

Research Article / Araştırma Makalesi

Systemic Inflammatory Response Index (SIRI) and Systemic Immune-Inflammation Index (SII) to Show Thrombus Localization in Patients with Acute Pulmonary Embolism
Akut Pulmoner Embolili Hastalarda Trombüs Lokalizasyonunu Göstermede Sistemik İmmün İnflamatuvar İndeks ve Sistemik İnflamatuvar Yanıt İndeks

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Abstract: Pulmonary embolism (PE) is a critical disease associated with mortality. Considerable markers related to this disease associated with inflammation have been used to catch thrombus localization. In this study, we wanted to examine the association between the Systemic inflammatory response index (SIRI), Systemic immune-inflammation index (SII) and thrombus localization in patients with PE. Our study consisted of patients diagnosed with PE between January 2020- June 2022. Laboratory parameters of patients diagnosed with PE, especially thrombus localization, thrombus location, SII, and SIRI, were recorded and compared with thrombus localization. One hundred patient with PE who met the inclusion criteria was incorporated in our study. When we grouped the patients according to PE localization, the thrombus was in the main pulmonary vein in 18%, in the lobar region in 51%, and in the distal pulmonary vein in 31% of the patients. In addition, mean SIRI and SII levels were encountered to be higher in patients with main pulmonary localization compared to those with thrombus in both lobar and segmental branches. SIRI has 78% sensitivity, and 72% specificity at the optimum cut-off value; in Level II, it detects thrombus with main pulmonary involvement with 66.7% sensitivity and 79.3% specificity. In patients with PE, high SII and SIRI values can be practical markers in predicting proximal thrombus.

Keywords: Pulmonary Embolism, Inflammation, Thrombosis

Özet: Pulmoner emboli (PE) mortalite ile de ilişkili önemli bir hastalıktır. İnflamasyon ile ilişkili olan bu hastalıkla ilgili birçok marker trombüs lokalizasyonu saptamak için kullanılmıştır. Biz bu çalışmada Systemic inflammatory response index (SIRI) ve Systemic immune-inflammation index (SII) ile PE li hastalardaki trombüs lokalizasyonu arasındaki ilişkiyi incelemek istedik. Çalışmamız Ocak 2020- Haziran 2022 yılları aranda PE tanısı alan hastalardan oluşmaktaydı. PE tanısı alan hastalar trombüs lokalizasyonu, trombüs yerleşkesi, SII ve SIRI başta olmak üzere labaratuvar parametreleri kaydedilmiş ve trombüs lokalizasyonu ile karşılaştırılmıştır. Çalışmamıza dahil edilme kriterlerini sağlayan 100 PE li hasta katılmıştır. Hastalarının PE lokalizasyonuna göre grupladığımızda trombüs %18 inde ana pulmoner, %51 hastada lobar bölgede iken, %31 inde ise distal pulmoner damardaydı. Ayrıca ortalama SIRI ve SII düzeyleri ana pulmoner lokalizasyonu olanlarda hem lobar hem de segmental dallarda trombüsü olanlara göre yüksek saptanmıştır. Optimum cut off değerinde SIRI %78 sensitivite, %72 spesifite; SII da %66.7 sensitivite, %79.3 spesifite ile ana pulmoner tutulumu olan trombüsü saptamaktadır. PE li hastalarda yüksek SII ve SIRI değerleri ile proksimal yerleşimli trombüsü tahmin etmede yararlı bir belirteç olabilir.

Anahtar Kelimeler: Pulmoner Emboli, İnflamatuvar, Tromboz

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1. Introduction

Pulmonary embolism (PE) is an insidious disease that causes patients to present to the emergency department with classic symptoms such as shortness of breath and pleuritic chest pain and is one of the typical diagnoses (1). On the other hand, some patients may have diagnostic hardships due to presentations other than respiratory patterns such as syncope (2). Differences in the clinical presentation of PE, known to be among the diseases associated with mortality, may cause difficulties in the diagnostic process. It is known that echocardiographic examination, lower extremity venous Doppler ultrasonography, and computed tomography pulmonary angiography, which are imaging techniques that can be used for diagnostic purposes, will bring additional costs in inpatient evaluation (3). Although imaging methods are the gold standard, inexpensive and rapidly accessible methods are needed. For this reason, the interest in biomarkers has been increasing in recent years due to their simple and easy application. Some of these markers are d-dimer, neutrophil-lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), and lymphocyte monocyte ratio (LMR). However, the superiority of these markers over each other has not been documented (4,5).

