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RESEARCH

The diagnostic value of the systemic immune-inflammatory index in acute appendicitis cases in the emergency department

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Abstract

Background and aim Acute appendicitis (AA) is one of the most common causes of acute abdomen conditions and continues to cause mortality and morbidity despite all the improvements. There is still a necessity for inexpensive and easily calculable index and scoring systems with fewer side effects for the diagnosis of AA and the detection of complications. Since the systemic immune-inflammation index (SIII) is an index that could be used in this context, we aimed to measure the success and reliability of SIII for the diagnosis of AA and related complications and to contribute to the literature.

Methods Our study was carried out retrospectively in a tertiary care hospital and conducted with 180 AA patients (study group-SG) and 180 control group (CG) patients. Demographic data, laboratory data, and clinical data of the cases, as well as the Alvarado score (AS), adult appendicitis score (AAS), and SIII and neutrophil/lymphocyte ratio (NLR) values calculated from laboratory data, were recorded in the previously created study form. $p<0.05$ was accepted as the significance level for the study.

Results In this study, age and gender were similar in the SG and CG groups. SIII and NLR levels calculated in SG cases were found to be significantly higher than CG. In addition, SIII and NLR levels were found to be significantly higher in complicated AA cases than in complicated cases. Although SIII was more significant in the diagnosis of AA, NLR was more successful than SIII in detecting the presence of complications. SIII, NLR, AAS, and AS were significantly positively correlated in the diagnosis of AA. In the presence of peritonitis, SIII and NLR were also found to be significantly higher when compared to cases without peritonitis.

Conclusions We found that SIII is a usable index in the diagnosis of AA and the prediction of complicated AA. However, NLR was found to be more significant than SIII in estimating complicated AA. In addition, it is recommended to be careful in terms of peritonitis in cases with high SIII and NLR levels.

Keywords Acute appendicitis · Complication · Systemic immune-inflammatory index · Alvarado score

Introduction

Acute appendicitis (AA) is one of the common causes of acute abdomen conditions [1]. The mortality rate of this surgically treatable pathology is low which is at the level of 7–70/1000 [2, 3]. In the physiopathology of AA, inflammation that occurs after lumen occlusion stands out. This inflammation is followed by necrosis, and in case of delays in its treatment, the process may lead to perforations [4]. Although it is known that surgical intervention is the golden standard in terms of treatment, for diagnosis, clinical presentation and imaging methods are included in addition to scoring systems such as the Alvarado scoring system. Computed tomography (CT) is the most widely used imaging method. However, new biomarkers and indices are needed for AA due to radiation exposure and economic burden [5].

Studies revealed that peripheral blood cells are associated with malignant tumors and inflammatory diseases [6–8]. In addition, systemic inflammation scores have been associated with many inflammatory diseases with

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the formula created using inflammatory cell counts such as neutrophil/lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) [8, 9].

The systemic immune inflammation index (SIII), with neutrophils, lymphocytes, and platelets, was first introduced by Hu in 2014 to evaluate the prognosis of hepatocellular carcinoma [10]. It has recently been used as an indicator to predict the presence and evaluate the progression of neurological diseases, inflammatory diseases, and carcinomas [11–13].

This study aimed to measure the success and reliability of SIII in the diagnosis of AA, to determine the presence of complications, and to contribute to the literature by so.

Material/method

Study setting and study population

The study was carried out retrospectively, in a single center, in the emergency department of a tertiary education and research hospital. One hundred eighty SG and CG patients with a confirmed diagnosis of AA who applied to the emergency department between January 1, 2021, and January 1, 2022, are included in this study.

Among the patients who came to the emergency department with abdominal pain, those who were diagnosed with AA after evaluation and whose diagnosis was confirmed from the pathology material sent, postoperatively, and those who met the study criteria were included in the study. For the study, data were obtained using patient files and an automation system. The automation system was scanned using the "K35.0, K35.1, K35.9, K36" ICD-10 diagnostic codes, and 253 suitable patients were identified. Among these patients, patients aged 18 years or older and diagnosed with AA after definitive pathological results were included in the study. Patients under the age of 18 (36 patients), pregnant patients (4 patients), and patients diagnosed with any condition other than AA after the pathological examination (11 patients) were not included in the study. In addition, patients with a diagnosis of malignancy in their medical history (2 patients), a history of hematological disease (8 patients), and septic patients (12 patients) with significant infectious findings according to the laboratory results were also excluded from the study. Patients with unstable vital signs who were in shock when they applied were not included either.

