

Evaluation of systemic immune-inflammation index efficacy in predicting complicated appendicitis in pediatric emergency department

✉ Aysun Tekeli, M.D.,¹ ✉ Mehmet Bahadır Çalışkan, M.D.,² ✉ Gökhan Berktuğ Bahadır, M.D.,²
✉ Övgücan Karadağ Erdemir, M.D.,³

¹Department of Pediatric Emergency Medicine, University of Health Sciences Gülhane Training and Research Hospital, Ankara-Türkiye

²Department of Pediatric Surgery, University of Health Sciences Gülhane Training and Research Hospital, Ankara-Türkiye

³Department of Actuarial Science, Faculty of Science, Hacettepe University, Ankara-Türkiye

ABSTRACT

BACKGROUND: Acute appendicitis (AA) is one of the most important causes of acute abdominal pain in children who are admitted to the pediatric emergency department. This study aims to determine the usefulness of the systemic immune-inflammation index (SII) in predicting complicated appendicitis (CA) in pediatric patients.

METHODS: The patients who underwent surgery with the diagnosis of AA were evaluated retrospectively. AA and control groups were formed. AA was divided into noncomplicated and CA groups. C-reactive protein (CRP), white blood cell (WBC) count, absolute neutrophil count (ANC), absolute lymphocyte count, neutrophil/lymphocyte ratio (NLR), platelet (PLT)/lymphocyte ratio (PLR), and SII values were recorded. The SII was calculated with the formula of PLT count \times neutrophil/lymphocyte. The efficacy of biomarkers in predicting CA was compared.

RESULTS: Our study included 1072 AA and 541 control patients. There were 74.3% of patients in the non-CA (NCA) group and 25.7% in the CA group. CRP, WBC count, ANC, NLR, PLR when AA and control group, complicated and NCA groups are compared in terms of laboratory parameters and SII level AA and it was higher in the CA group. While the SII value was 2164.91 ± 1831.24 in the patients with NCA and 3132.59 ± 2658.73 in those with CA ($P < 0.001$). When the cut-off values were determined according to the area under the curve, CRP and SII were found to be the best biomarkers in predicting CA.

CONCLUSION: Inflammation markers together with clinical evaluation may be useful in distinguishing noncomplicated and complicated AA. However, these parameters alone are not sufficient to predict CA. CRP and SII are the best predictors of CA in pediatric patients.

Keywords: Biomarker, Children; complicated appendicitis; systemic immune-inflammation index.

INTRODUCTION

Acute appendicitis (AA) is one of the most important causes of acute abdominal pain requiring emergency surgery in childhood. AA is seen in approximately 10% of pediatric patients admitted to the emergency department with the complaint of abdominal pain.^[1,2] A diagnosis is based on a complete an-

amnesis and physical examination findings; however, some patients require supportive imaging and laboratory tests. Early and rapid diagnosis is important because the complication rate increases over time.^[3] Diagnosis is difficult in children at the initial evaluation since up to 50% of pediatric AA cases present with non-specific symptoms. Young children cannot fully describe pain, and therefore, accurate anamnesis and

Cite this article as: Tekeli A, Çalışkan MB, Bahadır GB, Erdemir ÖK. Evaluation of systemic immune-inflammation index efficacy in predicting complicated appendicitis in pediatric emergency department. *Ulus Travma Acil Cerrahi Derg* 2023;29:566-573.

Address for correspondence: Aysun Tekeli, M.D.

University of Health Sciences Gülhane Training and Research Hospital, İstanbul, Türkiye

E-mail: aysunnakay@yahoo.com.tr

Ulus Travma Acil Cerrahi Derg 2023;29(5):566-573 DOI: 10.14744/tjtes.2022.42472 Submitted: 06.12.2022 Revised: 16.03.2023 Accepted: 30.03.2023
OPEN ACCESS This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).



physical examination are more difficult in this population than in adults.^[4,5] Due to these difficulties in diagnosis in pediatric patients, the risk of complications increases, causing the prolongation of treatment and follow-up periods. Therefore, it is important to predict complicated appendicitis (CA) as a factor negatively affecting the prognosis of the disease.^[6,7] Many studies have evaluated various biomarkers to differentiate non-CA (NCA) from CA. C-reactive protein (CRP) levels, white blood cell (WBC) count, absolute neutrophil count (ANC), neutrophil/lymphocyte ratio (NLR), and platelet (PLT)/lymphocyte ratio (PLR) are frequently used markers in the diagnosis and differentiation of NCA and CA.^[8-11]

Systemic immune-inflammation index (SII), a new marker of inflammation, is calculated using the combination of PLT, neutrophil, and lymphocyte counts (PLT × neutrophil/lymphocyte counts). SII may reflect systemic inflammation better than NLR or PLR alone. Its important advantages are that it can be easily calculated from the hemogram test results, and it does not incur extra costs or require additional blood collection. SII was initially considered a poor prognosis marker in patients with hepatocellular carcinoma, and later studies mostly focused on oncological diseases.^[12-14] It has also been reported that in addition to oncological diseases, SII can be used to predict prognosis in coronary artery disease, infective endocarditis, rheumatological diseases, and COVID-19 disease, as well as to evaluate disease activity in inflammatory bowel diseases.^[15-22]

In the literature, there are only limited studies evaluating SII in pediatric patients. In addition, studies investigating whether SII can be used to predict AA in this patient group are very few.^[23] This study is one of the first to evaluate the efficacy of SII in predicting CA in children.