Systemic inflammatory response index (SIRI) and Systemic immune-inflammation index (SII) have been the subject of research in the literature in recent years, with their easy applicability in many diseases, especially in the follow-up and treatment of malignancy patients (6,7). These markers, which can be obtained by the ratio of simple hemogram parameters to each other, are the subject of research in many diseases associated with inflammation (8). The relationship between SIRI and SII parameters in PE patients has been fully elucidated. Therefore, in this study, we evaluated the association of thrombus with SIRI and SII in patients with PE and explored the relationship between thrombus localization.

2. Materials and Methods

Our study consists of patients who were admitted to the chest diseases clinic from the emergency department with the diagnosis of PE between January 2020- June 2022. Our study is a single-center, retrospective study and all procedures were performed by following standard procedures following the Declaration of Helsinki. Approval for the study was granted by the Clinical Research Ethics Committee Antalya Training and Research Hospital (Date: January 16.02. 2023, Decision No: 3/22). The diagnosis of PE in the patients included in the study was made by multi-detector computed tomography (CT) pulmonary angiography scanning, and patients aged 18 years and older with a diagnosis of PE were included in the study. Pregnant women, those who use anticoagulant, steroid, or immunosuppressive drugs that may affect similar tests, those with chronic kidney or hematological disease, those with acute or chronic infections, patients aged <18 years, and patients with missing data were excluded from the investigation.

According to the thrombus localization of the patients diagnosed with PE, right, left, and bilateral localization of the thrombus was recorded. The thrombus is grouped as main PE if it is in the main pulmonary vessel, as lobar PE if it is in the lobar branch, and as distal PE if it is in segmental vessels. Demographic data and laboratory parameters of the patients were recorded from the files in the hospital data processing system. Among the hemogram parameters, white blood cell count, hemoglobin, neutrophil count, lymphocyte count, and platelet count were recorded. Calculated and recorded using the SIRI $\text{Neutrophil} \times \text{Platelet} / \text{Lymphocyte}$ formula. $\text{Neutrophil} \times \text{Monocyte} / \text{Lymphocyte}$ formula was used for SII formulation. The relationship between laboratory parameters and PE localization was investigated.

Statistical analysis

Statistical analysis of our study was done with SPSS 25.0. and p-value <0.05 was considered statistically significant. Probability analysis of our data was performed using the

Kolmogorov-Smirnov test, and the data were shown as percentage, mean, and standard deviation (SD) values. In the analysis between thrombus localization groups, comparisons between independent groups were used, the Mann-Whitney U test was used, and the chi-square test was used to evaluate numerical and categorical variables that did not show normal distribution. The optimum cut-off values of SIRI and SII values were calculated with the Receiver Operating Characteristic (ROC).

3. Results

One hundred patient with PE who met the inclusion criteria was included in our study. Fifty three(53%) of these patients were female patients. The median age of the patients was 68.5 years. When we grouped the study patients according to PE localization, the thrombus was classified as main pulmonary in 18 (18%) patients, in the lobar region in 51 (51%) patients, and the distal pulmonary vessel in 31 (31) patients. The in-hospital mortality rate was 13%. The general demographic data of the patients are given in Table 1.

In computed tomography pulmonary angiogram (CTPA) , which is used to detect thrombus in PE patients, the mean age of the patients according to the thrombus localization was found to be significantly lower in patients with thrombus in the main pulmonary region than in the lobar region (58.55±18.39 vs. 68.71±16.16, p:0.044). There was no significant difference between patients and localization region for genders. Those with right-sided thrombus localization were found to be significantly lower in the

