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Systemic inflammation response index and systemic immune-inflammation index for predicting complications of acute appendicitis: A retrospective study

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ABSTRACT

Objective: To investigate the value of systemic inflammatory response index (SIRI) and systemic immune-inflammation index (SII) in predicating acute appendicitis complications based on hemogram parameters.

Methods: Demographic data, histopathological studies, and laboratory results of the patients who were admitted to the emergency department with a complaint of abdominal pain between January 2020 and June 2022 and were hospitalized with the diagnosis of acute appendicitis for operation by general surgery were examined. Simple appendicitis and complicated appendicitis groups were compared in terms of parameters according to their histopathological examinations.

Results: A total of 220 patients who met the inclusion criteria were included in our study. Mean SIRI levels were found to be significantly higher in the complicated appendicitis group than in the simple appendicitis group [6.60 (4.07, 14.40) *vs*. 3.50 (2.20, 6.80); *P*=0.002]. Similarly, SII levels were found to be significantly higher in the complicated appendicitis group compared to the simple appendicitis group [2514.50 (1132.25, 5388.00) *vs.* 1207.00 (571.50, 2089.00), *P*<0.001]. The power of SIRI and SII to indicate complications was higher than white blood cell count and C-reactive protein (area under the curve: 0.753 and 0.786, respectively).

Conclusion: SIRI and SII could be used to indicate complications in patients with acute appendicitis.

KEYWORDS: Appendicitis; Diagnosis; SII; SIRI; Inflammation

1. Introduction

Acute appendicitis (AA) is one of the most common surgical conditions in patients presenting to the emergency department with abdominal pain, and the necessity of emergency surgical intervention was accepted by many physicians[1]. The lifetime risk of this disease is approximately 7% in men[2]. Many cases are in the form of simple appendicitis (SA) and there are no complications. However, the possibility of complicated appendicitis (CA) may occur in certain groups of patients, especially in the elderly[3]. The diagnosis can usually be made with a simple physical examination, history, and laboratory analyses, however, delayed diagnosis, especially in complicated patients, may result in longer hospital

Significance

Many inflammatory biomarkers are used in diagnosis and complications. This study compared inflamatory markes. The results showed that SIRI and SII are two simple parameters that can be used to show acute appendicitis complication with its easy applicability and fast calculation.

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stays, raised costs, and increased mortality rates. In these patients, early diagnosis and then rapid intervention should be performed to prevent complications[4,5].

Many studies have been done aiming to detect and diagnose CA early. Clinicians should pay attention to inflammation parameters such as white blood cell (WBC) count, C-reactive protein (CRP), mean platelet volume, red cell distribution width, and platelet distribution width, immature granulocyte as well as the ratio of hemogram parameters, *i.e.* neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR)[6-8]. If these biomarkers and imaging techniques are used together, they can provide the benefit of rapid diagnosis. Therefore, specific new biomarkers are needed to catch complications. The systemic inflammatory response index (SIRI), which is evaluated based on hemogram parameters that can be obtained by dividing neutrophil count×monocytes count to lymphocyte count, and is used as a biomarker in many inflammatory diseases, especially in oncological disorders[9,10]. Another biomarker calculated from hemogram parameters is the systemic immune-inflammation index (SII), which can be obtained as neutrophil count×thrombocyte count/lymphocyte count, and is similarly used by clinicians as an inflammation marker[11]. There is no clear determination in the literature regarding the utility of SIRI and SII in detecting complications of AA. Hence, in this study, we investigated the value of SIRI and SII for predicting complications in patients with AA.

2. Patients and methods

2.1. Study setting

This retrospective study included patients who were admitted to the emergency department with a complaint of abdominal pain between January 2020 and June 2022 and were hospitalized with the diagnosis of AA for operation by general surgery.

2.2. Ethical approval

Ethics approval of this study was obtained from the Non-Interventional Clinical Research Ethics Committee of Health Sciences University Antalya Training and Research Hospital (2022/12).

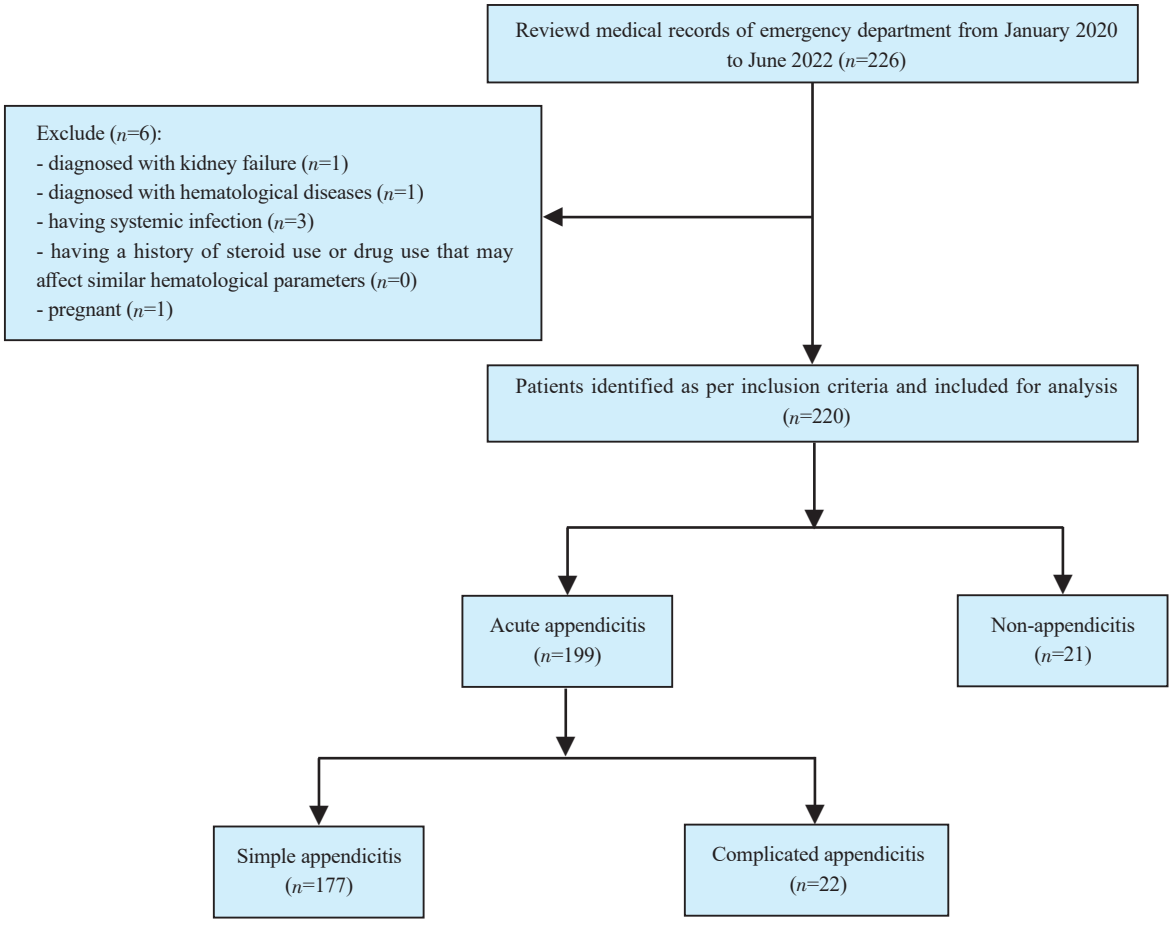

Figure 1. The study flowchart.

2.3. Inclusion criteria exclusion criteria

Patients aged 18 years or older, diagnosed with AA, and underwent general surgery were included in the study. Patients who were younger than 18 years of age, diagnosed with kidney failure and hematological diseases, having systemic infection findings and sepsis, having a history of steroid use or drug use that may affect similar hematological parameters, not undergoing surgery, referred to an external center, and pregnant, were excluded from the study. Demographic data, laboratory data, and pathology results of 220 patients who met the inclusion criteria were evaluated.

2.4. Data collection

The hemogram parameters taken within the first hour of the patient's entrance to the emergency department were evaluated in the emergency laboratory before the operation. WBC, neutrophils, lymphocytes, platelets, monocytes, and immature granulocytes were measured from the routine hemogram parameters of the patients. Demographic data, histopathological examinations, and CRP values were recorded. NLR and PLR values were obtained from the ratio of neutrophils or platelet to lymphocytes, respectively. SIRI was calculated as (neutrophil×monocytes)/lymphocyte and SII was calculated as (neutrophil×platelet)/lymphocyte. The patients included in the study were grouped as AA and non-appendicitis as a result of the histopathological examination after the operation. The patients with AA were then grouped as simple and complicated (gangrenous, perforated, and abscess) according to their histopathological examinations. All demographic and laboratory data were statistically compared.

2.5. Statistical analysis

SPSS 21.0 was used for the analysis of the statistical data of our study. A *P*-value of <0.05 was considered significant. Parametric or non-parametric methods were used according to the normal distribution. Student *t*-test or Mann-Whitney *U* test were used to compare continuous variables and the results were expressed as mean±standard deviation or medium, Q1, Q3. Chi-square or Fisher's exact tests were used to compare categorical variables and the results were expressd as frequency and percentage (%). The receiver operating characteristic analysis has been performed to show complications in patients with AA, and the higher the area under the curve (AUC) values, the better the diagnostic values.

3. Results

A total of 220 patients who met the inclusion criteria were included in our study, of which 199 (90.40%) were in the AA group and 21 (9.60%) were in the non-appendicitis group (Figure 1). Among the male patients, 118 (59.20%) of them had AA, and 7 (33.30%) were

Table 1. Comparison between acute appendicitis and non-acute appendicitis groups regarding the laboratory parameter.

Variables	Acute appendicitis (*n*=199)	Non–appendicitis (*n*=21)	$t/U/\chi^2$	*P*
Age, years, mean±SD	38.50±14.70	41.30±15.50	0.876^t	0.381
Male, *n*, %	118 (59.20)	7 (33.30)	5.194^C	0.022*
WBC, $\times10^3$/mL, mean±SD	12.11±5.07	10.20±2.57	2.615^t	0.009*
Neutrophils, $\times10^3$/mL, mean±SD	9.34±4.45	9.04±3.41	0.770^t	0.770
Lymphocytes, $\times10^3$/mL, mean±SD	1.58±0.44	1.57±0.77	0.662^t	0.662
CRP, mg/L, median, Q1, Q3	129.30 (83.60, 163.75)	103.20 (82.60, 121.25)	2.231^U	0.026*
NLR, median, Q1, Q3	7.20 (6.00, 8.50)	5.60 (4.25, 7.25)	0.075^U	0.941
PLR, median, Q1, Q3	179.80 (162.25, 193.75)	188.20 (165.25, 202.21)	0.124^U	0.902
SIRI, median, Q1, Q3	5.89 (4.90, 7.20)	3.12 (2.00, 4.20)	3.181^U	<0.001*
SII, median, Q1, Q3	1735.10 (823.80, 1989.25)	812.10 (662.10, 1012.32)	3.081^U	0.002*

[t]Student *t*-test; [C]Chi-squre test;[U] Mann-Whitney *U* test; WBC: white blood cell; CRP: C-reactive protein; NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; SIRI: systemic inflammatory response index; SII: systemic immune-inflammation index. *Significant at α=0.05.

Table 2. Comparison between complication groups regarding the laboratory parameter.

Variables	Simple appendicitis (*n*=177)	Complicated appendicitis (*n*=22)	$t/U/\chi^2$	*P*
Age, years, mean±SD	38.30±14.10	48.10±14.40	3.069^t	0.002*
Male, *n*, %	107 (60.50)	11 (50.00)	0.886^C	0.347
WBC, $\times10^3$/mL, mean±SD	11.57±4.01	16.38±9.25	2.615^t	0.009*
Neutrophils, $\times10^3$/mL, mean±SD	8.98±3.81	12.14±7.44	1.934^t	0.053
Lymphocytes, $\times10^3$/mL, mean±SD	1.63±0.72	1.04±0.54	3.708^t	<0.001*
CRP, mg/L, median, Q1, Q3	86.70 (44.55, 158.75)	118.00 (96.75, 186.75)	2.231^U	0.026*
NLR, median, Q1, Q3	5.55 (3.36, 9.36)	10.27 (4.22, 15.5)	2.369^U	0.018*
PLR, median, Q1, Q3	151.16 (104.37, 220.31)	181.18 (136.53, 306.21)	2.329^U	0.020*
SIRI, median, Q1, Q3	3.50 (2.20, 6.80)	6.60 (4.07, 14.40)	3.129^U	0.002*
SII, median, Q1, Q3	1207.00 (571.50, 2089.00)	2514.50 (1132.25, 5388.00)	3.837^U	<0.001*

