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A Novel Potential Biomarker for Predicting the Development of Septic Embolism in Patients with Infective Endocarditis: Systemic Coagulation Inflammation Index

Enfektif Endokarditli Hastalarda Septik Emboli Gelişimini Öngörmek İçin Yeni Bir Potansiyel Biyobelirteç: Sistemik Koagulasyon İnflamasyon İndeksi

ABSTRACT

Objective: Early diagnosis of septic emboli is crucial to prevent the associated morbidity and mortality. This study aimed to examine the relationship between the systemic coagulation ınflammation ındex (SCII) and septic embolism in patients with infective endocarditis (IE).

Methods: We retrospectively analyzed the data of 167 IE patients treated at our tertiary care hospital between January 2007 and January 2023. We collected information on symptoms, comorbidities, predisposing valve diseases, prosthetic valves, devices, history of injectable drug use, blood culture results, echocardiographic findings, and complications. The SCII index was calculated using the formula: [platelet count (PLT) × fibrinogen level (g/L) / white blood cell count (WBC)].

Results: The mean age of the patients was 61 years, with rheumatic valve disease being the most common predisposing factor. The most common etiologic microorganism was Staphylococcus species. Septic embolism developed in 25.7% of the patients, with the cerebral system being the most commonly affected (46.5%). The SCII was identified as an independent marker for the development of septic embolism. Receiver operating characteristic (ROC) curve analysis confirmed that an optimal SCII value of 59.8 predicted septic emboli with a sensitivity of 65.1% and a specificity of 59.6% (area under the ROC curve: 0.649 [95% confidence interval (CI): 0.556 - 0.743], *P* = 0.004).

Conclusion: This study demonstrates that high SCII levels are an independent predictor for the development of septic embolism in patients with IE.

Keywords: Infective endocarditis, septic embolism, systemic coagulation inflammation index

ÖZET

Amaç: Septik embolilerin erken teşhisi, bu durumla ilişkili morbidite ve mortaliteyi önlemek için çok önemlidir. Bu çalışma, İE hastalarında sistemik pıhtılaşma inflamasyon indeksi (SCII) ile septik emboli arasındaki ilişkiyi incelemeyi amaçladı.

Yöntem: Üçüncü basamak hastanemizde Ocak 2007 ile Ocak 2023 tarihleri arasında tedavi edilen 167 İE hastasının verileri retrospektif olarak incelendi. Semptomlar, komorbiditeler, predispozan kapak hastalıkları, protez kapak, cihaz, enjekte edilebilir ilaç kullanım öyküsü, kan kültürü sonuçları, ekokardiyografik bulgular ve komplikasyonlara ilişkin veriler toplandı. SCII indeksi [trombosit sayısı (PLT) × fibrinojen seviyesi (g/L)/ beyaz küre sayısı (WBC)] şeklinde hesaplandı.

Bulgular: Ortalama hasta yaşı 61 idi ve romatizmal kapak hastalığı en sık predispozan faktördü. En sık etiyolojik mikroorganizma Staphylococcus türleriydi. Septik emboli gelişme oranı %25,7 idi. En sık emboli yerleşim yeri serebral sistemdi (%46,5). SCII'nin septik emboli gelişimi için bağımsız bir belirteç olduğu bulundu. ROC eğrisi analizi, SCII için optimal değer olan 59,8'in %65,1 duyarlılık ve %59,6 özgüllükle septik emboli öngördüğünü doğruladı (ROC eğrisi altındaki alan: 0,649 [%95 GA:0,556–0,743], *P* = 0,004).

Sonuç: Yüksek SCII düzeylerinin EE'li hastalarda septik emboli gelişimi için bağımsız bir belirleyici olduğunu gösterdik.