The included cases were divided into two groups. One hundred eighty cases with AA were defined as SG. Then, 180 patients of similar age and gender, who had abdominal pain and no pathology was found as a result of the evaluation, were considered CG.

Data collection

Demographic data of the cases (age and gender), clinical data (fever presence at admission, complaints on admission (nausea, vomiting, loss of appetite, presence of pain, changes in the location of the pain, presence of rebound and defense), laboratory data (white blood cells (WBC), neutrophil level, neutrophil percentage, lymphocyte level, thrombocyte level, C-reactive protein (CPR) level, and SIII and NLR levels obtained using these values), definitive pathology results of the patients and presence of complications (complicated AA: gangrenous AA; perforated AA and abscess) recorded in the previously created form and archived with sequence numbers.

The data of CG were also recorded in the previously created form and archived similarly.

After the study was completed, the data were transferred to digital media, and statistical analysis was performed.

In our study, NLR was calculated with the formula: neutrophil level/lymphocyte level; SIII was calculated with the formula as (neutrophil level x platelet level)/lymphocyte level.

Statistical analysis

Statistical analysis was performed using SPSS 23.0 for Windows® statistical program (IBM Inc. Chicago, IL, USA). Number, percentage, mean, standard deviation, median, minimum, and maximum values were used in the presentation of descriptive data. The conformity of the data to the normal distribution was evaluated with the Kolmogorov-Smirnov test. Pearson's chi-square test was used to compare categorical data. *T*-test was used to compare two independent numerical data.

Pearson's correlation analysis was used for the correlation of the quantitative values of the cases. In addition, ROC curve analysis was performed to evaluate the predictive value of SIII and NLR for the diagnosis of AA and complicated AA, and AUC, cut-off, sensitivity, and specificity values were determined.

Results were considered significant at $p<0.05$, with a 95% confidence interval.

Results

Our study was conducted with a total of 180 SG and 180 CG patients. Seventy percent ($n=126$) of the SG were male, and the mean age was 31.12±9.20 years. 69.4% ($n=125$) of CG were male, and the mean age was

29.48±7.35 years. Age and gender ratios were similar in both groups.

In our study, the relationship between laboratory values in SG and CG was investigated and while the lymphocyte level was statistically significantly higher in CG; all other parameters were significantly higher in SG ($p<0.001$) (Table 1).

When the differences in clinical and laboratory values between complicated AA cases and uncomplicated AA cases were examined, it was observed that while lymphocyte level was significantly lower in complicated cases, WBC, neutrophil, neutrophil percentage, SIII, and NLR were found to be significantly higher. No significant correlation was found between CRP and PLT levels and complications. Moreover, in complicated AA cases, not only AAS and AS were found to be significantly higher but also the presence of peritonitis was significantly higher (Table 2).

Table 1 Comparison of demographic and laboratory data of SG and CG patients

Parameter		Study group (n=180) n (%)/mean±SD	Control group n (%)/mean±SD	%95 CI	p^t
Age (years)		31.12±9.20	29.48±7.35	−0.82 to 3.37	0.262
Gender	Male	126 (70.0)	125 (69.4)	-	0.909
Laboratory results	WBC ($\times10^3$/mm^3)	13.35±3.93	11.9±3.00	0.70–2.15	**<0.001**
	Neutrophil ($\times10^3$/mm^3)	10.71±4.15	7.81±2.68	2.17–3.62	**<0.001**
	Neutrophil Percentage	0.78±0.09	0.64±0.07	0.12–0.15	**<0.001**
	Lymphocyte ($\times10^3$/mm^3)	2.64±1.04	3.02±0.90	−0.58 to 0.17	**<0.001**
	PLT ($\times10^3$/mm^3)	379.02±133.81	253.31±68.21	173.69–247.72	**0.028**
	CRP (mg/dL)	36.53±60.59	3.95±.01	23.65–41.50	**<0.001**
	SIII ($\times10^3$/mm^3)	2438.88±1987.14	1282.90±1193.33	816.20–1495.74	**<0.001**
	NLR	5.10±3.89	2.89±1.64	1.59–2.83	**<0.001**

WBC, white blood cell; *PLT*, platelet; *CRP*, C reactive protein; *SIII*, systemic immune-inflammation index; *NLR*, neutrophil/lymphocyte ratio

Table 2 Comparison of demographic, clinical, and laboratory data of patients with complicated and uncomplicated AA

