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Original Article

Diagnostic Value of Systemic Immune-inflammation Index in Patients with Acute Pancreatitis

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Keywords: Acute pancreatitis; neutrophil–lymphocyte ratio; systemic immune-inflammatory index.

ABSTRACT

Objective: Acute pancreatitis is one of the most common causes of gastrointestinal diseases. Furthermore, it is a very common disease diagnosed in the emergency department (ED). However, the diagnosis of acute pancreatitis cannot be made with simple and inexpensive methods in the ED. The systematic immune-inflammation index (SII) is a scoring system that has recently been introduced for diagnosing inflammatory diseases. This study investigates the use of SII in diagnosing acute pancreatitis and predicting its severity.

Methods: This study was carried out retrospectively, in a single center, in the ED of a tertiary education and research hospital. The study included patients who presented to the ED between June 2021 and December 2021 and were diagnosed with acute pancreatitis and who met the inclusion criteria. Of 207 patients diagnosed with acute pancreatitis, 150 patients who met the inclusion criteria were included in the study.

Results: Comparison of SII and neutrophil-to-lymphocyte ratio (NLR) in diagnosing pancreatitis and predicting its severity showed that SII with a cutoff value of 938.82×109/L had 78.7% sensitivity and 46% specificity in diagnosing pancreatitis (area under the curve [AUC]: 0.685; 95% confidence interval [CI]: 0.626–0.745). NLR, with a cutoff value of 4.45, on the other hand, had 74.7% sensitivity and 50% specificity in diagnosing pancreatitis (AUC: 0.677; 95% CI: 0.617–0.737). SII performed better than NLR in diagnosing acute pancreatitis.

Conclusion: SII is more sensitive in the diagnosis of acute pancreatitis, and NLR is more sensitive in disease severity. SII can be used in the diagnosis of acute pancreatitis.

INTRODUCTION

Acute pancreatitis (AP) is an acute inflammation of the pancreas. AP is the most common disease of the gastrointestinal system, with a mortality rate of 1.0%–1.5%.[1] AP is clinically categorized into mild AP and severe AP (SAP).[2] SAP is associated with a high mortality rate and should, thus, be diagnosed early in patients at risk. Commencing the treatment early on affects the prognosis of these patients.[3]

Several scoring systems have been developed to assess the severity and establish the prognosis of AP. Of these scoring systems, the most widely used prognostic marker is Ranson's criteria. However, these scoring systems contain certain parameters that do not affect the prognosis of AP. Furthermore, Ranson's criteria that are sought within 48 h significantly restrict the use of this scoring system in the emergency department (ED). Hence, there is a need for simple and inexpensive scoring systems and indices that are practical for use in the ED. Against this background, the systemic immune-inflammation index (SII) is seen as a potentially useful index for use in the ED to diagnose AP. One study has proposed SII as a new prognostic marker based on neutrophils, lymphocytes, and platelets.[4]

SII has previously only been associated with the prognosis of patients with malignancies. However, it has recently been used as a prognostic marker in some inflammatory conditions, such as chronic obstructive pulmonary disease

and vasculitis.[5,6] Inflammatory responses involve several immune cells (neutrophils, lymphocytes, etc.).[7] SII has been reported to be a stronger prognostic marker than those of systemic inflammation, such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio, in some diseases.[8]

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.[4] Since SIII is easy to calculate, is inexpensive, requires only complete blood count, and relies on no subjective findings, it will provide more accurate results in the diagnosis of AA.

Quick and simple scoring systems and indices are needed to diagnose and determine the severity of AP. This study, thus, investigated the utility of SII in diagnosing and determining the severity of AP.

MATERIALS AND METHODS

Study Setting

This study was approved by the ethics committee of our tertiary training and research hospital (ethics committee decision dated March 24, 2021, no. 2021.03.32). It was a retrospective and single-center study. The study was conducted with patients who presented to the ED with abdominal pain between June 1, 2021, and December 1, 2021, were diagnosed with AP, and met the inclusion criteria. Patients' demographic characteristics, medical histories, laboratory results, SII scores, Ranson's criteria, and length of hospital stay were recorded in previously created case report forms. The patients with AP were classified into low-risk (with a score of 0–3) and high-risk (with a score of 4–11) groups according to Ranson's criteria (Table 1).[9]

The study included 150 patients with confirmed AP and 150 control subjects who presented to the ED with abdominal pain and in whom AP was ruled out.