Anahtar Kelimeler: Enfektif endokardit, septik emboli, sistemik pıhtılaşma inflamasyon

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

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Infective endocarditis (IE) is an inflammatory heart condition resulting from the microbial invasion of the heart valves and endocardium.[1] Historically, the incidence of IE ranged from 3 to 10 cases per 100,000 people; however, this has recently increased due to the widespread use of cardiac device treatments and prosthetic materials. Hospital mortality rates for IE hover between 15% and 30.[2] Notably, the primary causes of mortality in IE patients are heart failure and embolic complications. The rate of embolic complications in patients with IE is reported to be between 20-50%, and embolic events occur before IE is diagnosed in approximately half of the cases.[3] The most common site for embolic complications is the brain, accounting for approximately 50% of cases, followed by the spleen, lungs, kidneys, and extremities.[1,3]

In recent years, there has been growing interest in investigating clinical, laboratory, and echocardiographic predictors to identify patients at high risk of developing embolic complications in IE. Previous studies have identified several predictors, including the size of the vegetation (> 10 mm), its mobility, mitral valve involvement, multiple valve involvement, and a history of embolic complications in previous IE episodes.[1,4] On the other hand, laboratory parameters such as white blood cell count, C-reactive protein, procalcitonin, erythrocyte sedimentation rate, neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (TLR), and systemic immune inflammation index (SII) have been shown to predict hospital mortality and embolic complications.[1,4,5] The pathogenesis of IE involves a complex relationship between pathogenic microorganisms on the valve endothelium, and the host immune response, coagulation, and inflammation.[3,5] Previous studies have investigated the role of inflammatory parameters in predicting embolic complications in patients with IE, with integrated parameters such as NLR, TLR, and SII reported to be stronger predictors than single inflammation parameters.[5-7] In this study, we aim to investigate whether the systemic coagulation-inflammation index (SCII), a new biomarker that integrates inflammation and coagulation parameters such as platelet count, fibrinogen level, and leukocyte count, has a prognostic role in the development of embolic events in patients with IE.

Materials and Methods

We conducted a retrospective analysis of the medical records of 167 patients diagnosed with infective endocarditis between January 2007 and January 2023. Patients with inflammatory disorders, autoimmune conditions, malignant tumors, hypercoagulable conditions, or any other blood system-related disorders were excluded from the study. We collected data on clinical manifestations, medical history, pre-existing valvular disorders, prosthetic valves, implanted devices, history of injectable drug use, microbial culture outcomes, echocardiographic evaluations, clinical outcomes, cardiac rhythm, and laboratory parameters at the time of hospital admission from electronic medical records. Following hospital admission, we collected blood cultures from at least three separate venous sites at one-hour intervals for all study participants. Additionally, we drew samples for the examination of specific antibodies. During any surgical procedures, we examined and sent for culture any extracted valves and structures. We administered empiric antibiotic treatment based on the guidelines of either the American Heart Association or the European Society of Cardiology.[8,9] We calculated the SII, a biomarker reflecting the balance between systemic inflammation and immune function in the body, [Neutrophil count (Neu) x platelet count (PLT) / Lymphocyte count (Lym)].[10] We calculated the SCII index as [platelet count (PLT) × fibrinogen level (g/L) / white blood cell count (WBC)].[6]

On the first day of hospitalization, we conducted a transthoracic echocardiographic examination on all patients using either Vivid S70 or Vivid 7 Pro devices (GE, Horten, Norway). An experienced cardiologist, who was blinded to the participants' results, analyzed the echocardiogram records. Transesophageal echocardiography (TEE) was conducted in almost all patients to confirm suspected infection of the prosthetic heart valve, assess valve dysfunction, detect septal defects, identify any other mechanical complications, and evaluate patients with clinical suspicion of IE but negative transthoracic echocardiographic findings. Septic embolism was diagnosed according to the European Society of Cardiology (ESC) guideline criteria, following a comprehensive physical examination and a detailed anamnesis of symptoms. Imaging methods appropriate to the relevant symptoms were employed, including but not limited to fever, chills, shortness of breath, neurological deficits, skin changes, chest pain, and abdominal pain.[11] The study was approved by the Trakya University Medical Faculty Ethics Committee (Approval Number: TUTF-GOBAEK 2023/39, Date: 13.02.2023), and it complied with the Helsinki Declaration.

Statistical Analysis

Statistical analysis of the data was performed using version 26.0 of the Statistical Package for the Social Sciences (SPSS) software (SPSS Inc., Chicago, Illinois USA,). The Kolmogorov-Smirnov test was utilized to determine the normality of the data distribution. Depending on the normality of the distribution, descriptive statistics were reported as either mean ± standard deviation or median (minimum-maximum). Nominal variables were described using frequencies and percentages. The independent-samples t-test was applied to compare normally distributed quantitative variables, while the Mann-Whitney U test was used for non-normally distributed quantitative variables. Categorical variables were presented as percentages or numbers, with the chi-squared test employed for comparison. Binary logistic regression analysis was conducted to identify predictors of septic embolism. All tests were deemed statistically significant at a