Parameter		Complicated AA (n=36) n (%)/mean±SD	Uncomplicated AA (n=144) n (%)/mean±SD	p
Fever (°C)		37.38±0.99	36.73±0.78	**<0.001**
Laboratory results	WBC ($\times10^3$/mm^3)	17.37±2.88	12.34±3.50	**<0.001**
	Neutrophil ($\times10^3$/mm3)	15.62±2.77	9.48±3.48	**<0.001**
	Lymphocyte ($\times10^3$/mm3)	1.74±0.67	2.86±1.00	**<0.001**
	PLT ($\times10^3$/mm3)	406.83±168.95	372.06±123.22	0.164
	CRP (mg/dL)	30.44±49.49	38.05±63.12	0.503
	SIII ($\times10^3$/mm3)	5099.19±2456.82	1773.80±1112.83	**<0.001**
	NLR	10.39±4.90	3.78±2.08	**<0.001**
Adult appendicitis score		18.22±3.33	13.85±3.47	**<0.001**
Adult appendicitis score	Low risk	0 (0.0)	27 (18.8)	**<0.001**
	Moderate risk	7 (19.4)	68 (47.2)	
	High risk	29 (80.6)	49 (34.0)	
Alvarado score		7.25±1.40	4.47±1.73	**<0.001**
Alvarado score	Low possibility of AA	2 (5.6)	70 (48.6)	**<0.001**
	Possible AA	7 (19.4)	61 (42.4)	
	Likely to have AA	21 (58.3)	13 (38.2)	
	Strong possibility of AA	6 (16.7)	0 (0.0)	
Peritonitis status	No peritonitis	0 (0.0)	68 (47.2)	**<0.001**
	Local peritonitis	10 (27.8)	74 (54.1)	
	Peritonitis	26 (72.2)	2 (1.4)	

WBC, white blood cell; *PLT*, platelet; *CRP*, C reactive protein; *SIII*, systemic immune-inflammation index; *NLR*, neutrophil/lymphocyte ratio; *AAS*, adult appendicitis score; *AS*, Alvarado score; *AA*, acute appendicitis

Table 3 Comparison of correlation between AAS, AS, SIII, and NLR in the diagnosis of SG and CG patients

Parameter		AAS	AS	SIII	NLR
AAS	Pearson's correlation	1	0.576	0.450	0.429
	p	-	**<0.001**	**<0.001**	**<0.001**
	n	180	180		
AS	Pearson's correlation	0.576	1	0.487	0.533
	p	**<0.001**	-	**<0.001**	**<0.001**
	n	180	180	180	180
SIII	Pearson's correlation	0.450	0.487	1	0.900
	p	**<0.001**	**<0.001**	-	**<0.001**
	n	180	180	360	360
NLR	Pearson's correlation	0.429	0.533	0.900	1
	p	**<0.001**	**<0.001**	**<0.001**	-
	n	180	180	360	360

AAS, adult appendicitis score; *AS*, Alvarado score; *SIII*, systemic immune-inflammation index; *NLR*, neutrophil/lymphocyte ratio

When the correlation between AAS, AS, SIII, and NLR was examined in the diagnosis of the cases, there was a moderate (0.576; $p<0.001$) correlation between AAS and AS. There was a weak correlation (0.450 and 0.429, respectively; $p<0.001$ for both parameters) between SIII and NLR. A moderate correlation was identified between AS and both AAS and NLR (0.576 and 0.533, respectively; $p<0.001$ for both parameters) whereas a weak correlation was present (0.487; $p<0.001$) with SIII (Table 3).

In the study, the valence, sensitivity, and specificity of SIII and NLR in the diagnosis of AA and detection of complicated AA were examined. According to the values obtained, SIII has a higher AUC level compared to NLR at the diagnostic level (AUC: 0.750; 95% CI: 0.700–0.800 and AUC: 0.716; 95% CI: 0.663–0.768), but in the detection of complicated AA, NLR was found to have a higher AUC level (AUC: 0.927; 95% CI: 0.889–0.965) than SIII, AAS, and AS (Table 4 and Fig. 1).