Population

The study included patients who presented to the ED with abdominal pain and in whom AP was confirmed (study group) and AP was ruled out (control group). The exclusion criteria were patients under 18 years of age, pregnancy, patients lost to follow-up, history of malignancy, history of hematologic diseases, bone marrow pathology, and use of anti-inflammatory or immunosuppressive drugs. The study also excluded patients having a focus of infection other than AP. Patients who were diagnosed with AP and did not meet any of these exclusion criteria were included in the study.

Data Collection

Patients were identified via screening of medical files and the automation system (Hospital Information Management System). AP cases were extracted from the automation system using ICD10 diagnostic codes "K85, K85.0, K85.1, K85.8, K85.9," yielding 207 patients with AP. Of the 207 detected patients, 17 were excluded for having a history of malignancy, 7 for being lost to follow-up, 11 for insufficient data, 6 for using anti-inflammatory or immunosuppressive medications, 4 for having a history of hematologic disease, and 2 for pregnancy. Finally, 150 of the remaining 160 patients were included in the study randomly.

The control group was randomly composed of age-matched patients selected on the basis of inclusion and exclusion criteria; it consisted of 150 patients who presented with "abdominal pain" and in whom AP was ruled out.

Data Calculation

The data obtained about the patients were used for calculating NLR, PLR, and SII. SII was calculated using the

Table 1. Ranson's criteria

	Biliary acute pancreatitis	Non-biliary acute pancreatitis
At admission		
Age	>70	>55
White blood cells (WBC)	>18,000/mm^3	>16,000/mm^3
Glucose	>220 mg/dL	>200 mg/dL
Lactate dehydrogenase	>400 U/L	>350 U/L
Aspartate aminotransferase	>250 U/L	>250 U/L
In 48 h		
Hematocrit decrease	>10%	>10%
Blood urea nitrogen (BUN) elevation	2 mg/dL despite fluid	5 mg/dL despite fluid
Serum calcium	<8 mg/dL	<8 mg/dL
pO2	<60 mm Hg	<600 mm Hg
Base deficit	>5 mEq/L	>4 mEq/L
Fluid sequestration	>4000 mL	>6000 mL

formula (Neutrophils×Platelets)/Lymphocytes. Since the study was retrospective, it also assessed inhospital outcomes (discharge, mortality, etc.).

Statistical Analyses

Data were analyzed using the SPSS Software Suite version 24.0. Descriptive data were presented as number, percentage, mean, standard deviation, median, minimum, and maximum. The normality of the distribution was assessed using the Kolmogorov-Smirnov test. Continuous variables exhibiting normal distribution in univariate analysis were expressed as mean±standard deviation and compared using the t-test. Categorical variables were analyzed using Pearson's Chi-square test. Fisher's exact test was used when less than five observations were present in the categorical variables. The t-test was used to compare two groups of independent numerical data. Diagnostic accuracy was assessed using receiver operating characteristic curve analysis. Appropriate cutoff values were determined, and sensitivity and specificity were calculated for parameters with an area under the curve (AUC) of >0.600. Statistical significance was set at $p<0.05$.

RESULTS

Our study included a total of 300 patients: 150 in the study group and 150 in the control group. The control group was randomly composed of patients who matched the age and sex of the patients in the study group. The mean age was 55.71±18.12 years in the study group and 57.56±18.78 years in the control group. In laboratory tests, mean levels of white blood cells (WBCs), neutrophils, and C-reactive protein (CRP) were found to be significantly higher in the study group than in the control group, but lymphocyte levels were found to be significantly low. There was no significant difference between the two groups in mean platelet levels (Table 2).

As for the ratios of laboratory parameters, mean SII, NLR, and PLR were found to be significantly higher in the study group diagnosed with AP as compared with the control group (Table 2).

The disease was classified into mild and severe according to the Ranson's criteria. This classification showed no significant difference in terms of sex between patients with mild and severe pancreatitis. The mean age in the severe pancreatitis group was found to be significantly higher than that in the mild pancreatitis group. Moreover, mean levels of WBC, neutrophil, lymphocyte, and CRP were found to be significantly higher in the severe pancreatitis group as compared with the mild pancreatitis group. There was no significant difference between the two groups in terms of mean platelet levels (Table 3).

Analysis of ratios and indices obtained from laboratory parameters showed that mean SII, NLR, and PLR scores were significantly higher in patients with severe pancreatitis (Table 3). Furthermore, the mean length of hospital stay was significantly higher in patients with severe pancreatitis than in those with mild pancreatitis (Table 3).