ABBREVIATIONS

CRP	C-Reactive Protein
EF	Ejection Fraction
IE	Infective Endocarditis
Lym	Lymphocyte
MRCNS	Methicillin-Resistant Coagulase-Negative Staphylococci
MRSA	Methicillin-Resistant *Staphylococcus aureus*
MSCNS	Methicillin-Sensitive Coagulase-Negative Staphylococci
MSSA	Methicillin-Sensitive *Staphylococcus aureus*
Neu	Neutrophil
PLT	Platelet
SCII	Systemic Coagulation Inflammation Index
SII	Systemic Immune-Inflammation Index
WBC	White Blood Cell

p-value of < 0.05. The area under the curve (AUC) for the SCII index was calculated using the receiver operating characteristic (ROC) curve to estimate the incidence of septic embolism.

Results

The data of 167 participants diagnosed with IE, who met the inclusion criteria, were analyzed. Of the total number of patients, 25.7% (n = 43) were diagnosed with septic emboli, and the median age of these patients was 64 years (range: 40-82 years). The median age of the second group, which did not have septic embolism, was 60.5 years (range: 34-84 years). A comparison of hospital admission complaints and demographic data of the patients included in the study is presented in Table 1. The mean age of all the patients in the study was 61 years, and there were no statistically significant differences in terms of demographic data and risk factors between the groups. The predominant symptoms reported by the patients were high fever (66.5%), aching joints and muscles (62,9%), dyspnea (55.7%), weakness (53.3%), and syncope (30.5%). Syncope was more common in the septic embolism group (P < 0.001).

The laboratory parameters, embolic, and echocardiographic features during hospitalization are compared in Table 2. Upon examining the laboratory measurements, no significant differences were found in renal function, left ventricular ejection fraction ratio, and hemoglobin counts between the two groups (P > 0.05). However, the group with septic embolism exhibited higher SCII values and inflammation markers compared to the control group. Regarding vegetation localization, although mitral valve involvement was more common in the septic embolism group, the difference between the groups was not statistically significant. In the septic embolism group, the most frequent embolization site was the brain (46.5%), followed by the coronary arteries (2.3%) and mesenteric arteries (2.3%). Abscess was the most common valve complication in both groups, but dehiscence was more prevalent in the septic embolism group. Staphylococcus species were identified as the most common pathogen causing infective endocarditis in our study, with no significant differences in pathogens between the two groups. The vegetation size was significantly larger in the septic embolism group than in the other groups (P < 0.001).

To investigate the impact of various risk factors on the development of septic embolism, we performed logistic regression analysis, and the results are presented in Table 3 and Table 4. The findings indicated that patients with septic embolism had elevated inflammatory markers and SCII values. Additional measurements are provided in Tables 3 and 4. The multivariate analysis results were illustrated in the relative importance plot of the multivariate analysis models (Figure 2). Figure 3 displays the effect of the systemic immune inflammation index, neutrophil, PLT, and lymphocyte values on the development of septic embolism, as determined by ROC analysis.

Receiver Operating Characteristic (ROC) curve analysis revealed that an SCII cut-off value of ≥ 59.8 optimally predicted the development of septic embolism, with a sensitivity of 65.1% and a specificity of 59.6%. The area under the ROC curve was 0.65 (95% confidence interval: 0.556 - 0.743), demonstrating the effectiveness of SCII in predicting septic embolism development (Figure 1). ROC analysis for septic embolism development also showed that a vegetation size ≥ 11.4 mm was significant, with a specificity of 66.9% and a sensitivity of 67.4%.

