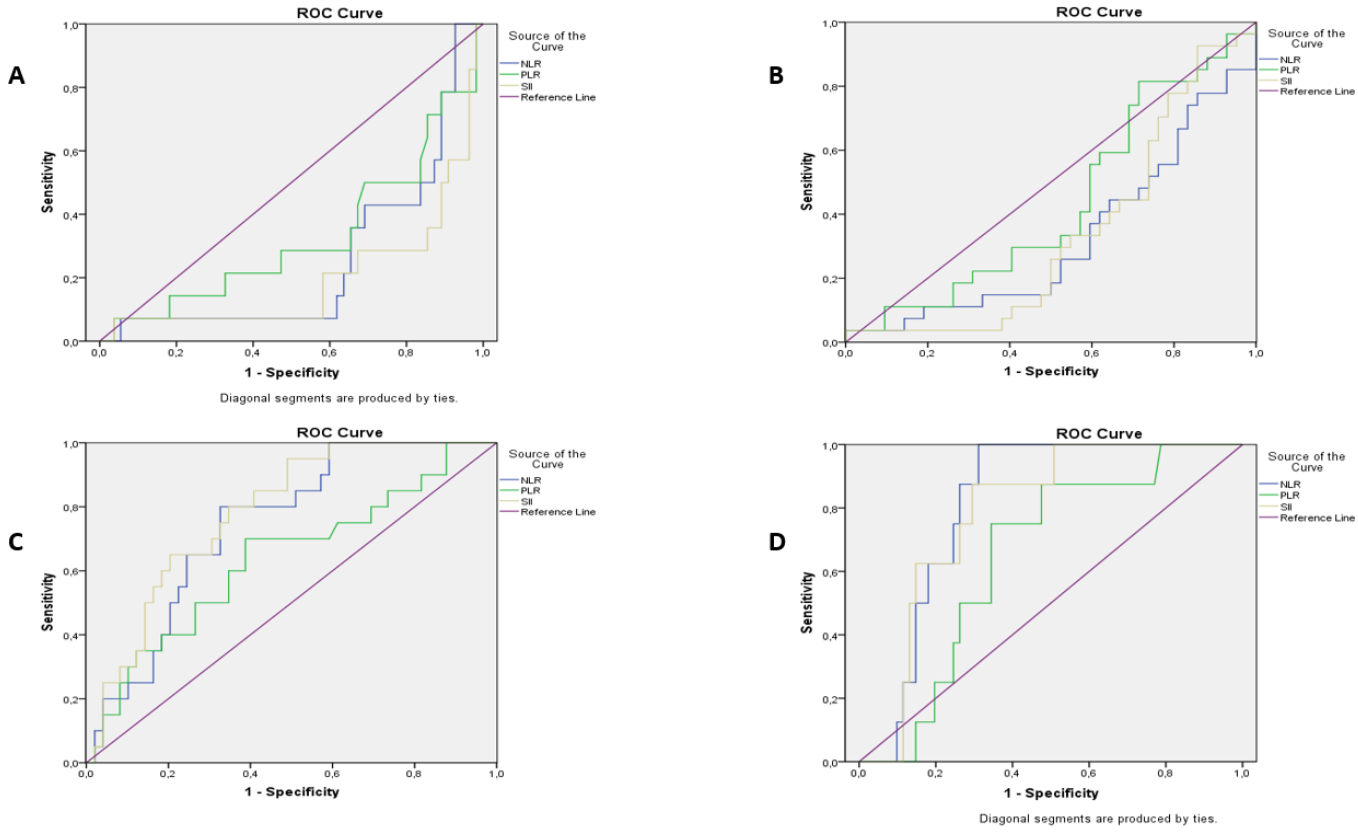

Figure 1. ROC analysis of groups with NLR, PLR and SII according to Alvarado score. A) The Alvarado score group is 4 or below (no risk), B) The Alvarado score group is 5-6 (low risk), C) The Alvarado score group is 7-8 (moderate risk), D) The Alvarado score group is 9-10 (high risk)
NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index

for the diagnosis of AA would not be a misstatement. While the proportion of female (49.5%) and male (50.5%) patients was very similar in the study by Al Amri et al. (3), the study by Berhuni et al. (4) found 54.65% to be male, and similarly, the study by Shrestha et al. (5) found 54% to be male. Rajalingam et al. (6) reported 41.3% to be male. In our study, 46.4% of the patients were found to be male. Based on these data, a patient's gender alone does not appear to be a reliable determinant of AA diagnosis.

Regarding age distribution, AA typically affects young adults presenting with acute abdomen. Previous studies reported mean ages ranging from 28.58±16.65 to 38.16±14.50 (5-9). Our study found a mean age of 41.25±17.46, slightly higher but attributable to increasing life expectancy in the population.