main pulmonary vein branch compared to the lobar and segmental branches (p=0.002; p=0.041, respectively). The mean SIRI values of the patients were found to be significantly higher in those with main pulmonary localization compared to the lobar region (6.74±4.91 vs. 3.53±2.66; p<0.001). In addition, mean SIRI values were found to be higher in patients with main pulmonary localization than those with distal thrombus (6.74±4.91 vs. 2.13±1.16; p<0.001). It was found to be significantly higher in those with localization in the lobar region compared to the distal region (3.53±2.66 vs. 2.13±1.16; p=0.002). The mean SII values of the patients were found to be significantly higher in those with main pulmonary localization compared to the lobar region (2700.51±1651.81vs. 1335.73±1012.16; p<0.001). In addition, mean SII values were found to be higher in patients with main pulmonary localization than those with distal thrombus (2700.51±1651.81 vs. 1196.31±820.63; p<0.001). It was found to be significantly higher in those with localization in the lobar region compared to the distal region (1335.73±1012.16vs. 1196.31±820.63; p<0.001). Demographic and laboratory parameters data of patients according to thrombus localization are given in Table 2.

AUC values of the variables including SIRI and SII values were discovered significant in the ROC analysis. For the optimum cut-off value of 1538.44, SIRI detects thrombus with main pulmonary involvement with 78% sensitivity and 72% specificity. For the optimum cut-off value of 4.12, it notices a thrombus with main pulmonary involvement with 66.7% sensitivity and 79.3% specificity in SII (Table 3, Figure 1).

Table 1. Demographic and clinical characteristics of patients

<i>Demographic features</i>	
Female/male (% female)	53/47 (53)
Median age (years)	68.5 (26.5)
Age over 65 years n(%)	57 (57)
<i>Localization of thrombus</i>	
Main pulmonary arteries, n (%)	18 (18)
Lobar arteries , n (%)	51 (51)
Segmental and subsegmental arteries , n (%)	31 (31)
In-hospital mortality, n (%)	13 (13)

Table 2. Distribution of the characteristics of pulmonary embolism patients according to thrombus localization

Parameter	Main PA (n=18)	Lobar PA (n=51)	Distal PA (n=31)	p1	p2	p3
Age (years)	58.55±18.39	68.71±16.16	62.48±20.79	0.044	NS	NS
Gender (female / male)	11/7	28/23	14/17	NS	NS	NS
Location of thrombus, n (%)						
Right PA	1 (5.6)	27 (52.9)	15(48.3)	0.002	0.041	NS
Left PA	2 (11.1)	6(11.8)	9(29.2)	NS	NS	NS
Bilateral PA	15 (83.3)	18(35.3)	7(22.5)	NS	NS	NS
White blood cell (×10 ³ /mm ³)	10.31±4.22	12.01±6.28	10.38±4.78	NS	NS	NS
Neutrophils (×10 ³ /mm ³)	7.91±4.22	9.41±4.78	8.01±2.54	NS	NS	NS
Platelets(×10 ³ /mm ³)	234.33±56.46	257.84±99.71	244.54±119.88	NS	NS	NS
C-reactive protein	99.11±23.02	96.37±12.51	89.87±14.16	NS	NS	NS
SIRI	6.74±4.91	3.53±2.66	2.13±1.16	<0.001	<0.001	0.002
SII	2700.51±1651.81	1335.73±1012.16	1196.31±820.63	<0.001	<0.001	<0.001

NS: non-specific;SIRI: Systemic inflammatory response index; SII: Systemic immune-inflammation index , PA: Pulmonary artery

p1=comparison between main PA group and Lobar PA group

p2=comparison between main PA group and Distal PA group

p3=comparison between Lobar PA group and Distal PA group

Table 3. Diagnostic accuracy of parameters for predicting the presence of main pulmonary arteries thrombus

	AUC	Cut-off value	Sensitivity (%)	Specificity (%)	95% CI	p Value
SIRI	0.843	1538.44	78	72	0.713 to 0.917	<0.001
SII	0.815	4.12	66.7	79.3	0.760 to 0.926	<0.001

SIRI: Systemic inflammatory response index; SII Systemic immune-inflammation index, AUC: Area under the curve