[t]Student *t*-test; [C]Chi-squre test;[U] Mann-Whitney *U* test; WBC: white blood cell; CRP: C-reactive protein; NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; SIRI: systemic inflammatory response index; SII: systemic immune-inflammation index. *Significant at α=0.05.

Table 3. Receiver operating characteristic analysis of parameters in the prediction of complicated appendicitis.

Variables	Cut-off	AUC (95% *CI*))	Sensitivity (%)	Specificity (%)	*P*
WBC, $\times 10^3$/mL	>11.26	0.673 (0.549-0.798)	72.7	56.8	0.008*
CRP, mg/L	>100	0.673 (0.539-0.745)	63.6	54.6	0.031*
SIRI	>4.65	0.753 (0.648-0.858)	68.2	60.5	0.002*
SII	>1465	0.786 (0.586-0.820)	72.7	64.2	<0.001*

WBC: white blood cell; CRP: C-reactive protein; SIRI: systemic inflammatory response index; SII: systemic immune-inflammation index. *Significant at α=0.05.

in the non-appendicitis group. There was a significantly higher percentage of male patients in the AA group (*P*=0.022). WBC, CRP, SII, and SIRI values were significantly higher in the AA group than in that of the non-appendicitis group. While the mean SII levels were 1735.10 (823.80, 1989.25) in the AA group, it was 812.10 (662.10, 1012.32) in the non-appendicitis group (*P*=0.002). The mean SIRI levels were 5.89 (4.90, 7.20) in the AA group, while it was 3.12 (2.00, 4.20) in the non-appendicitis group (*P*<0.001). The investigation between the AA and non-appendicitis group was listed in Table 1.

According to the pathology results, the patients in the AA were then separated into two groups of SA and CA. The mean age of the CA group was significantly higher than the SA group (48.10±14.00 *vs*. 38.30±14.10; *P*=0.002). The mean lymphocyte count was significantly lower in the CA group compared to the SA group (1.04±0.54 *vs*. 1.63±0.72; *P*<0.001). Mean WBC, CRP, NLR, and PLR levels were significantly higher in the CA group (*P*<0.05). Mean SIRI levels were found to be significantly higher in the CA group than in the SA group (*P*=0.002). While the mean SIRI levels were 6.60 (4.07, 14.40) in the CA group, it was 3.50 (2.20, 6.80) in the SA group. In addition, SII levels were found to be significantly higher in the CA group than in the SA group (*P*<0.001). While the mean SII levels were 2514.50 (1132.25, 5388.00) in the CA group, it was 1207.00 (571.50, 2089.00) in the SA group. The comparison between the parameters in establishing the complication in patients with AA is given in Table 2.

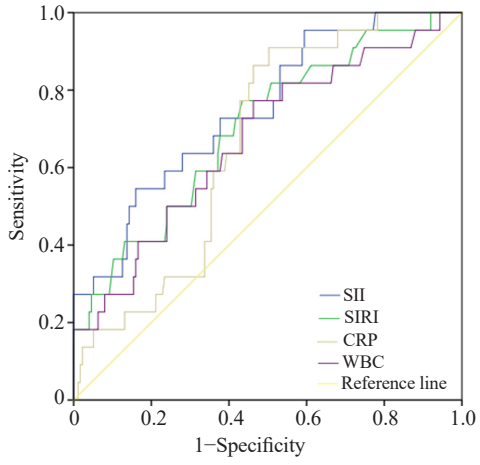

Figure 2. Receiver operating characteristic curve showing the efficiency of SII, SIRI, CRP and WBC parameters. SII: systemic immune-inflammation index; SIRI: systemic inflammatory response index; CRP: C-reactive protein; WBC: white blood cell.