The Alvarado score has been repeatedly evaluated to determine its effectiveness in preventing unnecessary imaging and laparotomy in the diagnosis of AA. We found a significant correlation between NLR and the Alvarado score. Hajibandeh et al. (10) reported NLR sensitivity of 90.91% and specificity of 88.89% for diagnosing and grading appendicitis severity. Kahramanca et al. (11) indicated that NLR aids in diagnosing and differentiating simple from complicated appendicitis, with 65.3% sensitivity and 54.7% specificity, complementing clinical examination. Ahmad et al. (12) reported sensitivity and specificity of 75.23% and 68.70%, respectively, for NLR in AA diagnosis. Markar et al. (13) ROC analysis yielded an AUC of 0.83 for NLR. Our results demonstrate statistically significant discrimination among low-, moderate-, and high-risk AA groups using NLR, suggesting its utility for clinical risk stratification and classification.

Rajalingam et al. (6) investigated PLR and NLR as surrogate biomarkers to differentiate complicated from uncomplicated appendicitis, finding both statistically significant, though PLR (sensitivity 75.9%, specificity 40.8%) lagged behind NLR (sensitivity 80.6%, specificity 47.2%). Kalayci and Kartal (14) found no significant difference in NLR and PLR between complicated and uncomplicated AA (p=0.926 and p=0.642, respectively). Chen et al. (15) compared NLR and PLR efficacy for differentiating AA from right ureterolithiasis, concluding that NLR (specificity 81.82%, sensitivity 68.87%) was more accurate and reliable than PLR (specificity 84.85%, sensitivity 37.74%). Celik et al. (16) reported

that both NLR (61.1% sensitivity, 73.2% specificity) and PLR (42% sensitivity, 86% specificity) effectively differentiate complicated from uncomplicated AA, with NLR having superior sensitivity and specificity. Our data indicate that, although PLR has lower discriminatory capacity than NLR, it can serve as a supportive biomarker above certain threshold values.

Şener et al. (17) reported that SII sensitivity for AA diagnosis was 82% and specificity 66.7%, also playing a role in distinguishing complicated and uncomplicated appendicitis. Mutlu et al. (18) identified SII as an independent predictor for complicated AA and noted its superior predictive power (AUC 0.809) over NLR (AUC 0.729) and CRP (AUC 0.732). Aydın and Tatlıparmak (19) found that SII had 78% sensitivity and 79% specificity for the diagnosis of AA (AUC 0.81). Our findings align with the literature, supporting that SII showed the strongest associations with higher clinical risk categories, reflecting their relationship with the magnitude of systemic inflammation.

Reported sensitivity and specificity of the Alvarado score at cut offs ≥5 and ≥7 vary across studies. Awayshih et al. (20) concluded that the Alvarado score is not sufficiently sensitive, reporting 54% sensitivity and 75% specificity. Din et al. (21) prospective study demonstrated that a cutoff value of 7.0 yielded 71.1% sensitivity and 75.8% specificity. Bouali et al. (22) reported higher diagnostic performance at increased Alvarado scores, with a decline in positive predictive value as the score decreased. In line with these findings, our results indicate that higher Alvarado score categories are associated with improved discriminatory performance of SII, NLR, and PLR across risk strata, with SII demonstrating the strongest association with the scoring system.

Study Limitations

• The absence of a non-appendicitis control group precludes the assessment of true diagnostic accuracy metrics, such as sensitivity and specificity.

• Single-center data collection limits generalizability; multicenter studies with larger samples are recommended.

• The sample size was limited. Larger cohorts would allow advanced analyses, including subgroup analyses.

• A retrospective design limits causal inference; prospective studies would better evaluate the efficacy of clinical decision-making.

• No distinction between complicated and uncomplicated appendicitis was made; this differentiation could strengthen the results, given the higher inflammatory markers observed in complicated cases.

• Potential inaccuracies or missing data inherent in retrospective electronic medical records may have influenced the results.

Conclusion

Our study suggests that SII is a supportive biomarker, parallel to the Alvarado score, in assessing the risk of AA. Both SII and NLR can be used in conjunction with the Alvarado score for risk assessment. However, these markers alone are insufficient, and larger-scale, multicenter, prospective studies are needed to improve diagnostic accuracy.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Tekirdağ Namık Kemal University Faculty of Medicine (approval number: 2025.70.04.06, date: 30.07.2025).

Informed Consent: This is a retrospective descriptive study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.Ö., A.T.D., U.Ç., B.Y., M.B., M.Ç., Concept: S.Ö., A.T.D., U.Ç., B.Y., F.G., Design: S.Ö., A.T.D., U.Ç., B.Y., F.G., Data Collection or Processing: S.Ö., A.T.D., U.Ç., B.Y., M.B., M.Ç., F.G., Analysis or Interpretation: S.Ö., Literature Search: S.Ö., A.T.D., U.Ç., B.Y., M.B., M.Ç., F.G., Writing: S.Ö., A.T.D., U.Ç., B.Y.

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