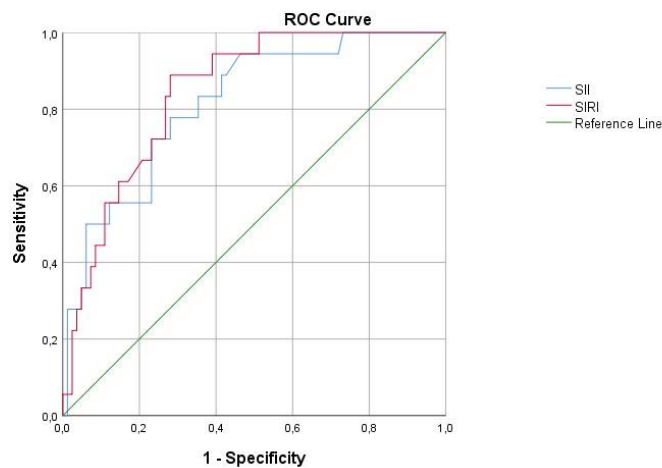


Figure 1. The receiver operating characteristic (ROC) curves of systemic immune-inflammation index (SII) and Systemic inflammatory response index (SIRI) in predicting main pulmonary arteries thrombus in pulmonary embolism patients

4. Discussion

In recent years, the role of biomarkers reflecting inflammation and inflammatory conditions in many atherothrombotic diseases, especially cardiovascular diseases, has been investigated. Conditions such as hypoxia or trauma have been shown to trigger conditions such as inflammation and pulmonary endothelial dysfunction. Many markers, both diagnostic and prognostic, have therefore been used for patients with PE (4-9). In this study, we showed that there is a significant relationship between high SIRI and SII levels and thrombus localization.

The role of inflammation in the pathophysiology of acute PE has been shown in many studies. Studies have demonstrated the role of many inflammatory markers in the course of the disease (9). Although many inflammation markers are affected in both mortality and diagnostic processes, there are very few studies in the literature regarding the marker showing thrombus localization in patients with PE (10). Since it is a life-threatening disease, early detection of thrombus that may occur in the main branches with non-invasive easily accessible markers will accelerate the diagnosis and treatment processes (11). Studies have shown the relationship between inflammatory markers such as d-dimer and NLR and thrombus localization (4,12). However, the relationship between SIRI or SII and thrombus in patients with PE has not been demonstrated in the literature. Based on the data in our study, the relationship between SIRI and SII and thrombus localization has been demonstrated. Significantly higher SII and SIRI values were found in thrombi in the main pulmonary vessels than in those with thrombi in more distal branches. For the optimum cut-off value of 1538.44, SIRI with 78% sensitivity and 72% specificity; detects thrombus with main pulmonary involvement with 66.7% sensitivity and 79.3% specificity in SII for the optimum cut-off value of 4.12. Our study showed that SIRI and SII can predict PE in the proximal region in patients with PE. Therefore, in patients with high SIRI and SII values, a relationship with thrombus in the main branches has been shown.

SIRI and SII have been used in many diseases in recent years, both for diagnostic and prognostic processes (7). They are the main inflammation-based parameters and have entered the medical literature systematically as biomarkers, especially for cardiovascular, gastrointestinal system, and pulmonary diseases (6-8,13). In one study, increased SII values were associated with an increased risk of postoperative recurrence of AF and is a parameter that can be used to independently predict late recurrence of AF after mitral valve surgery (14). Ocal et al. reported that it may be a better predictor of mortality compared to traditional risk factors in coronary artery patients who underwent SII coronary angiography (15). Kudlinsk et al. in a study conducted by patients with COVID-19, it was shown that it may be an independent risk factor in the prognostic process of the disease (16). In a study by Chen et al., SII was reported as a more powerful parameter to predict survival outcomes in patients with colorectal cancer, and its usefulness was demonstrated in patients with high-risk malignancies (17). In our study, it was observed that there was a significant correlation between the high SII values of the patients and the thrombus in the proximal region.

SIRI, another inflammatory marker, is similarly a useful prognostic and diagnostic marker and is useful in many studies (6-8). Chao et al. showed that SIRI can be an objective and reliable marker for the survival of patients with cervical cancer after radical surgery (18). Cakmak et al. reported its usefulness in complications in patients with cholecystitis (19). In a similar study, it was shown that it may be a marker of complication in patients with acute appendicitis (6). In our study, we found a significant relationship between high SII values and proximal PE.

The first of the limitations of our study is that it is retrospective and single-centered. More prospective studies on the patient population are needed to better analyze the data. Since SIRI and SII are inflammatory markers, we think that comparing patients with intermittent follow-up results will give more accurate

results. Another limitation is that we cannot compare it with other inflammation markers. In addition, the inclusion of many scoring systems and patient clinical findings in the study may have affected the results of our study.

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