Table 1. Demographic Characteristics and Symptoms of the Study Populations

	Septic Embolism Group (n = 43)	Non-Embolic Group (n = 124)	*P*
Age, n (%)	64 (40 - 82)	60.5 (34 - 84)	0.51
Hypertension, n (%)	30 (69.8)	82 (66.1)	0.80
Diabetes Mellitus, n (%)	9 (20.9)	21 (16.9)	0.35
Drinking, n (%)	18 (41.9)	51 (41.1)	0.53
Smoking, n (%)	21 (48.8)	61 (49.2)	0.55
Chronic Heart Failure, n (%)	6 (14)	15 (12.1)	0.46
Prior Stroke, n (%)	2 (4.7)	5 (4)	0.57
IV Drug User, n (%)	2 (4.7)	4 (3.2)	0.46
Dialysis, n (%)	1 (2.3)	3 (2.4)	0.72
Intracardiac Device, n (%)	3 (7)	11 (8.9)	0.69
Atrial Fibrillation, n (%)	5 (11.6)	13 (10.5)	0.51
Syncope, n (%)	23 (53.5)	28 (22.6)	<0.001
Fever, n (%)	25 (58.1)	86 (69.4)	0.17
Dyspnea, n (%)	20 (46.5)	73 (58.9)	0.22
Weakness, n (%)	21 (48.8)	68 (54.8)	0.61
Aching Joints and Muscles, n (%)	25 (58.1)	80 (64.5)	0.28

Table 2. Laboratory Findings, Embolic, and Echocardiographic Characteristics of the Study Populations

	Septic Embolism Group (n = 43)	Non-Embolic Group (n = 124)	*P*
WBC Count (10^3/μL)	14.2 (9.8 - 18.9)	11.7 (5.8 - 17.9)	<0.001
Lymphocyte Count (10^3/μL)	1.7 (1 - 2.5)	1.6 (0.7 - 2.2)	0.01
Neutrophil Count (10^3/μL)	10.1 ± 1.8	9.3 ± 1.6	0.01
Platelet Count (10^3/μL)	236.8 ± 59.3	200.8 ± 40.4	<0.001
CRP	98 ± 25.1	70.3 ± 19.3	<0.001
Fibrinogen (g/L)	4.1 ± 1.6	3 ± 1.2	<0.001
Creatinine	1 (0.5 - 1.4)	0.9 (0.5 - 1.5)	0.03
Hemoglobin (mg/dL)	11.1 ± 2.2	11.2 ± 2	0.90
Left Ventricular Ejection Fraction (%)	59 (47 - 68)	61 (48 - 74)	0.05
Vegetation Size	13.2 (4.1 - 22.5)	9.1 (4 - 23.6)	<0.001
SCII	69.1 ± 28.7	54.7 ± 27	0.003
SII	1,444.1 (504.3 – 3,339.6)	1,094.6 (364.2 – 3,294)	0.02
Embolic Complication			
Cerebral	20 (12)		
Splenic	8 (4.8)		
Pulmonary	7 (4.2)		
Renal	3 (1.8)		
Peripheral	3 (1.8)		
Coronary	1 (0.6)		
Mesenteric	1 (0.6)		
Vegetation Location			
Aortic Vegetation	12 (27.9)	58 (46.8)	0.23
Mitral Vegetation	23 (53.5)	53 (42.7)	
Tricuspid Vegetation	4 (9.3)	6 (4.8)	
Pulmonary Vegetation	0 (0)	1 (0.8)	
Device Vegetation	1 (2.3)	3 (2.4)	
Prosthetic Valve	3 (7)	3 (2.4)	
Valvular Complication			
Abscess	3 (7)	16 (12.9)	0.18
Fistula	1 (2.3)	2 (1.6)	
Pseudoaneurysm	1 (2.3)	4 (3.2)	
Dehiscence	3 (7)	1 (0.8)	
Culture*			
Coagulase Negative Staph.			0.42
MRCNS	15 (34.8)[a]	28 (22.6)[a]	
MSCNS	3 (7)[a]	17 (13.7)[a]	
Staphylococcus aureus			
MRSA	3 (7)[a]	9 (7.3)[a]	
MSSA	11 (25.6)[a]	21 (16.9)[a]	
Streptococcus	2 (4.7)[a]	7 (5.6)[a]	
Enterococcus Faecalis	0 (0)[a]	9 (7.3)[a]	
Gram negative	3 (7)[a]	8 (6.5)[a]	
Brucella	0 (0)[a]	3 (2.4)[a]	
Candida	1 (2.3)[a]	2 (1.6)[a]	
Culture Negative	5 (11.6)[a]	20 (16.1)[a]	
Group Comparison (Staph. Etiology)			
Staph. Species	32 (84.2)	75 (72.1)	0.1
Non-Staph. Species	6 (15.8)	29 (27.9)	

[a]There is no significant difference between groups with the same letter. *Compared the column proportions with the Bonferroni method. CRP, C-reactive protein; EF, ejection fraction; MRCNS, methicillin resistant coagulase negative Staphylococcus; MRSA, methicillin resistant *Staphylococcus aureus*; MSCNS, methicillin sensitive coagulase negative Staphylococcus; MSSA, methicillin sensitive *Staphylococcus aureus*; SICI, systemic inflammation and coagulation index; SII, systemic immune-inflammation index; WBC, white blood cell.