The aim of this study was to evaluate the utility of SII in diagnosing AA and predicting CA in children and to compare its usability with routine laboratory parameters.

MATERIALS AND METHODS

Patient Selection And Study Example

The research was planned as a retrospective study. The study was carried out in the Pediatric Emergency Department and Pediatric Surgery Clinic of the University of Health Sciences Gülhane Training and Research Hospital in Ankara, Turkey.

The data of the patients who admit to the pediatric emergency department with the complaint of abdominal pain and were operated on with a pre-diagnosis of AA between January 2017 and December 2021 were scanned through the file registry system.

Patients under the age of 18 who were operated on with a pre-diagnosis of AA and whose preoperative hemogram and

CRP tests were evaluated in the emergency department were included in the study. Patients with a normal appendix after surgery and a known chronic inflammatory disease were excluded from the study. The patients were divided into two groups NCA and CA according to the results of the surgeon's operation evaluation and histopathological examination report. Perforated appendicitis, gangrenous appendicitis, intra-abdominal fecalitis, and abscess were defined as CA.

Children of similar age and gender, who were admitted to the pediatric surgery outpatient clinic for umbilical hernia, inguinal hernia, and circumcision, were included in the control group.

Patients with chronic disease, drug use, and history of appendectomy were excluded from the control study group.

Data Collection And Laboratory Tests

The patients' age, gender, complaints, duration of complaints, and length of hospital stay were recorded. CRP levels, WBC count, absolute lymphocyte count (ALC), ANC, NLR, PLT, PLR, and SII values at the first admission to the pediatric emergency department were recorded from the hemogram analysis. SII, PLT count × neutrophil count /lymphocyte count was calculated using the formula.

Ethical Approval

The study protocol was in line with the tenets of the Declaration of Helsinki. The study was reviewed and approved by the Ethics Committee of Gülhane Health Sciences Faculty Hospital (2022-64).

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS) version 23 and R Studio. Descriptive statistics were calculated separately for total appendicitis, the two patient groups (NCA and CA), and the control group.

Quantitative parameters were expressed as mean and standard deviation values, and categorical parameters as frequency (n) and percentages (%). The normality of data was analyzed with the Kolmogorov–Smirnov goodness-of-fit test. For normally distributed parameters, the independent-samples t-test was used to analyze the mean differences between the control, NCA and CA groups. For non-normally distributed parameters, the Mann–Whitney U test was used. The Pearson Chi-square test was carried out for categorical variables. The Youden index (YI) method was used to find the optimal cutoff value. The area under the curve (AUC), sensitivity, specificity, the positive predictive value (PPV), and negative predictive value (NPV) were calculated. The receiver operating characteristic (ROC) analysis was used to analyze the sen-

Table 1. Comparison of demographic, clinical and laboratory characteristics of patients diagnosed with acute appendicitis and control group

Parameters	Acute appendicitis (n=1072) Mean±SD	Control (n=514) Mean±SD	P-value
Age, years	11.52±3.74	10.35±2.98	0.130 ^a
WBC/mm ³	14724.53±6196.27	7614.79±1830.86	<0.001 ^a
ANC/mm ³	11393.55±6715.68	3804.28±1868.98	<0.001 ^a
ALC/mm ³	1887.74±1385.84	3022.96±916.29	<0.001 ^a
NLR	8.52±6.76	1.38±0.77	<0.001 ^a
PLT/mm ³	285243.40±81158.90	314303.50±71927.54	<0.001 ^a
PLR	200.70±126.24	112.43±39.96	<0.001 ^a
SII ×10 ⁹ /L	2426.61±2129.25	430.45±246.68	<0.001 ^a
Gender	n (%)	n (%)	
Male	689 (64.27)	334 (64.98)	0.831 ^b
Female	383 (35.73)	180 (35.02)	

SII: Systemic immune-inflammation index; WBC: White blood cell; ANC: Absolute neutrophil count; ALC: Absolute lymphocyte count; NLR: Neutrophil/lymphocyte ratio; PLT: Platelets; PLR: Platelet/lymphocyte ratio; SD: Standard deviation; ^aP-value significant at the 0.05 level (two-tailed), ^aIndependent-samples t-test; ^b Pearson Chi-square test

sitivity and specificity of these biomarkers. A value of P<0.05 was considered statistically significant.

RESULTS

The study included a total of 1586 patients, of whom 514 control group and 1072 AA group. There were 796 (74.3%)

children in the NCA and 276 (25.7%) in the CA. Demographic, clinical, and laboratory characteristics of all patients are presented in Tables 1 and 2.