SII and NLR values were compared in terms of diagnosing and predicting the severity of pancreatitis. In diagnosing pancreatitis, SII with a cutoff value of 938.82 × 109/L had 78.7% sensitivity and 46% specificity (AUC: 0.685; 95% confidence interval (CI): 0.626–0.745); SII with a cutoff value of 1995.65×10^9/L had 50% sensitivity and 79.3% specificity (AUC: 0.685; 95% CI: 0.626–0.745). In addition, NLR with a cut-off value of 4.45 had 74.7% sensitivity and 50% specificity (AUC: 0.677; 95% CI: 0.617–0.737) in diagnosing pancreatitis. SII was found to perform better than

Table 2. Comparison of demographic and laboratory data between the study and control groups

Parameter	Study group (n=150) Mean±SD	Control Group (n=150) Mean±SD	p-value
Demographic Data			
Male n (%)	74 (49.3)	86 (57.3)	0.165*
Age (years)	55.71±18.12	57.56±18.78	0.622**
Laboratory Tests			
WBC ($\times10^9$/L)	13.43±4.41	11.08±4.53	<0.001**
Neutrophil ($\times10^9$/L)	11.04±4.53	8.24±4.39	<0.001**
Lymphocyte ($\times10^9$/L)	1.52±0.82	1.78±0.80	0.006**
Platelet ($\times10^9$/L)	254.88±106.38	243.86±72.42	0.295**
CRP (mg/dL)	53.84±93.56	23.46±19.46	<0.001**
Ratios			
SII ($\times10^9$/L)	2859.59±3870.81	1599.51±2577.22	0.001**
NLR	11.52±13.01	6.73±9.99	<0.001**
PLR	230.47±192.53	177.53±169.13	0.012**

*: Pearson $\chi2$ Test has been used; **: T-test has been used; SD: Standard deviation; CRP: C-reactive protein; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SII: Systemic immune-inflammation index.

Table 3. Comparison of demographic and laboratory data by severity of pancreatitis

Parameter	Mild pancreatitis (n=39) Mean±SD	Severe pancreatitis (n=111) Mean±SD	p-value
Demographic data			
Male n (%)	51 (45.9)	23 (59.0)	0.162*
Age (years)	51.19±16.15	68.59±17.75	<0.001**
Laboratory Tests			
WBC (109/L)	12.25±3.24	16.82±5.47	<0.001**
Neutrophil (×109/L)	8.29±6.77	20.70±20.36	<0.001**
Lymphocyte (×109/L)	1.63±0.79	1.20±0.81	0.005**
Platelet (×109/L)	256.13±76.16	251.30±166.02	0.808**
CRP (mg/dL)	44.53±89.61	80.35±100.53	0.039**
Ratios			
SII (×109/L)	2081.18±1872.60	5075.08±6464.65	<0.001**
NLR	8.29±6.77	20.70±20.36	<0.001**
PLR	198.44±128.24	321.64±293.61	<0.001**
Length of hospital stay	5.23±3.64	8.10±4.85	<0.001**

*: Pearson χ 2 Test has been used; **: T-test has been used. SD: Standard deviation; CRP: C-reactive protein; NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio; PNR: Platelet-to-neutrophil ratio; LNR: Lymphocyte-to-neutrophil ratio; SII: Systemic immune-inflammation index.

Table 4. ROC analysis results for SII and NLR in diagnosing and predicting the severity of pancreatitis

Parameter	Cutoff value	Sensitivity	Specificity	Area under the curve (AUC)	95% CI Lower Bound	95% CI Upper Bound	p-value
SII in diagnostic use (×10⁹/L)	938,82	78,7	46	0,685	0,626	0,745	<0.001
	1995,65	50	79,3	0,685	0,626	0,745	<0.001
NLR in diagnostic use	4,45	74,7	50	0,677	0,617	0,737	<0.001
SII in the severity of pancreatitis (×10⁹/L)	1872,07	76,9	57,7	0,711	0,614	0,808	<0.001
NLR in the severity of pancreatitis	7,44	82,1	60,4	0,750	0,653	0,847	<0.001

NLR: Neutrophil-to-lymphocyte ratio; SII: Systemic immune-inflammation index.

NLR in diagnosing AP (Table 4 and Figure 1).

On the contrary, in predicting the severity of pancreatitis, SII, with a cutoff value of 1872.07 × 109/L, had 76.9% sensitivity and 57.7% specificity (AUC: 0.711; 95% CI: 0.614–0.808). NLR, with a cutoff value of 7.44, had 82.1% sensitivity and 60.4% specificity (AUC: 0.750; 95% CI: 0.653–0.847). These results showed that NLR was better than SII in determining the severity of pancreatitis (Table 4 and Figure 1).