Table 3. Univariate Predictors of Septic Embolism in Patients with Infective Endocarditis

	Univariate Analysis*		
	Odds Ratio	**(95% C.I. for Odds Ratio)**	***P***
Age	1.007	(0.977 - 1.038)	0.656
WBC	1.559	(1.339 - 1.911)	<0.001
Lym	1.71	(1.089 - 2.62)	0.004
Neu	1.334	(1.077 - 1.651)	0.008
Fibrinogen	1.801	(1.359 - 2.389)	<0.001
PLT	1.017	(1.008 - 1.025)	<0.001
Vegetation Size	1.232	(1.122 - 1.351)	<0.001
SCII	1.018	(1.006 - 1.031)	0.004
SII	1.001	(1.000 - 1.004)	0.038

*Univariate analysis conducted via Logistic Regression (Method = Enter).

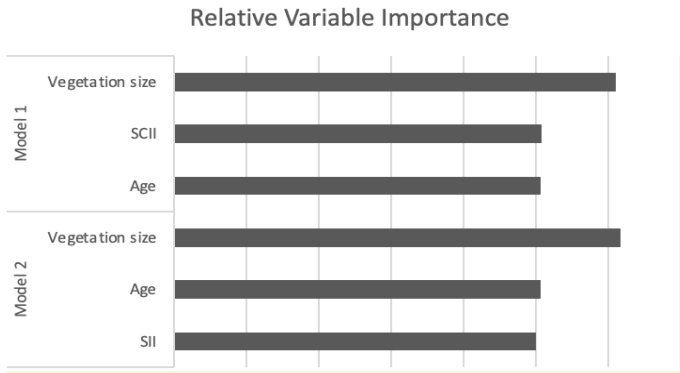

Figure 2. Graph of the relative importance of multivariate analysis models.

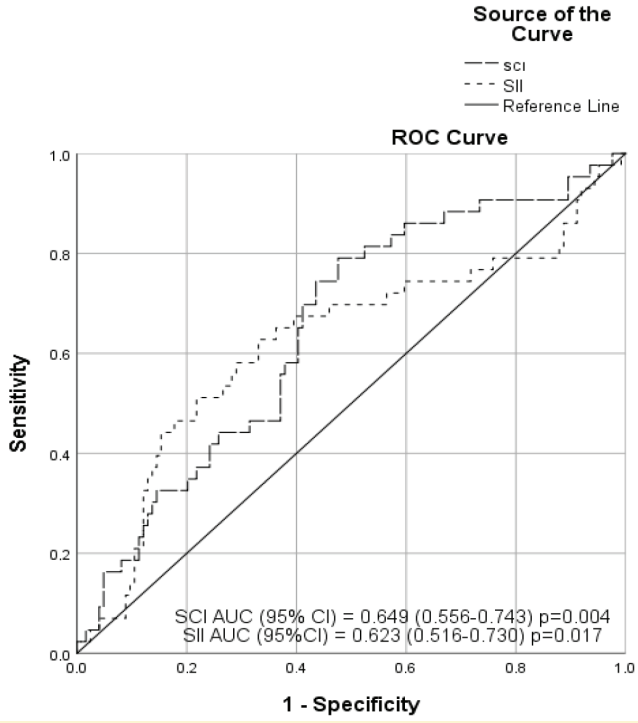

Figure 1. Effect of systemic coagulation inflammation index (SCII) and systemic immune inflammation index (SII) on the development of septic embolism, analyzed using Receiver Operating Characteristic (ROC) curves.