The mean age of the control group was 10.35±2.98 years. Of all the patients of the control group, 334 (64.98%) were

Table 2. Comparison of demographic, clinical and laboratory characteristics of patients diagnosed with non-complicated and complicated appendicitis

Parameters	Total AA (n=1072) Mean±SD	Non-complicated appendicitis (n=796) Mean±SD	Complicated appendicitis (n=276) Mean±SD	P-value
Age, years	11.52±3.74	11.92±3.56	11.12±3.98	0.161 ^a
Duration of abdominal pain, days	1.49±1.102	1.28±0.68	2.13±1.73	<0.001 ^a
Length of hospital stay, days	3.70±2.287	2.66±0.76	6.69±2.57	<0.001 ^a
CRP mg/L	49.70±68.96	25.18±35.55	115.87±90.57	<0.001 ^a
WBC/mm ³	14724.53±6196.27	14296.98±6452.82	15877.91±5291.31	0.002 ^a
ANC/mm ³	11393.55±6715.68	10734.70±4441.76	13170.93±10473.95	0.004 ^a
SII ×10 ⁹ /L	2426.61±2129.25	2164.91±1831.24	3132.59±2658.73	<0.001 ^a
NLR	8.52±6.76	7.77±5.99	10.56±8.17	<0.001 ^a
ALC/mm ³	1887.74±1385.84	1959.91±1479.97	1693.02±1071.95	0.013 ^a
PLT/mm ³	285243.40±81158.90	276525.43±70652.75	308761.63±100902.05	<0.001 ^a
PLR	200.70±126.24	183.52±106.65	247.06±159.44	<0.001 ^a
Gender	n (%)	n (%)	n (%)	
Male	689 (64.27)	507 (63.69)	182 (65.94)	0.780 ^b
Female	383 (35.73)	289 (36.31)	94 (34.06)	

CRP: C-reactive protein; SII: Systemic immune-inflammation index; WBC: White blood cell; ANC: Absolute neutrophil count; ALC: Absolute lymphocyte count; NLR: Neutrophil/lymphocyte ratio; PLT: Platelets; PLR: Platelet/lymphocyte ratio; SD: Standard deviation. ^aP-value significant at the 0.05 level (two-tailed); ^aindependent-samples t-test; ^b Mann-Whitney U-test; ^c Pearson Chi-square test.

Table 3. The performance of biomarkers in predicting acute appendicitis

Biomarkers	Cut-off	AUC	YI	Sensitivity	Specificity	PPV	NPV
WBC count/mm ³	11100	0.915	0.7238	77.83	94.55	97.25	63.28
ANC/mm ³	6600	0.937	0.7733	82.39	94.94	97.58	68.54
NLR	2.36	0.952	0.8081	88.21	92.61	96.72	76.04
PLR	141.07	0.771	0.4422	62.89	81.32	89.29	46.97
SII × 10 ⁹ /L	923	0.927	0.7363	78.30	95.33	97.65	63.97

WBC: White blood cell; ANC: Absolute neutrophil count; NLR: Neutrophil/lymphocyte ratio; SII: Systemic immune-inflammation index; PLR: Platelet/lymphocyte ratio; AUC: Area under the curve; YI: Youden index; PPV: Positive predictive value; NPV: Negative predictive value

male. For the WBC count, ANC, ALC, NLR, PLT, PLR, and SII biomarkers, the differences between the total AA and control groups were found to be statistically significant ($P < 0.05$) (Table 1).

The mean age of the AA patients was 11.52 ± 3.74 years. Of all the patients, 689 (64.27%) were male, and the number of male patients in the CA groups was 182 (65.94%). The mean duration of abdominal pain was 1.28 ± 0.68 days in the NCA group and 2.13 ± 1.73 days in the CA group. The most common symptoms accompanying abdominal pain were nausea and vomiting in 86.3% of patients and anorexia in 30.8% of patients. The mean length of hospital stay was 2.66 ± 0.76 in the NCA group and 6.69 ± 2.57 days in the CA group. Abdominal pain duration (days) and hospital stay (days) were statistically significant between the two groups ($P < 0.05$), these durations were longer in the CA group compared to the NCA group.

For the CRP, WBC count, ANC, NLR, PLT, SII, and PLR biomarkers, the differences between the NCA and CA groups were also found to be statistically significant ($P < 0.05$). The mean values were significantly higher in the CA group for these biomarkers. However, the NCA and CA groups did not significantly differ in relation to age ($P = 0.161$). Furthermore, as regards to Pearson Chi-square test, for gender, the difference between non-complicated and complicated groups was

also found statistically insignificant ($P = 0.780$) (Table 2).

The AUC of SII to predict AA was 0.927 (95% confidence interval [CI] 0.911–0.943, $P = 0.000$); for WBC count, it was 0.915 (95% CI 0.897–0.933, $P = 0.000$); for ANC it was 0.937 (95% CI 0.921–0.953, $P = 0.000$); for NLR it was 0.952 (95% CI 0.938–0.965, $P = 0.000$) and for PLR it was 0.771 (95% CI 0.740–0.801, $P = 0.000$). AUC, YI, sensitivity, specificity, PPV, and NPV were calculated for AA and are given in Table 3. ROC curves in AA for WBC count, ANC, NLR, PLR, and SII are given in Fig. 1.

The AUC of SII to predict CA was 0.646 (95% [CI] 0.600–0.692, $P = 0.000$); for CRP, it was 0.858 (95% CI 0.823–0.892, $P = 0.000$); for WBC count it was 0.600 (95% CI 0.549–0.652, $P = 0.000$); for ANC it, was 0.595 (95% CI 0.545–0.644, $P = 0.000$); for NLR it was 0.621 (95% CI 0.574–0.668, $P = 0.000$) and for PLR it, was 0.624 (95% CI 0.575–0.673, $P = 0.000$). Considering the AUC data of the biomarkers at their optimal cut-off values, the best markers for the prediction of CA were determined as CRP, SII, PLR, and NLR (AUC; 0.858, 0.646, 0.624, and 0.621, respectively) (Table 4). ROC curves in CA for CRP, WBC count, ANC, NLR, PLR, and SII are given in Fig. 2.