When the mean SIII and NLR values in the presence of peritonitis were compared, SIII and NLR values of cases with peritonitis were found to be significantly higher than local

Table 4 ROC curve analysis results of SIII and NLR values in the diagnosis of AA and prediction of complicated AA in SG and CG patients

Parameter	AUC	Cut off	Sensitivity	Specificity	*p*	%95 CI	
SIII (diagnosis for AA)	0.750	2726.26	88.9	85.4	<0.001	0.700	0.800
NLR (diagnosis for AA)	0.716	6.13	91.7	86.8	**<0.001**	0.663	0.768
SIII (diagnosis for complicated AA)	0.927	1239.77	70.6	72.8	**<0.001**	0.889	0.965
NLR (diagnosis for complicated AA)	0.935	3.47	54.4	80.0	**<0.001**	0.900	0.970
AAS (diagnosis for complicated AA)	0.818	15.50	80.6	66.0	**<0.001**	0.738	0.898
AS (diagnosis for complicated AA)	0.888	5.50	86.1	69.4	**<0.001**	0.828	0.949

AAS, adult appendicitis score; *AS*, Alvarado score; *SIII*, systemic immune-inflammation index; *NLR*, neutrophil/lymphocyte ratio

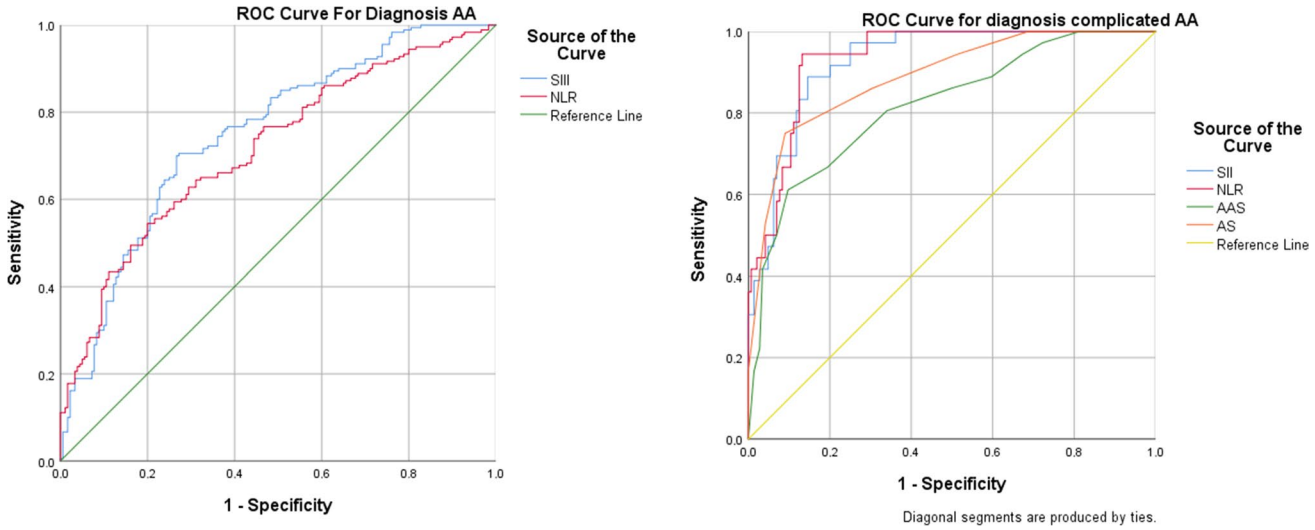

Fig. 1 The ROC curve analysis of SIII and NLR values in the diagnosis of AA and prediction of complicated AA in SG and CG patients

peritonitis cases and cases without peritonitis (95% CI for SIII with local peritonitis cases: 1551.21–3321.57; $p<0.001$ and 95% CI with non-peritonitis cases: 2242.49–3676.43; $p<0.001$; for NLR, 95% CI with local peritonitis cases: 3.32–6.73; $p<0.001$ and 95% CI without peritonitis cases: 4.60–7.39; $p<0.001$). In cases of local peritonitis, SIII and NLR values were borderline significantly higher in cases without peritonitis (95% CI for SIII: 29.36–1016.77; $p=0.038$ and 95% CI:0.01–1.92 for NLR: $p=0.047$). In the presence of elevated SIII and NLR (cut off for SIII: 2068.61; AUC: 0.845; 95% CI: 0.766–0.925; $p<0.001$; cut off for NLR: 6.00; AUC: 0.862; 95% CI: 0.82–0.941; p<0.001), professionals should be careful in terms of peritonitis.

Discussion

In this study, the success and reliability of SIII in the diagnosis of AA and prediction of complicated AA were evaluated. In addition, the results obtained were compared with the diagnostic value of NLR.