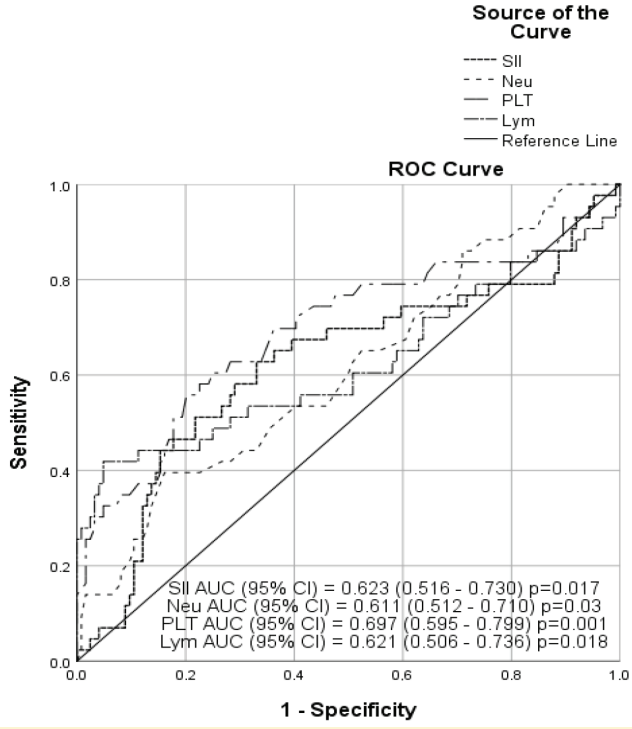

Figure 3. Effect of systemic immune inflammation index (SII), neutrophil count, platelet (PLT) count, and lymphocyte count on the development of septic embolism, analyzed using Receiver Operating Characteristic (ROC) curves.

Table 4. Multivariate Predictors of Septic Embolism in Patients with Infective Endocarditis

		Multivariate Analysis*			
		Odds Ratio	**(95% C.I. for Odds Ratio)**	***P***	**Chi-Square**
Model 1	Age	1.014	(0.980 - 1.050)	0.414	8.163
	Vegetation Size	1.221	(1.111 - 1.341)	<0.001	
	SCII	1.016	(1.003 - 1.031)	0.02	
Model 2	Age	1.013	(0.979 - 1.048)	0.456	13.613
	Vegetation Size	1.233	(1.122 - 1.354)	<0.001	
	SII	1.001	(1.000 - 1.001)	0.051	

*Logistic Regression (Method = Enter). Model 1: Cox & Snell R Square = 0.377, Nagelkerke R Square = 0.554; Model 2: Cox & Snell R Square = 0.376, Nagelkerke R Square = 0.553.

Discussion

The most significant finding of our study is that an increase in the SCII serves as an independent predictor for the development of septic emboli in patients with IE.

The valve endothelium is structurally resistant to infection, but mechanical damage to the endothelium leads to the exposure of extracellular matrix proteins, resulting in local inflammation and the accumulation of fibrin and platelets in this region. This also promotes platelet activation and additional fibrin formation.[12] These changes may contribute to the adhesion of bacteria to the endothelial surface, thrombus formation, and the progression of the infected material through adhesins.[13] Thrombin, the product of the coagulation cascade, plays a bridging role in this process, called immunothrombosis.[14] This strong relationship between inflammation and coagulation has led its description as "coagulation at the core of IE".[15] Septic embolism, a condition in which fragmented material from the source of infection travels through the circulatory system, causes vascular obstruction and results in two types of tissue damage. The first is an early ischemic event due to occlusion of blood vessels, leading to infarction. The second is inflammation and abscess formation secondary to infection, owing to the presence of infected material.[16] Early prediction and intervention in this clinical condition, which is associated with high mortality and morbidity, are crucial. Previous studies have shown that early initiation of antimicrobial therapy is the most effective method for preventing embolic events, as it suppresses inflammation and inhibits the maturation of vegetative material.[9,17] The value of surgical removal of infective material, however, is debatable due to concerns regarding timing and surgical risks.

In this study, we retrospectively analyzed data from 167 patients. The mean age of the patients included in the study was 61. The patients were divided into two groups based on the presence or absence of septic emboli. Consistent with the literature, the rate of septic emboli in IE patients was 25.7%.[1] Syncope was more common in the septic embolism group than in the control group. Other demographic data and symptoms were similar between the two groups.