When the cut-off value for CRP was determined as 39 mg/L

Table 4. The performance of biomarkers in predicting complicated appendicitis

Biomarkers	Cut-off	AUC	YI	Sensitivity	Specificity	PPV	NPV
CRP mg/L	39	0.858	0.5918	79.65	79.53	59.05	91.34
WBC count/mm ³	14400	0.600	0.1699	65.70	51.29	33.33	80.13
ANC/mm ³	12600	0.595	0.1500	48.84	66.16	34.85	77.72
NLR	5.36	0.621	0.1953	73.84	45.69	33.51	82.49
PLR	223	0.624	0.1891	66.19	44.77	39.09	78.36
SII × 10 ⁹ /L	2358.03	0.646	0.2407	56.40	67.67	39.27	80.72

CRP: C-reactive protein; WBC: White blood cell; ANC: Absolute neutrophil count; NLR: Neutrophil/lymphocyte ratio; SII: Systemic immune-inflammation index, PLR: Platelet/lymphocyte ratio; AUC: Area under the curve; YI: Youden index; PPV: Positive predictive value; NPV: Negative predictive value

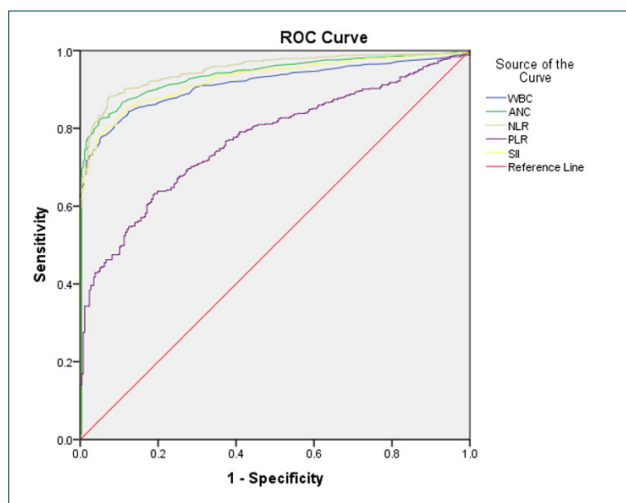


Figure 1. Receiver operating characteristic curve of biomarkers to predict acute appendicitis

in predicting CA, the sensitivity and specificity were found 79.65% and 79.53%; and when the cut-off value for SII was 2358.03, the sensitivity was 56.40% and the specificity was 67.67%. For SII the values of PPV and NPV were calculated as 39.27% and 80.72%, respectively.

DISCUSSION

Acute appendicitis is one of the most common causes of emergency surgical pathology in patients presenting to the pediatric emergency department with abdominal pain.^[24] It occurs at any age, but often in the second decade. In our study, the mean age of the patients was around 11 years, which is similar to the literature.^[25,26] The male gender constitutes the majority of AA cases in children.^[27] In our study, AA was also seen more frequently in the male gender (64.27%). The most common symptom in AA is abdominal pain, and the duration of symptoms has been reported to be longer in CA. In the literature, the length of hospital stay was found to be longer in CA. Similarly, in our study, the time from the onset of abdominal pain to admission to the hospital, and the length of hospital stay were longer in the CA cases than in the NCA cases, and the difference between the two groups was statistically significant ($P < 0.05$).^[28,29]

Although the diagnosis of AA in children is primarily made clinically, the combination of laboratory and imaging methods supports the diagnosis. Among the laboratory parameters, CRP level, WBC count, ANC, NLR, and PLR are frequently used markers. In previous studies, WBC count, ANC, NLR, and PLR rates were found to be significantly higher in the AA group when compared to the control group.^[8,9,30] In our study, the WBC count, ANC, NLR, and PLR rates were significantly higher in the AA group than in the control group ($P < 0.05$).

Delay in the diagnosis of AA in children due to difficulties in defining pain and examination may cause complications such

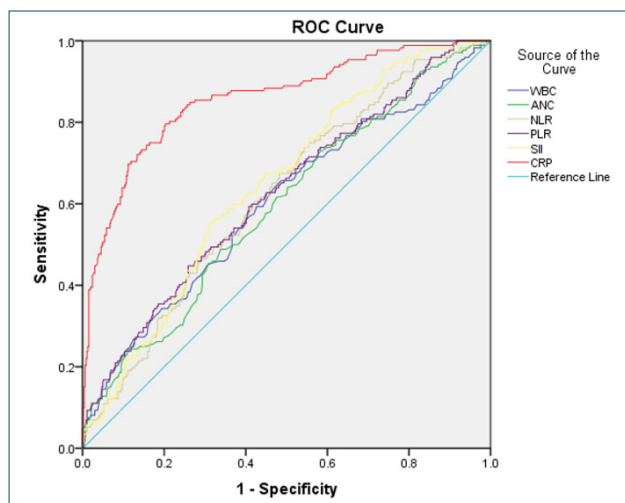


Figure 2. Receiver operating characteristic curve of biomarkers to predict complicated appendicitis

as perforation, abscess, and peritonitis.^[31] In our study, 25.7% of AA cases were complicated. The early diagnosis of CA is vital for appropriate medical treatment and the timing of surgery to prevent complications. Therefore, some auxiliary tests were needed to achieve early diagnosis. To date, many biomarkers have been used to differentiate non-complicated and CA.^[8,9,32,33]

WBC count and ANC are the most commonly used diagnostic laboratory parameters in the diagnosis of AA. Studies have shown that WBC count and ANC are high in AA and are strong markers of CA.^[33-35] The results of our study were similar to the literature, and the WBC count was found to be higher in Jung et al.^[36] determined the WBC count cut-off value of 10600/mm³ in CA (sensitivity 71.2%; specificity 68.2%) and reported the AUC value of this parameter as 0.664. This study, the cut-off value for WBC count in CA was found to be 14400/mm³ and AUC 0.600 (sensitivity 65.70%; specificity 51.29%).

In a prospective study conducted with 200 patients, Boshnak et al.^[24] reported the sensitivity and specificity of ANC for AA as 72.4% and 81.8%, respectively, at a cut-off value of 9400/mm³. In another study, it was reported that ANC has no diagnostic value for the diagnosis of CA.^[33] In our study, the cut-off value of ANC for CA was 12600/mm³ (sensitivity 48.84% and specificity 66.16%). When ANC was compared between the two groups, the difference was statistically significant ($P < 0.001$). Decreased lymphocyte count is a stress marker, and lymphopenia has been reported to be associated with appendicitis.^[36] In the current study, the lymphocyte count was found to be lower than CA and there was statistically significant difference between the groups ($P = 0.013$).

Systemic inflammatory states can increase NLR by causing an increase in neutrophil count and a decrease in lymphocyte count, and increased NLR and PLR levels, which are signs

of inflammation, can be observed in AA.^[33,37-39] In a study by Kart and Uğur^[23] in the prediction of AA; the cut-off value for NLR was found to be 2.235, AUC value was 0.996; the cut-off value for PLR was found to be 137.055, the AUC value was 0.848.

In this study, the cut-off value for NLR was found to be 2.36, AUC value was 0.952; the cut-off value for PLR was found to be 141.07, and the AUC value was 0.771. NLR was found to be the most significant biomarker in AA prediction.

Many studies are reporting different cut-off values for the diagnostic power of NLR in the diagnosis of CA. In studies using a cut-off value of 4.8–7.32, the sensitivity of NLR was found to be 78.4–95.2% and specificity 41.7–83.8%.^[40-43] In our study, similar to the literature, at a cutoff value of 5.36 for NLR, the sensitivity was 73.84% and the specificity was 45.69%.

PLR has been investigated in several studies on AA. In a study by Celik et al.,^[44] it was shown to have a good predictive value in the diagnosis of CA with a sensitivity of 42% and a specificity of 86% at a cut-off value of 284 for PLR. In another study evaluating 558 patients who underwent appendectomy, the cutoff value for PLR was found to be 163.27, AUC value 0.660, sensitivity 64.3%, and specificity 67.5% for the distinction between NCA and perforated appendicitis.^[45] In our study, at a cut-off value of 223, PLR had a sensitivity and specificity of 66.19% and 44.77%, respectively in the prediction of CA.

CRP is an acute-phase reactant and can be used as a diagnostic marker in acute inflammatory conditions. CRP, together with clinical and radiological findings, is a laboratory parameter with a good diagnostic value in AA. In the literature, it has been found that CRP is an important parameter in the diagnosis of CA and is more sensitive than increased leukocyte count.^[33,35,46] In the current study, CRP was shown to be the best diagnostic marker for differentiation between NCA and CA. In a study by Sengul et al.,^[43] the cutoff value of CRP in CA was reported to be 13 mg/L (sensitivity 81%; specificity 80%). In our study, the cut-off value of CRP was 39 mg/L, at which it had a sensitivity of 79.65% and specificity of 79.53%. CRP had the highest sensitivity and specificity in the prediction of CA.

In the literature, elevated WBC count, ANC, and CRP levels were found in CA patients.^[33,36] Similarly, in our study, the WBC count, ANC, and CRP levels were significantly higher in the CA group ($P < 0.05$).

Research is ongoing for laboratory markers that show better diagnostic benefits than CRP and hemogram, which are commonly used to assess inflammation. In recent years, SII has been shown as a new marker of inflammation that can be easily calculated with hemogram parameters, reflecting the balance between the patient's immune status and inflam-

mation. To date, a high SII has been shown to be generally associated with poor outcomes in various malignancies. It has also appeared to be associated with poor outcomes in many different clinical conditions, including cardiovascular disease and autoimmune disorders.^[15-19] However, studies evaluating the usability of SII in pediatric patients are limited.^[47-49] In our study, a cut-off value of 923 (sensitivity 78.30% and specificity 95.33%) was found for SII to diagnose AA. Kart and Uğur^[23] the optimum cutoff value of SII was determined as 651.475 by using ROC curve analysis in the diagnosis of AA, and its sensitivity was 95% and its specificity was 98%.

This study considering the AUC value of the biomarkers at their optimal cut-off values, the best markers for the prediction of AA were determined as NLR, ANC, SII, and WBC count (AUC 0.952, 0.937, 0.927, and 0.915, respectively).

This study is one of the first to evaluate the efficacy of SII in predicting CA in children. In our study, when the SII cut-off was taken as 2358.03, its AUC value was calculated as 0.646 in the prediction of CA. We determined CRP, then SII to be the best AUC values for the prediction of CA.