In the literature, it has been reported that NLR has a significant predictive value in the diagnosis of AA [14–16]. Eun et al. stated that in addition to its diagnostic value, NLR can be used to decide which imaging technique to be used in diagnostically in-between patients [16]. In the results of our study, it was seen that the diagnostic value of SIII for AA was significantly higher than NLR. However, in our study, NLR was found to have higher valence in predicting complicated AA. Şener et al. reported that SIII is a significant predictive value in the diagnosis of AA. In this context, our study supports the study data of Şener et al. [17] and the results of the studies reporting the value of NLR in the diagnosis of AA in the literature [14–16].

Many scoring systems have been designed and developed to reduce the rate of negative appendectomy and to increase the rate of a positive diagnosis of appendicitis [18]. Among these, "Alvarado Scoring" is a comprehensive scoring system developed by Alvarado in 1986 and provides practical diagnostic support in the interpretation of the diagnosis of AA [19]. In addition, in a study by Reddy et al., it has been reported that the use of AS prevents false-negative surgery in patients applied to emergency clinics with clinical findings of AA [20]. Another scoring system is AAS. Sammalkorpi et al. reported that AAS predicts AA more reliably than AS and clinical surgery decision [21]. However, there is little explanation for a clear distinction in the guidelines in distinguishing between complicated AA and uncomplicated AA cases [22, 23]. In the literature, it has been mentioned in several studies that complicated and uncomplicated AA can be distinguished by using the Alvarado score [24, 25]. Besides these studies, Atema et al. reported that they developed appendicitis severity scoring systems that combine both clinical and biochemical features and reported that they distinguish complicated AA with high sensitivity [26]. In our study, we compared SIII, NLR, AAS, and AS index and scoring systems in estimating complicated AA, and according to the results, SIII, NLR, AAS, and AS were found to be significantly valuable in the diagnosis of complicated AA. In the ROC analysis results, we found that NLR had the highest AUC value over SIII, AAS, and AS in estimating complicated AA. Whereas secondly, SIII was found to have a higher AUC value than AAS and AS. In this context, considering the success of AS and AAS at predicting AA level in the literature, we think that SIII is a usable index.

Peritonitis is a clinical condition that may occur in complicated AA cases. The clinical situation is worse in cases with peritonitis, and it causes prolongation in the medical treatment plan and length of stay both preoperatively and postoperatively. For this reason, conditions that cause peritonitis such as perforation should be diagnosed in the early period, and their treatment should be started. In fact, some researchers report that negative AA operation is acceptable to avoid delays considering the risk of peritonitis development [27]. Again, according to the study of Schietroma et al., in cases with peritonitis, higher neutrophil count and acute phase reactant levels were detected, and these levels were higher in laparotomy cases than in laparoscopic cases [28]. In the results of our study, SIII and NLR were found to be significantly higher in cases with peritonitis compared to cases with local peritonitis and without peritonitis. Also, it was observed that it was higher in cases with local peritonitis compared to cases without peritonitis. Therefore, in cases with very high SIII and NLR (cut off for SIII: 2068.61; AUC: 0.845; 95% CI: 0.766–0.925; $p<0.001$; cut off for NLR: 6.00; AUC: 0.862; 95% CI: 0.82–0.941; $p<0.001$), considering peritonitis is crucial. In this context, more studies are needed to generalize our study data.

Limitations of study

Our study has several limitations. The first of these is that our study is retrospective, and the data were obtained from the records. Later, our study is single-centered, and multicenter studies are needed to generalize our results to other health institutions. Thirdly, since chronic disease information of the cases is obtained from the patients and their relatives, errors that might have occurred in this information cannot be detected. Our last limitation is the fact that the time of admission and waiting duration in the emergency department are different from each other, and this data cannot be standardized. However, we think that these limitations are not at a level to affect our study results.

Conclusion

In our study, we found that SIII is a usable index in the diagnosis of AA and the prediction of complicated AA. However, NLR was found to be more significant than SIII in estimating complicated AA. In addition, it is necessary to be careful in terms of peritonitis in cases with high SIII and NLR levels. In order to generalize our results, they should be supported by multicenter studies with higher patient numbers.

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Authors' contribution MAT: concept, data collection and entry, analysis and interpretetion, writing, critical review, and supervisor. MY: data collection and entry, literature search, and critical review.

Declarations

Ethics approval Ethics committee approval was obtained from the university hospital ethics committee (with the ethics committee decision number of Erzurum BEAH KAEK 2022/02-03 dated 07.02.2022). Due to the retrospective nature of the study, obtaining voluntary consent from the patients included in the study was waived. The entire study was performed in accordance with the Declaration of Helsinki and the statement of good clinical practice.

Conflict of interest The authors declare no competing interests.

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