Previous studies have indicated that systemic inflammation can affect the prognosis of IE. Agus et al.[5] reported that an increase in SII values may indicate a higher mortality risk in patients with IE. Hu et al. [18] showed that high levels of inflammation and SII values may predict the occurrence of septic emboli. In our study, the SII values were higher in the septic emboli group, consistent with findings in the literature. Additionally, levels of inflammation biomarkers such as WBC, C-reactive protein (CRP), PLT, Neu, and Lym were also elevated in this group, which aligns with previous research.[5]

Studies have shown that matrix metalloproteinases, mean platelet volume, Anti-ß2-glycoprotein I antibodies, parameters affecting coagulation, and D-dimer levels, which indicate serum coagulation level and fibrin turnover, may also serve as predictors of septic embolism.[19-21] The SCII is a new hematological parameter that reflects inflammation and coagulation levels, providing a comprehensive assessment of these pathways. It is a useful tool for assessing an individual's overall inflammatory and coagulation status and has previously demonstrated utility in other clinical situations where inflammation and coagulation play significant roles.[6] In our study, the SCII values were significantly higher in the septic embolism group when compared between the groups.

After microorganisms invade the valve endothelium, tissue factor expression begins, prompted by monocyte migration and endothelial cell activation in the region.[15] This leads to an increase in inflammation, coagulation, and fibrin accumulation in the vegetated area. Fibrin acts as a scaffold for white blood cells, platelets, and microorganisms in this region.[15] Consequently, the aggregation of microbial agents, fibrin, and blood cells leads to the formation of larger vegetations. Studies have indicated that vegetation size (especially ≥ 10 mm) and mitral valve involvement can result in a higher incidence of septic emboli.[22] Our study aligns with the literature regarding vegetation location and size, with a higher SCII value and larger vegetations observed in the septic embolism group. This is consistent with the literature, considering that the parameters involved in vegetation growth are used in calculating the index.

In retrospective analyses, IE-related septic emboli were most frequently found in the cerebral system (occurring in approximately 40-50% of cases, with higher rates in recurrent IE patients).[23,24] In cranial Magnetic Resonance Imaging (MRIs) performed regardless of symptoms, this rate rose to as much as 80%.[25] In our study, the most common embolism location was also the cerebral system (46.5%), followed by the spleen and pulmonary system. Upon examining etiologic pathogens, staphylococci emerged as the most common pathogens in culture-positive patients. Recent studies have shown an increase in the incidence of staphylococci, which can be attributed to a decrease in the incidence of rheumatic heart disease and an increase in invasive procedures. Our study results are similar to those reported in the literature.[26,27] When the groups were evaluated in terms of valve complications, abscesses were the most common. Although dehiscence was observed at the same rate in the septic emboli group, pseudoaneurysm was the second most common complication in the group without emboli. No statistically significant differences were found between the groups.

In our study, factors affecting the development of septic embolism were evaluated using univariate analysis. High SCII values were found to be significantly correlated with septic embolism. Similarly, an increase in inflammatory markers was also found to be significant, consistent with the literature. This strong correlation continued to be observed in multivariate analysis. ROC curve analysis confirmed that an optimal SCII value of 59.8 predicted septic emboli with 65.1% sensitivity and 59.6% specificity (area under the ROC curve: 0.649 [95% CI: 0.556 - 0.743], $P = 0.004$).

Study Limitations

The main limitation of our study is that it was a single-center retrospective study with a relatively small number of patients. Additionally, septic emboli were diagnosed using imaging methods when symptoms developed in the patient, leaving the condition of asymptomatic patients with septic emboli uncertain. This index should be evaluated prospectively in larger studies.

Conclusion

Our study is valuable for predicting the development of septic emboli in patients with infective endocarditis. This condition is

becoming more common due to the increasing use of minimally invasive surgical procedures, percutaneous valve operations, and intracardiac devices. Our findings can be particularly useful for the early diagnosis and treatment of complications such as septic emboli, which increase mortality and morbidity. Additionally, we have observed a decrease in streptococcal positive endocarditis due to the reduced incidence of rheumatic heart diseases. It would be beneficial to re-evaluate the frequency of pathogens causing infective endocarditis in larger studies.

Ethics Committee Approval: The study was approved by the Trakya University Medical Faculty Ethics Committee (Approval Number: TUTF-GOBAEK 2023/39, Date: 13.02.2023).

Informed Consent: Written informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - U.Ö., M.G.; Design - U.Ö., M.G.; Supervision - U.Ö., M.G.; Resource - U.Ö., M.G.; Materials - U.Ö., M.G.; Data Collection and/or Processing - U.Ö., M.G.; Analysis and/or Interpretation - U.Ö., M.G.; Literature Review - U.Ö., M.G.; Writing - U.Ö., M.G.; Critical Review - U.Ö., M.G.

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