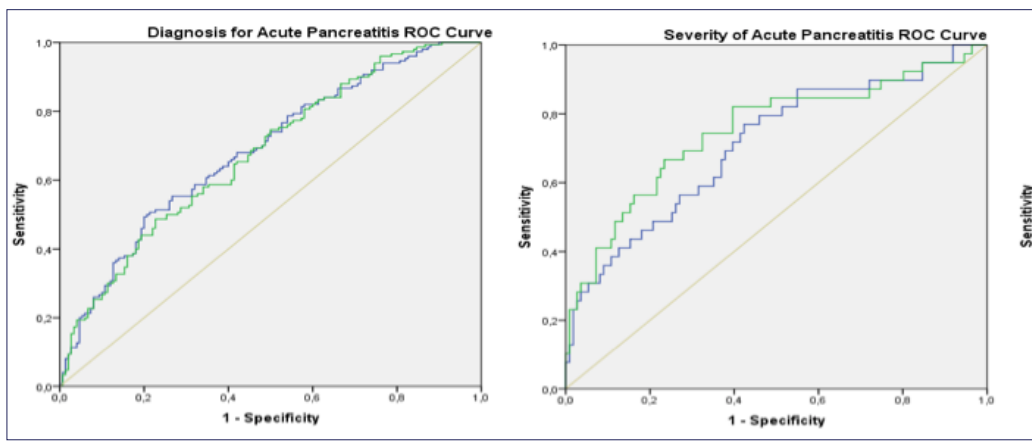

Figure 1. Receiver operating characteristic analysis of systematic immune-inflammation index and neutrophil-to-lymphocyte ratio in diagnosing and predicting the severity of pancreatitis.

DISCUSSION

AP is an inflammatory disease with a sudden onset, rapid progress, and a high risk of morbidity and mortality. Therefore, it is crucial to diagnose and determine the severity of AP in a timely and accurate manner. However, the methods currently used to determine the severity of AP are not sufficiently sensitive and specific. Hence, this study investigated the use of SII in diagnosing and determining the severity of AP.

Inflammation plays an important role in the development of AP and disease progression. The early phases of SAP are characterized by a complex state of inflammation and immunosuppression that leads to intestinal mucosal barrier dysfunction.[10] Studies have reported that, during the pancreatitis process, neutrophils and reactive oxygen radicals exert synergistic effects on damaged cells.[11] Platelets are directly involved in the systemic inflammatory processes of AP.[12] Neutrophils are thought to play a role in the chemokine and cytokine cascades that accompany inflammation in the pathogenesis of SAP.[13] Therefore, SII is viewed as a potential marker in diagnosing and determining the severity of AP.

Gürleyik et al. reported the mean age of patients with AP to be 57 years.[14] Another study documented the mean age to be 57±15.6 years.[15] The mean age of patients with AP in our study was similar to that reported in other studies in the literature. As the age advances, AP becomes more severe, thus leading to increased mortality.[16] Studies have noted longer hospital stay in patients with SAP.[1] Most of the patients included in our study had initially presented to other hospitals. Therefore, clinical manifestations of the study were visible at the time of presentation to our hospital, which resulted in a high incidence of SAP in our study.

Numerous clinical and laboratory parameters are used for diagnosing and determining the severity of pancreatitis. The most widely used clinical prognostic scoring system is the Ranson's criteria.[17] Ranson's scoring system contains a significant number of parameters, including those that are calculated at 48 h of presentation, which makes its use significantly difficult for clinicians in the ED. Therefore, an index capable of rapid and direct assessment is needed for diagnosing AP.[18] Recent studies have investigated the use of NLR and PLR, particularly in predicting the severity of pancreatitis.[19] NLR and PLR provide easier and inexpensive calculation for use in the ED.

NLR and PLR scores have been used in diagnosing several inflammatory and neoplastic diseases.[20] Previous studies reported elevated NLR in SAP in the follow-up of the inflammatory process.[19] Sepsis is characterized by elevated NLR as a result of increased neutrophils and decreased lymphocytes. Kaplan et al. showed NLR and PLR to be significant markers in SAP.[21] The results of our study are in line with those in the literature; owing to the delayed presentation of patients to our hospital after referral from other hospitals, NLR and PLR were found to be significant.

SII has only recently been used to determine disease severity in patients with AP. The parameters used in SII are obtained from hemogram, which is an inexpensive and quick test. SII is calculated using neutrophil, platelet, and lymphocyte counts. Thus, easy, inexpensive, and quick application of SII makes it a practical index for use in inflammatory diseases. One study found SII to be more specific than NLR and PLR in determining the severity of AP.[22] Another study reported SII to be significant in establishing the prognosis of AP.[23] Our study, however, found NLR and PLR to be more significant than SII in determining the severity of AP. This discrepancy may be because of the delayed presentation of patients referred to our hospital from other institutions. However, we believe that future prospective studies with larger samples might show SII to be a more significant parameter.

To the best of our knowledge, there are no reports on the relationship between SII and the diagnosis of AP. Our results suggest that SII is a valuable parameter in the diagnosis of AP. Comprehensive studies in the future might come up with results similar to those from our study and increase the use of SII in the diagnosis of AP. In such a scenario, SII can replace other scoring systems that are difficult to use in the ED.

Limitations

This study has some limitations. First, the data used were obtained retrospectively from a single center. Second, SII was calculated only once at the time of presentation to the ED; it needs to be measured at different time points in the future. The third limitation is the limited number of patients. Future studies should be conducted with a greater number of patients to confirm our results. Fourth, some of the patients included in the study were referred from other hospitals. Delayed presentation of these patients resulted in different SII, NLR, and PLR values.

Conclusion

SII is an inexpensive, quick, and easy method that can be used in diagnosing and determining the severity of AP and can, thus, reduce the need for diagnostic imaging methods that involve exposure to radiation, such as contrast-enhanced abdominal computed tomography. Furthermore, using SII in conjunction with the Ranson's criteria can reduce the rate of misdiagnosis and prevent delays in treatment.

Ethics Committee Approval

This study approved by the Başakşehir Çam and Sakura City Hospital Clinical Research Ethics Committee (Date: 15.04.2021, Decision No: 2021.03.32).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: E.A., R.G.; Design: E.A., K.Ş.; Supervision: E.A., H.K.; Fundings: E.A., G.E.; Materials: E.A., K.Ş., H.K.; Data: E.A., A.Ç.; Analysis: A.Ç., Ç.E., E.A.; Literature search: E.A., R.G., A.Ç.; Writing: E.A., A.Ç., R.Ç.; Critical revision: E.A., R.Ç.

Conflict of Interest

None declared.

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Akut Pankreatitte Sistemik İmmün-İnflamasyon İndeksinin Tanısal Değeri

Amaç: Akut pankreatit, gastrointestinal hastalıkların en yaygın nedenlerinden biridir. Ayrıca, acil serviste (AS) teşhis edilen çok yaygın bir hastalıktır. Ancak acil serviste basit ve ucuz yöntemlerle akut pankreatit tanısı konulamamaktadır. Sistematik immün-enflamasyon indeksi (SII), enflamatuvar hastalıkların teşhisi için son zamanlarda tanıtılan bir puanlama sistemidir. Bu çalışma, SII'nin akut pankreatit tanısında ve ciddiyetini tahmin etmede kullanımını araştırmaktadır.

Gereç ve Yöntem: Bu, üçüncü basamak bir hastanenin acil servisinde yapılan retrospektif ve tek merkezli bir çalışmadır. Çalışmaya Haziran 2021-Aralık 2021 tarihleri arasında acil servise başvuran, akut pankreatit tanısı alan ve dahil edilme kriterlerini karşılayan hastalar alındı. Akut pankreatit tanısı alan 207 hastadan dahil edilme kriterlerini karşılayan 150 hasta çalışmaya alındı.

Bulgular: Pankreatit tanısında ve şiddetini tahmin etmede SII ve nötrofil-lenfosit oranının (NLO) karşılaştırılması, 938.82×10^9/L kesme değeri olan SII'nin pankreatit (alan) tanısında %78.7 duyarlılığa ve %46 özgüllüğe sahip olduğunu gösterdi. Eğrinin altında (EAA): 0.685; %95 güven aralığı (CI): 0.626–0.745). Kestirim değeri 4.45 olan NLO ise pankreatit tanısında %74.7 duyarlılığa ve %50 özgüllüğe sahipti (EAA: 0.677; %95 GA: 0.617–0.737). SII, akut pankreatit tanısında NLR'den daha iyi performans gösterdi.

Sonuç: SII, akut pankreatit tanısında NLR'den daha fazla duyarlılık göstermektedir. Ancak hastalığın ciddiyetini belirlemede NLR daha duyarlıdır. Sonuç olarak SII acil serviste akut pankreatit tanısında kullanılabilir.

Anahtar Sözcükler: Akut pankreatit; nötrofil-lenfosit oranı; sistemik immün enflamatuvar indeks.