

The Influence of Characteristics and Indexes (NLR, PNI, and SII) Evaluated at Admission on the Mortality Prediction of Infectious Endocarditis Patients

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Background: Infective endocarditis (IE) is a serious and potentially life-threatening infection with high morbidity and mortality. Early risk identification is critical for enabling timely treatment and preventing adverse outcomes. Recently, several low-cost and accessible inflammatory markers, such as the neutrophil-to-lymphocyte ratio (NLR), prognostic nutritional index (PNI), and systemic immune-inflammation index (SII), have gained attention for their potential prognostic value in infectious diseases.

Methods: This retrospective study evaluated patients diagnosed with definite IE between May 2014 and May 2024 at Bakirkoy Dr. Sadi Konuk Training and Research Hospital. Clinical characteristics, laboratory parameters, complications, and outcomes were compared between survivors and non-survivors. The predictive value of NLR, PNI, and SII for in-hospital mortality was assessed.

Results: A total of 78 patients with IE were included, with an overall mortality rate of 52.5%. Non-survivors were significantly older ($p = 0.001$) and had higher rates of cardiac complications ($p < 0.05$). PNI values were significantly lower in non-survivors ($p = 0.014$). Undergoing cardiac surgery was associated with a lower mortality rate ($p = 0.024$).

Conclusion: PNI, a simple, inexpensive, and readily available marker, may provide valuable prognostic information in patients with infective endocarditis. This index could help in early risk stratification and clinical decision.

Keywords: biomarkers, infective endocarditis, mortality, neutrophil-to-lymphocyte ratio, systemic immune-inflammation index, prognostic nutritional index

Introduction

Infectious endocarditis (IE) is a life-threatening infection of the inner lining of the heart muscle (endocardium) and cardiac valves. IE has significant morbidity and high mortality rates. Rapid diagnosis, causative agent identification, prognostic evaluation and timely treatment initiation are critically important. Managing IE is complex; following procedures should include clinical signs, imaging, and laboratory results.^{1,2}

With the rapid development of medical knowledge in recent years, significant progress has been made in diagnosing and treating IE. However, the frequency of IE, which is approximately 13/100,000, has increased in recent years.^{3,4} IE-associated mortality rates (15–30%) continue to be high,⁴ and there are various severe complications. Identifying high-risk patients is essential in improving infective endocarditis (IE) outcomes. Although early diagnosis and prompt treatment are critical in the management of infective endocarditis, accurate prediction of patient prognosis is also crucial. This study focuses on the prognostic value of inflammation-based indices assessed at admission. Risk stratification helps

us determine the appropriate time to perform surgery, prevent complications, and identify patients at risk of mortality. However, there is limited data on the prognostic significance of NLR, PNI, and SII specifically in IE, and their comparative predictive performance has not been well defined in this context in the literature.

Many potential biomarkers associated with pro-inflammatory and anti-inflammatory processes represent pathophysiological pathways of disease processes. