ORIGINAL ARTICLE

https://doi.org/10.1590/1806-9282.20221003

# Diagnostic value of systemic immune inflammation index in acute appendicitis

Kemal Şener[1*], Adem Çakır[1], Hüseyin Kılavuz[2], Ertuğrul Altuğ[1], Ramazan Güven[1]

## SUMMARY

**OBJECTIVE:** Clinical diagnosis of acute appendicitis is often difficult and involves a synthesis of clinical, laboratory, and radiological findings. The aim of this study was to investigate whether the systemic immune inflammation index can be used as an effective parameter in the diagnosis of acute appendicitis and its reliability in the differentiation of complicated vs. non-complicated appendicitis.

**METHODS:** The study was conducted retrospectively with patients admitted to the emergency department with abdominal pain and diagnosed with acute appendicitis. In total, 150 patients and 150 control cases were included in the study. Demographic data, medical history, white blood cell count, platelet count, neutrophil count, systemic immune inflammation index values, Alvarado score, adult appendicitis score, and pathology result of appendectomy material were retrieved from the hospital automation system and recorded in the data form.

**RESULTS:** Neutrophil-lymphocyte ratio and systemic immune inflammation index were significantly higher, and platelet-neutrophil ratio and lymphocyte-neutrophil ratio were significantly lower in the patient group compared to the control group ($p<0.001$). Receiver operating characteristic analysis revealed that the sensitivity and specificity of systemic immune inflammation index with a cutoff value of 840.13 was 82 and 66.7%, respectively, for the diagnosis of acute appendicitis. Correlation analysis revealed that systemic immune inflammation index, Alvarado score, and adult appendicitis score were positively correlated, and this correlation was statistically significant.

**CONCLUSION:** Systemic immune inflammation index may be used to promote the diagnosis of acute appendicitis and may reduce the need for radiation exposure and diagnostic imaging tests such as contrast-enhanced abdominal computed tomography. It can also be used to differentiate between complicated and non-complicated acute appendicitis cases.

**KEYWORDS:** Appendicitis. Inflammation mediators. Systemic immune-inflammation index.

## INTRODUCTION

Acute appendicitis (AA) is one of the most common abdominal emergencies worldwide[1]. Lifetime risk is 8.6% in men and 6.7% in women[2]. In addition, AA is one of the most common causes of hospitalization in patients admitted to the emergency department with abdominal pain.

Clinical diagnosis of AA is often difficult and involves a synthesis of clinical, laboratory, and radiological findings. The diagnosis of AA can be made more accurately and reliably by using physical examination findings and inflammation markers. In addition, many scoring systems are used to estimate AA risk, including Alvarado score, acute appendicitis score, adult appendicitis score (AAS), Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score, appendicitis inflammatory response (AIR) score, and modified Alvarado score. Studies have shown that these scoring systems are helpful in the diagnosis and treatment of AA[3,4].

The systemic immune inflammation index (SIII) is a novel systemic inflammatory prognostic indicator associated with outcomes in patients with different tumors. Studies have shown an association between SIII and many chronic/acute inflammatory diseases[5]. Since SIII is easy to calculate, inexpensive, requires only complete blood count, and relies on no subjective findings, it will provide more accurate results in the diagnosis of AA.

Therefore, the aim of this study was to determine whether the diagnostic value SIII can be used as an effective parameter in the diagnosis of AA and its reliability in the distinction between complicated and non-complicated appendicitis.

## METHODS

### Study setting

This study began after obtaining the study approval from the ethics committee of our hospital (Ethics committee decision no.

[1]Başakşehir Çam ve Sakura Şehir Hastanesi, Department of Emergency Medicine – Istanbul, Turkey.
[2]Başakşehir Çam ve Sakura Şehir Hastanesi, Department of General Surgery – Istanbul, Turkey.
*Corresponding author: drkemalsener@hotmail.com
Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
Received on September 21, 2022. Accepted on October 23, 2022.

2021.04.35; dated: April 28, 2021). The study was conducted retrospectively and in a single center. The study was conducted between May 1, 2021, and May 1, 2022, with patients who were admitted to the emergency department with abdominal pain, diagnosed with AA, and met the criteria for inclusion in the study. Demographic data, medical history, WBC, platelet count, neutrophil count, SIII values, Alvarado scores, AAS, and pathology results of appendectomy material were retrieved from the hospital automation system [Hospital Information Management System (HIMS)] and recorded in the case form. The Alvarado score is a diagnostic score that is based on the symptoms (migratory pain, anorexia, nausea, and/or vomiting), signs (tenderness, rebound tenderness, and elevated body temperature), and laboratory findings (leukocytosis and left shift). One point was given to the presence of each indicator, except 2 points for tenderness and leukocytosis, making a total score of 10. AA cases were divided into two groups as complicated appendicitis and non-complicated appendicitis based on the presence of complications (gangrenous, perforated, and abscess formation). The study included 150 confirmed cases of AA and 150 control cases who were admitted to the emergency department with abdominal pain and not diagnosed with AA.

Study group patients with confirmed AA diagnosis and control group patients who were not diagnosed with AA after being admitted to the emergency department with abdominal pain were included in the study. In all, 3 patients under the age of 18 years, 5 pregnant patients, and 12 patients with missing data were excluded from the study. Also, 10 patients whose outcome could not be followed and whose medical history was unknown were not included in the study. In addition, 12 patients with any medical history of malignancy, a history of hematological disease, bone marrow pathology, and those taking anti-inflammatory or immunosuppressive drugs were also excluded from the study. In addition, patients with non-appendicitis infection focus were excluded from the study.

### Patient group

The control group was randomized from age- and gender-matched patients meeting the inclusion and exclusion criteria. As the control group, 150 patients who presented to the emergency department with the complaint of "abdominal pain" but were not diagnosed with AA were included. The group consisted of volunteers with a known medical history and no chronic disease history.

### Data calculation

In the study, calculations were made from the obtained results of the cases. P, N, and L refer to peripheral platelet, neutrophil, and lymphocyte counts, respectively. Accordingly, NLR (N/L ratio), PLR (P/L ratio), PNR (P/N ratio), and LNR (L/N ratio) were calculated. SIII calculated as $[(P\times N)/L)]^5$. Mortality evaluation was based on the mortality rates of the patients during hospital stay. Due to the retrospective design of the study, mortality after discharge and its causes were not evaluated.

### Statistical analyses

The data were analyzed with SPSS Package Program version 24.0. Number, percentage, mean, standard deviation, median, minimum, and maximum values were used in the presentation of descriptive data. The conformity of the data to normal distribution was evaluated by the Kolmogorov-Smirnov test. In the univariate analysis, continuous variables with normal distribution were expressed as mean±SD and compared using the t-test. Pearson's $\chi^2$ test was used in the analysis of categorical variables. For categorical variables, Fisher's exact test was used in cases with less than five variables. Spearman's correlation test was used in correlation analysis of multiple variables. Diagnostic accuracy was assessed using receiver operating characteristic (ROC) curve analysis. The appropriate cutoff values were determined, and the sensitivity and specificity values were calculated for the parameters with an area below the curve (AUC) above 0.600. A $p<0.05$ was accepted as statistically significant in all analyses.

## RESULTS

A total of 150 patients and 150 control cases were included in the study. The control group was randomly generated from age- and gender-matched patients. Mean age was 33.47±11.01 years in the patient group and 35.67±12.23 years in the control group. Mean pulse rate was significantly higher in the patient group compared to the control group. There was no significant difference between other vital parameters. WBC and neutrophil count were significantly higher and lymphocyte level was significantly lower in the patient group compared to the control group. There was no significant difference in platelet count between the two groups (Table 1).

Neutrophil-lymphocyte ratio (NLR) and SIII were significantly higher, and PNR and LNR were significantly lower in the patient group compared to the control group. There was no significant difference between the two groups with respect to mean PLR (Table 1).

The patient group was further subdivided as complicated and non-complicated cases based on the complication status. In all, 18 cases were evaluated as complicated appendicitis cases and 132 cases as non-complicated appendicitis cases. Both defense and rebound findings in physical examination

were significantly more common in complicated appendicitis cases. WBC and neutrophil count were significantly higher and lymphocyte count was significantly lower in complicated appendicitis cases compared with non-complicated cases. SIII, NLR, and PLR were significantly higher and PNR and LNR were significantly lower in complicated appendicitis cases.

Mean Alvarado score (14.5±2.83 and 11.40±1.98; p<0.001) and AAS (7.33±1.08 and 4.33±1.38; p<0.001) were significantly higher in complicated appendicitis cases. Peritonitis findings were significantly more pronounced in complicated appendicitis cases (p=0.003). There was no significant difference between the two groups in terms of mortality.

The ROC analysis revealed that the sensitivity and specificity of SIII with a cutoff value of 840.13 was 82 and 66.7%, respectively, for the diagnosis of AA. Furthermore, a cutoff value of 1782.94 for SIII had 88.9% sensitivity and 68.9% specificity for distinguishing between complicated vs. non-complicated cases (Figure 1 and Table 2).

Correlation analysis revealed that SIII, Alvarado score, and AAS were positively correlated, and this correlation was statistically significant.

## DISCUSSION

Acute appendicitis is one of the leading abdominal emergencies worldwide. The diagnosis of AA is still not clearly established in emergency room conditions with tests that prolong the process, are cost-ineffective, and lead to radiation exposure. There is a search for new diagnostic tools in order to make the diagnosis of AA more accurate, more reliable, and cheaper. Recent studies show that SIII is both an accurate indicator of inflammation and a useful ratio that helps predict the diagnosis and prognosis of many diseases[6-8]. SIII is a newly defined, simple, and inexpensive index that reflects the balance between inflammatory and immune responses. Based on the results of this study, it was found that SIII is a reliable index that can be used both in the diagnosis of AA and in the differentiation of complicated and non-complicated AA cases.

Leukocyte count is one of the most commonly used diagnostic methods in the diagnosis of AA. However, the sensitivity and specificity of leukocyte count for the diagnosis of AA is limited[9]. In this study, leukocyte count was higher in the patient group diagnosed with AA. Likewise, NLR and PLR have been used as auxiliary parameters in the diagnosis and prognosis of many diseases[10-12]. In this study, NLR was significantly higher in patients diagnosed with AA, while no significant difference was found in PLR. In addition, based on the results of this study, PNR and LNR are also diagnostic ratios that can be used in the diagnosis of AA.

In patients with suspected AA, these ratios can optimize the use of risk classification with clinical scoring systems and diagnostic imaging, as well as guide decision-making to prevent negative exploratory surgeries. Due to these scoring systems, both unnecessary radiological examinations for AA diagnosis

**Table 1.** Comparison of demographic and clinical data of the patient and control groups.

| Parameter | Subparameter | Patient group | Control group | p |
|---|---|---|---|---|
| Age | | 33.47±11.01 | 35.67±12.23 | 0.102* |
| Gender | Female | 65 (48.5) | 69 (51.5) | 0.642* |
| | Male | 85 (51.2) | 81 (48.8) | |
| Vital parameters | Systolic BP (mmHg) | 128.65±26.47 | 132.29±20.85 | 0.187** |
| | Diastolic BP (mmHg) | 77.50±16.57 | 77.43±13.88 | 0.970** |
| | Pulse (pulse/min) | 94.03±19.71 | 88.79±16.81 | **0.014**** |
| Laboratory values | WBC (×10$^9$/L) | 13.42±4.57 | 8.72±2.89 | **<0.001**** |
| | Neutrophil (×10$^9$/L) | 7.75±5.41 | 4.10±4.84 | **<0.001**** |
| | Lymphocytes (×10$^9$/L) | 1.75±0.75 | 2.07±1.04 | **0.004**** |
| | Platelet (×10$^9$/L) | 238.06±68.98 | 254.89±66.18 | 0.032** |
| Ratios | NLR | 7.75±5.41 | 4.10±4.84 | **<0.001**** |
| | PLR | 162.27±90.03 | 156.88±113.04 | 0.648** |
| | PNR | 27.13±16.18 | 51.78±24.04 | **<0.001**** |
| | LNR | 0.21±0.17 | 0.43±0.265 | **<0.001**** |
| | SIII (×10$^9$/L) | 1759.62±1263.92 | 979.96±1032.33 | **<0.001**** |

*Pearson's $\chi^2$ test was used; **t-test was used. BP: blood pressure; NLR: neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; PNR: platelet-neutrophil ratio; LNR: lymphocyte-neutrophil ratio; SIII: systemic immune inflammatory index; WBC: white blood cells. Bold indicates statistically significant p-values.

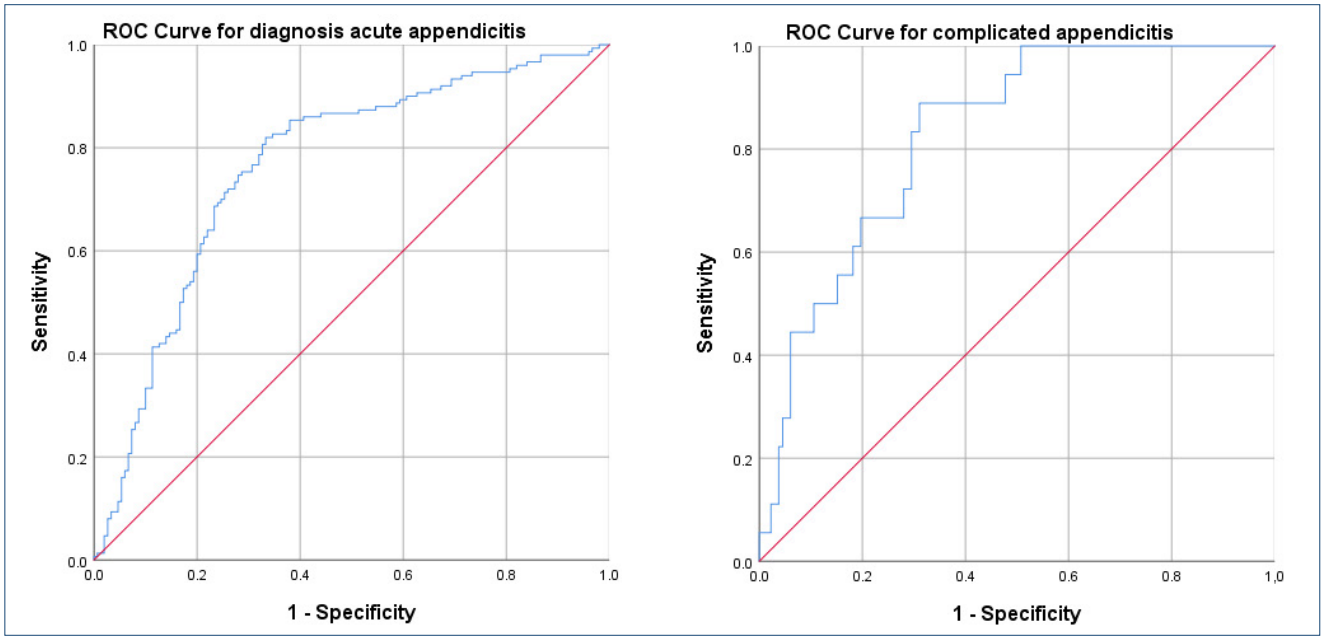


**Figure 1.** Systemic immune inflammation index receiver operating characteristic analysis for diagnosis of acute appendicitis and identifying complications.

**Table 2.** Systemic immune inflammation index receiver operating characteristic analysis results for the diagnosis of acute appendicitis and identifying complications.

| Parameter | Cutoff value | Sensitivity | Specificity | Area under curve (AUC) | 95%CI | | p |
|---|---|---|---|---|---|---|---|
| | | | | | Lower bound | Upper bound | |
| Diagnostic value of SIII | 840.13 | 82.0 | 66.7 | 0.764 | 0.709 | 0.819 | **<0.001** |
| SIII for differentiating between complicated vs. non-complicated cases | 1782.94 | 88.9 | 68.9 | 0.826 | 0.744 | 0.909 | **<0.001** |

ROC: receiver operating characteristic; SIII: systemic immune inflammatory index. Bold indicates statistically significant p-values.

and unnecessary surgeries are prevented. Many scoring systems such as Alvarado score, AAS, and AIR can be used in the diagnosis and risk classification of AA. In a meta-analysis, Kularatna et al. reported that the AIR scoring system was the most successful scoring system in terms of sensitivity and specificity[3,4,13,14]. Among the scoring systems evaluated in this study, Alvarado score and AAS were more successful in complicated AA cases compared to non-complicated cases. This is due to the fact that physical examination and peritoneal irritation findings and inflammatory markers are more prominent in complicated AA patients.

To the best of our knowledge, there are no studies in the literature investigating the diagnostic power of SIII for AA. Similarly, there are no studies investigating the efficacy of SIII in the distinction of complicated vs. non-complicated AA. In this study, the cutoff value of 840.13 ($\times 10^9$/L) for SIII had 82% sensitivity and 66.7% specificity. In addition, the cutoff value of 1,782.94 ($\times 10^9$/L) had 88.9% sensitivity and 88.9% specificity for differentiating between complicated and non-complicated cases. Compared to the study by Khairol et al., the sensitivity of SIII obtained in this study is higher than that of NLR, and its specificity is the same[15].

Dey et al. examined AA cases that were diagnosed histopathologically and found that there were misdiagnosed cases. For this reason, they investigated the correlation between histopathological diagnosis and Alvarado score and found a statistically significant positive correlation[16]. Canbak et al. investigated the correlation between Alvarado score and ultrasonography in the diagnosis of AA and found that their combined use reduced the rates of misdiagnosis and missed diagnosis[17]. In another study, Sousa-Rodrigues et al. found that the Alvarado score and the macroscopic appearance of the appendix were correlated for the diagnosis of AA; however,

this correlation only occurred in the advanced stage of AA[18]. In this study, both Alvarado score and AAS were positively correlated with SIII. This indicates that SIII can be successfully used in the diagnosis of AA. When evaluated together with Alvarado score and AAS, SIII will reduce the rates of misdiagnosis and missed diagnosis in AA cases.

## CONCLUSION

Based on the results of this study, SIII may be used to promote the diagnosis of AA, and it can reduce the need for diagnostic imaging tests with radiation exposure, such as contrast-enhanced abdominal computed tomography. SIII is cost-effective and easy to calculate, and its use with Alvarado score and AAS will reduce both misdiagnosis and unnecessary operation rates.

### Limitations

The limitations of our study are that it is a retrospective, single-center study. There is a need for multicenter, prospective studies with more patients.

## ETHICAL APPROVAL

This study was approved by the Ministry of Healthy Başaksehir Çam and Sakura State Hospital Ethics Committee (decision no.: 2021.04.34). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

## AVAILABILITY OF DATA AND MATERIALS

Ministry of Healthy Başaksehir Çam and Sakura State Hospital computer data system was used.

## AUTHORS' CONTRIBUTIONS

**KŞ**: Conceptualization, Methodology, Writing – review & editing. **AÇ**: Conceptualization, Methodology, Writing – review & editing. **HK**: Conceptualization, Writing – review & editing. **EA**: Methodology, Writing – review & editing. **RG**: Conceptualization, Methodology.

## REFERENCES


1. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet. 2015;386(10000):1278-87. https://doi.org/10.1016/S0140-6736(15)00275-5. Erratum in: Lancet. 2017;390(10104):1736. PMID: 26460662.
2. Snyder MJ, Guthrie M, Cagle S. Acute appendicitis: efficient diagnosis and management. Am Fam Physician. 2018;98(1):25-33. PMID: 30215950
3. Di Saverio S, Podda M, De Simone B, Ceresoli M, Augustin G, Gori A, et al. Diagnosis and treatment of acute appendicitis: 2020 update of the WSES Jerusalem guidelines. World J Emerg Surg. 2020;15(1):27. https://doi.org/10.1186/s13017-020-00306-3
4. Kularatna M, Lauti M, Haran C, MacFater W, Sheikh L, Huang Y, et al. Clinical prediction rules for appendicitis in adults: which is best? World J Surg. 2017;41(7):1769-81. https://doi.org/10.1007/s00268-017-3926-6
5. 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(23):6212-22. https://doi.org/10.1158/1078-0432.CCR-14-0442
6. Liu X, Guan G, Cui X, Liu Y, Liu Y, Luo F. Systemic immune-inflammation index (SII) can be an early indicator for predicting the severity of acute pancreatitis: a retrospective study. Int J Gen Med. 2021;14:9483-9. https://doi.org/10.2147/IJGM.S343110
7. Chen JH, Zhai ET, Yuan YJ, Wu KM, Xu JB, Peng JJ, et al. Systemic immune-inflammation index for predicting prognosis of colorectal cancer. World J Gastroenterol. 2017;23(34):6261-72. https://doi.org/10.3748/wjg.v23.i34.6261
8. Mazza MG, De Lorenzo R, Conte C, Poletti S, Vai B, Bollettini I, et al. Anxiety and depression in COVID-19 survivors: role of inflammatory and clinical predictors. Brain Behav Immun. 2020;89:594-600. https://doi.org/10.1016/j.bbi.2020.07.037
9. Agrawal CS, Adhikari S, Kumar M. Role of serum C-reactive protein and leukocyte count in the diagnosis of acute appendicitis in Nepalese population. Nepal Med Coll J. 2008;10(1):11-5. PMID: 18700623
10. Yao C, Liu X, Tang Z. Prognostic role of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio for hospital mortality in patients with AECOPD. Int J Chron Obstruct Pulmon Dis. 2017;12:2285-90. https://doi.org/10.2147/COPD.S141760
11. Wang D, Bai N, Hu X, Ou Yang XW, Yao L, Tao Y, et al. Preoperative inflammatory markers of NLR and PLR as indicators of poor prognosis in resectable HCC. PeerJ. 2019;7:e7132. https://doi.org/10.7717/peerj.7132
12. Paliogiannis P, Fois AG, Sotgia S, Mangoni AA, Zinellu E, Pirina P, et al. Neutrophil to lymphocyte ratio and clinical outcomes in COPD: recent evidence and future perspectives. Eur Respir Rev. 2018;27(147):170113. https://doi.org/10.1183/16000617.0113-2017
13. Andersson M, Kolodziej B, Andersson RE, STRAPPSCORE Study Group. Randomized clinical trial of appendicitis inflammatory response score-based management of patients with suspected appendicitis. Br J Surg. 2017;104:1451-61. https://doi.org/10.1002/bjs.10637
14. Coleman JJ, Carr BW, Rogers T, Field MS, Zarzaur BL, Savage SA, et al. The Alvarado score should be used to reduce emergency department length of stay and radiation exposure in select patients with abdominal pain. J Traum Acute Care Surg. 2018;84(6):946-50. https://doi.org/10.1097/TA.0000000000001885

15. Ahmad KA, Ideris N, Aziz SHSA. A cross-sectional study of neutrophil-to-lymphocyte ratio in diagnosing acute appendicitis in hospital melaka. Malays J Med Sci. 2019;26(6):55-66. https://doi.org/10.21315/mjms2019.26.6.6

16. Dey S, Mohanta PK, Baruah AK, Kharga B, Bhutia KL, Singh VK. Alvarado scoring in acute appendicitis-a clinicopathological correlation. Indian J Surg. 2010;72(4):290-3. https://doi.org/10.1007/s12262-010-0190-5

17. Canbak T, Acar A. Does alvarado score reduce the need for ultrasonography in the diagnosis of acute appendicitis? Niger J Clin Pract. 2020;23(6):764-7. https://doi.org/10.4103/njcp.njcp_328_19

18. Sousa-Rodrigues CF, Rocha AC, Rodrigues AK, Barbosa FT, Ramos FW, Valões SH. Correlation between the Alvarado Scale and the macroscopic aspect of the appendix in patients with appendicitis. Rev Col Bras Cir. 2014;41(5):336-9. https://doi.org/10.1590/0100-69912014005007