The efficiency of WBC, SIRI, SII, and CRP parameters in differentiating SA and CA was estimated by drawing the receiver operating characteristic curves (Figure 2). The efficacy of WBC, SIRI, SII, and CRP in demonstrating complications was statistically significant. The power of SIRI and SII was higher AUC value in indicating complications. The AUC for SIRI was 0.753 (sensitivity: 0.682, specificity: 0.605, *P*=0.002). The AUC for SII was 0.786 (sensitivity: 0.727, specificity: 0.642, *P*<0.001) (Table 3, Figure 2).

4. Discussion

AA is one of the most common reasons for admission to the emergency department, and anamnesis, physical examination, and laboratory tests often help the diagnosis. Recently developed biomarkers and imaging methods are also important because they can show both the diagnosis and the complications that may develop in these patients[12,13]. Our study showed that SIRI and SII can predict complications in patients with AA.

Many inflammatory markers have been used in recent years both in the diagnosis of patients with AA and to show complications. The main ones are WBC, sedimentation, CRP, mean platelet volume, and red cell distribution width[7,14]. Since almost none of these markers can demonstrate in the diagnosis and complication of AA, studies are shifting towards inflammatory markers obtained by the ratio of these parameters to each other. The most commonly used one is the ratio of NLR, PLR, and neutrophil/CRP ratio[2,6]. In recent years, it has been shown that SIRI and SII can be used effectively, especially in studies on the prognosis of cardiovascular patients[15]. In our study, we demonstrated the usability of SIRI and SII in patients with AA.

SII has been used in many studies in current years as a marker of systemic inflammation that can be used in the prognosis and diagnosis of many diseases, especially in malignancy patients[10]. Gok *et al*. found that there is a significant relationship between high levels of SII and the severity of patients with pulmonary embolisms. In this study, it was emphasized that SII has a more practical use than its routine role as an inflammatory marker[16]. Xu *et al*. reported that SII might show the interaction of thrombocytosis, inflammation, and immunity in the development of cerebrovascular diseases in middle-aged and elderly populations[17]. In Candemir *et al*.'s study of SII, a significant correlation was demonstrated between the easily accessible SII and the severity of coronary artery disease in patients

with stable angina pectoris[18]. When studying the Behçet disease, Tanacan *et al* found that it was shown that increased SII levels can be used with high sensitivity and specificity in demonstrating disease activity[19]. In the study conducted by Cakcak *et al*., although SII has shown that it can predict complications in patients with AA, it was reported that this study included patients with delayed surgery during the COVID-19 pandemic period[20]. In our study, we showed that the optimum cut-off value of SII is 1 465, and it can predict complications with a sensitivity of 0.727 and a specificity of 0.642 in patients with AA.

SIRI, which is used likewise to SII, has also been used as an inflammatory marker in many diseases, especially oncological diseases. Since this parameter is a peripheral blood-based parameter, it is easily available by physicians and has been used as a biomarker for the diagnosis and prognosis of many diseases[21]. Lattanzi *et al*. emphasized that SIRI may be a predictor of endovascular reperfusion in stroke patients[22]. In another study, it was reported that SIRI could be used as an independent prognostic index in patients with esophageal squamous cell carcinoma after radical resection, and the nomogram integrating SIRI could help clinicians to screen high-risk patients and formulate individualized treatment schemes[23]. In the study conducted by Zhang *et al*., it was shown that increased SIRI was associated with the severity of stroke[24]. In our study, we found a significant association between increased SIRI values and AA complications.

Our study had some limitations. The first one is the retrospective single-center design. Another one is that taking inflammation markers at the time of admission to the emergency department does not rule out the dynamic change of these markers. The other limitation of our study is the inability to detect the relationship between SII and SIRI, and other inflammation markers such as interleukins and thromboxane. Prospective multicenter studies are needed for the analysis of the data in our study.

In conclusion, in this study, we showed that SIRI and SII are two of the parameters that can predict complications in patients with AA. However, there is a need for prospective studies involving many biochemical parameters.

Conflict of interest statement

The authors report no conflict of interest.

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Authors' contributions

GY, ÖZ, and FS collected and curated the data. GY, FS, CB and ÖZ contributed to writing the manuscript. All authors read and approved the final manuscript.

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