This study has certain limitations, with the major examples being the data reflecting the situation in a single-center and retrospective design. However, we consider that our findings will contribute to the literature since it is a study conducted with a large number of patients to investigate the predictive ability of CA in pediatric patients.

Conclusion

Inflammation markers, together with clinical evaluation may be useful in differentiating AA. However, these parameters alone are not sufficient to predict AA. In this study, according to the AUC; NLR, ANC, SII, and WBC count were the best biomarkers to predict AA. To predict CA, the best AUC values were associated with the CRP level and the SII. SII can be used as a good biomarker to predict CA. However, prospective and multicenter studies are needed to evaluate the effectiveness of SII in distinguishing between CA and NCA in children.

Ethics Committee Approval: This study was approved by the Gülhane Training and Research Hospital Clinical Research Ethics Committee (Date: 17.02.2022, Decision No: 2022-64)

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: A.T.; Design: A.T., M.B.Ç., G.B.B.; Supervision: M.B.Ç., Ö.K.E.; Fundings: A.T., G.B.B.; Materials: A.T., G.B.B., M.B.Ç.; Data: A.T., G.B.B., M.B.Ç.; Analysis: A.T., Ö.K.E.; Literature search: A.T., G.B.B.; Writing: A.T.; Critical revision: A.T., Ö.K.E., G.B.B., M.B.Ç.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

- Reynolds SL, Jaffe DM. Diagnosing abdominal pain in a pediatric emergency department. *Pediatr Emerg Care* 1992;8:126–8. [CrossRef]
- Magnúsdóttir MB, Róbertsson V, Þorgrímsson S, Rósmundsson Þ, Agnarsson U, Haraldsson A. Abdominal pain is a common and recurring problem in paediatric emergency departments. *Acta Paediatr* 2019;108:1905–10. [CrossRef]
- Gadiparthi R, Waseem M. Pediatric appendicitis. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2022.
- Téoule P, Laffolie J, Rolle U, Reissfelder C. Acute appendicitis in childhood and adulthood. *Dtsch Arztebl Int* 2020;117:764–74.
- Duman L, Karaibrahimoğlu A, Büyükyavuz BI, Savaş MC. Diagnostic value of monocyte-to-lymphocyte ratio against other biomarkers in children with appendicitis. *Pediatr Emerg Care* 2022;38:e739–42. [CrossRef]
- Rentea RM, St Peter SD. Pediatric appendicitis. *Surg Clin North Am* 2017;97:93–112. [CrossRef]
- Williams RF, Blakely ML, Fischer PE, Streck CJ, Dassinger MS, Gupta H, et al. Diagnosing ruptured appendicitis preoperatively in pediatric patients. *J Am Coll Surg* 2009;208:819–25. [CrossRef]
- Acharya A, Markar SR, Ni M, Hanna GB. Biomarkers of acute appendicitis: Systematic review and cost-benefit trade-off analysis. *Surg Endosc* 2017;31:1022–31. [CrossRef]
- Beltrán MA, Almonacid J, Vicencio A, Gutiérrez J, Cruces KS, Cumsille MA. Predictive value of white blood cell count and C-reactive protein in children with appendicitis. *J Pediatr Surg* 2007;42:1208–14. [CrossRef]
- Malia L, Sturm JJ, Smith SR, Brown RT, Campbell B, Chicaiza H. Predictors for acute appendicitis in children. *Pediatr Emerg Care* 2021;37:e962–8. [CrossRef]
- Liu L, Shao Z, Yu H, Zhang W, Wang H, Mei Z. Is the platelet to lymphocyte ratio a promising biomarker to distinguish acute appendicitis? Evidence from a systematic review with meta-analysis. *PLoS One* 2020;15:e0233470. [CrossRef]
- Hu B, Yang XR, Xu Y, Sun YF, Sun C, Guo W, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. *Clin Cancer Res* 2014;20:6212–22.
- Fest J, Ruiter R, Mulder M, Koerkamp BG, Ikram MA, Stricker BH, et al. The systemic immune-inflammation index is associated with an increased risk of incident cancer—a population-based cohort study. *Int J Cancer* 2020;146:692–8. [CrossRef]
- Jomrich G, Paireder M, Kristo I, Baierl A, Ilhan-Mutlu A, Preusser M, et al. High systemic immune-inflammation index is an adverse prognostic factor for patients with gastroesophageal adenocarcinoma. *Ann Surg* 2021;273:532–41. [CrossRef]
- Dai X, Kong T, Zhang X, Luan B, Wang Y, Hou AJ. Relationship between increased systemic immune-inflammation index and coronary slow flow phenomenon. *BMC Cardiovasc Disord* 2022;22:362. [CrossRef]
- Yang YL, Wu CH, Hsu PF, Chen SC, Huang SS, Chan WL, et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. *Eur J Clin Invest* 2020;50:e13230.
- Hu W, Su G, Zhu W, Zhou E, Shuai X. Systematic immune-inflammation index predicts embolic events in infective endocarditis. *Int Heart J* 2022;63:510–6. [CrossRef]
- Wu J, Yan L, Chai K. Systemic immune-inflammation index is associated with disease activity in patients with ankylosing spondylitis. *J Clin Lab Anal* 2021;35:e23964. [CrossRef]
- Taha SI, Samaan SF, Ibrahim RA, Moustafa NM, El-Sehsah EM, Youssef MK. Can complete blood count picture tell us more about the activity of rheumatological diseases? *Clin Med Insights Arthritis Musculoskelet Disord* 2022;15:11795441221089182. [CrossRef]
- Muhammad S, Fischer I, Naderi S, Jouibari MF, Abdolreza S, Karimialavijeh E, et al. Systemic inflammatory index is a novel predictor of intubation requirement and mortality after SARS-CoV-2 infection. *Pathogens* 2021;10:58. [CrossRef]
- Wijeratne T, Wijeratne C. Clinical utility of serial systemic immune inflammation indices (SSII) in the context of post covid-19 neurological syndrome (PCNS). *J Neurol Sci* 2021;423:117356. [CrossRef]
- Xie Y, Zhuang T, Ping Y, Zhang Y, Wang X, Yu P, et al. Elevated systemic immune inflammation index level is associated with disease activity in ulcerative colitis patients. *Clin Chim Acta* 2021;517:122–6. [CrossRef]
- Kart Y, Uğur C. Evaluation of systemic immune-inflammation index as novel marker in the diagnosis of acute appendicitis in children. *J Contemp Med* 2022;12:593–7. [CrossRef]
- Boshnak N, Boshnaq M, Elgohary H. Evaluation of platelet indices and red cell distribution width as new biomarkers for the diagnosis of acute appendicitis. *J Invest Surg* 2018;31:121–9. [CrossRef]
- Wu HP, Fu YC. Application with repeated serum biomarkers in pediatric appendicitis in clinical surgery. *Pediatr Surg Int* 2010;26:161–6. [CrossRef]
- Brown RL. Appendicitis. In: Zeigler MM, Azizkhan RG, Von Allmen D, Weber TR, editors. *Operative Pediatric Surgery*. 2nd ed., Ch. 48. New York: McGraw-Hill Education; 2014. p. 613–31.
- Goodman DA, Goodman CB, Monk JS. Use of the neutrophil: Lymphocyte ratio in the diagnosis of appendicitis. *Am Surg* 1995;61:257–9.
- Baird DL, Simillis C, Kontovounisios C, Rasheed S, Tekkis PP. Acute appendicitis. *BMJ* 2017;357:j1703. [CrossRef]
- Stringer MD. Acute appendicitis. *J Paediatr Child Health* 2017;53:1071–6. [CrossRef]
- Yardımcı S, Uğurlu MÜ, Coşkun M, Attaallah W, Yeğen ŞC. Neutrophil-lymphocyte ratio and mean platelet volume can be a predictor for severity of acute appendicitis. *Ulus Travma Acil Cerrahi Derg* 2016;22:163–8. [CrossRef]
- Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: Modern understanding of pathogenesis, diagnosis, and management. *Lancet* 2015;386:1278–87. [CrossRef]
- Sack U, Biereder B, Elouahidi T, Bauer K, Keller T, Tröbs RB. Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. *BMC Surg* 2006;6:15. [CrossRef]
- Zani A, Teague WJ, Clarke SA, Haddad MJ, Khurana S, Tsang T, et al. Can common serum biomarkers predict complicated appendicitis in children? *Pediatr Surg Int* 2017;33:799–805. [CrossRef]
- Birchley D. Patients with clinical acute appendicitis should have pre-operative full blood count and C-reactive protein assays. *Ann R Coll Surg Engl* 2006;88:27–32. [CrossRef]
- Yu CW, Juan LI, Wu MH, Shen CJ, Wu JY, Lee CC. Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. *Br J Surg* 2013;100:322–9. [CrossRef]
- Jung SK, Rhee DY, Lee WJ, Woo SH, Seol SH, Kim DH, et al. Neutrophil-to-lymphocyte count ratio is associated with perforated appendicitis in elderly patients of emergency department. *Aging Clin Exp Res* 2017;29:529–36. [CrossRef]
- Greer D, Bennett P, Wagstaff B, Croaker D. Lymphopaenia in the diagnosis of paediatric appendicitis: A false sense of security? *ANZ J Surg* 2019;89:1122–5. [CrossRef]
- Ishizuka M, Shimizu T, Kubota K. Neutrophil-to-lymphocyte ratio has a close association with gangrenous appendicitis in patients undergoing appendectomy. *Int Surg* 2012;97:299–304. [CrossRef]
- Zahorec R. Ratio of neutrophil to lymphocyte counts—rapid and simple

- parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy 2001;102:5–14.
40. Shimizu T, Ishizuka M, Kubota K. A lower neutrophil to lymphocyte ratio is closely associated with catarrhal appendicitis versus severe appendicitis. Surg Today 2016;46:84–9. [CrossRef]
41. Khan A, Riaz M, Kelly ME, Khan W, Waldron R, Barry K, et al. Prospective validation of neutrophil-to-lymphocyte ratio as a diagnostic and management adjunct in acute appendicitis. Ir J Med Sci 2018;187:379–84. [CrossRef]
42. Sevinç MM, Kinacı E, Çakar E, Bayrak S, Özakay A, Aren A, et al. Diagnostic value of basic laboratory parameters for simple and perforated acute appendicitis: An analysis of 3392 cases. Ulus Travma Acil Cerrahi Derg 2016;22:155–62. [CrossRef]
43. Sengul S, Guler Y, Calis H, Karabulut Z. The role of serum laboratory biomarkers for complicated and uncomplicated appendicitis in adolescents. J Coll Physicians Surg Pak 2020;30:420–4. [CrossRef]
44. Celik B, Nalcacioglu H, Ozcatal M, Torun YA. Role of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in identifying complicated appendicitis in the pediatric emergency department. Ulus Travma Acil Cerrahi Derg 2019;25:222–8. [CrossRef]
45. Pehlivanlı F, Aydın O. Role of platelet to lymphocyte ratio as a biomedical marker for the pre-operative diagnosis of acute appendicitis. Surg Infect (Larchmt) 2019;20:631–6. [CrossRef]
46. Wu HP, Lin CY, Chang CF, Chang YJ, Huang CY. Predictive value of C-reactive protein at different cutoff levels in acute appendicitis. Am J Emerg Med 2005;23:449–53. [CrossRef]
47. Winker M, Stössel S, Neu MA, Lehmann N, El Malki K, Paret C, et al. Exercise reduces systemic immune inflammation index (SII) in childhood cancer patients. Support Care Cancer 2022;30:2905–8. [CrossRef]
48. Güneşlioğlu MM, Güngör A, Göktaş A, Üner Ç, Bodur İ, Yaradılmış RM, et al. Evaluation of the efficiency of the systemic immune-inflammation index in differentiating parapneumonic effusion from Empyema. Pediatr Pulmonol 2022;57:1625–30. [CrossRef]
49. Taranu I, Lazea C, Creț V, Răcătăianu N, Iancu M, Bolboacă SD. Inflammation-related markers and thyroid function measures in pediatric patients: Is the grade of obesity relevant? Diagnostics (Basel) 2021;11:485.

ORJİNAL ÇALIŞMA - ÖZ

Çocuk acilde komplike apandisit öngörmede sistemik immün inflamasyon indeksi etkinliğinin değerlendirilmesi

Dr. Aysun Tekeli,¹ Dr. Mehmet Bahadır Çaliskan,² Dr. Gökhan Berktaş Bahadır,² Dr. Övgücan Karadağ Erdemir³

¹Sağlık Bilimleri Üniversitesi, Gülhane Eğitim ve Araştırma Hastanesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Çocuk Acil, Ankara

²Sağlık Bilimleri Üniversitesi, Gülhane Eğitim ve Araştırma Hastanesi, Çocuk Cerrahisi Anabilim Dalı, Ankara

³Hacettepe Üniversitesi, Aktüerya Bilimleri Bölümü, Ankara

AMAÇ: Akut apandisit, çocuk acil servisine başvuran çocuklarda akut karın ağrısının en önemli nedenlerinden biridir. Bu çalışma, pediatrik hastalarda komplike apandisit öngörmede sistemik immün-inflamasyon indeksinin yararlılığını belirlemeyi amaçlamaktadır.

GEREÇ VE YÖNTEM: Akut apandisit tanısı ile ameliyat edilen hastalar geriye dönük olarak incelendi. Akut apandisit ve kontrol grubu oluşturuldu. Akut apandisit, nonkomplike ve komplike apandisit grubu olarak ikiye ayrıldı. C-reaktif protein, beyaz küre sayısı, mutlak nötrofil sayısı, mutlak lenfosit sayısı, nötrofil/lenfosit oranı, trombosit/lenfosit oranı ve sistemik immün-inflamasyon indeksi değerleri kaydedildi. Sistemik immün inflamasyon indeksi trombosit sayısı x nötrofil/lenfosit formülü ile hesaplandı. Biyobelirteçlerin komplike apandisit öngörmedeki etkinliği karşılaştırıldı.

BULGULAR: Çalışmamıza 1072 akut apandisit ve 541 kontrol hasta dahil edildi. Nonkomplike apandisit grubunda %74.3 hasta, komplike apandisit grubunda %25.7 hasta vardı. Akut apandisit ve kontrol grubu, komplike ve nonkomplike apandisit grubu laboratuvar parametreleri açısından karşılaştırıldığında C-reaktif protein, beyaz küre, mutlak nötrofil sayısı, nötrofil/lenfosit oranı, trombosit/lenfosit oranı ve sistemik immün-inflamasyon indeksi düzeyi akut apandisit ve komplike apandisit grubunda daha yüksek tespit edildi. Nonkomplike apandisit hastalarında sistemik immün-inflamasyon indeksi değeri 2164.91 ± 1831.24 iken komplike apandisit hastalarında 3132.59 ± 2658.73 idi ($p < 0.001$). Eğri altındaki alana göre kestirim değerleri belirlendiğinde, komplike apandisit öngörüsünde en iyi biyobelirteçler C-reaktif protein ve sistemik immün-inflamasyon indeksi bulundu.

TARTIŞMA: Nonkomplike ve komplike akut apandisit ayırımında, klinik değerlendirme ile birlikte inflamasyon belirteçleri faydalı olabilir. Fakat bu parametreler tek başına komplike apandisit öngörmede yeterli değildir. Çocuklarda komplike apandisit tahmin etmek için C-reaktif protein ve sistemik immün-inflamasyon indeksi en iyi biyobelirteç tespit edilmiştir.

Anahtar sözcükler: Biyobelirteç; çocuk; komplike apandisit; sistemik immün-inflamasyon indeksi.

Ulus Travma Acil Cerrahi Derg 2023;29(5):566-573 doi: 10.14744/tjtes.2022.42472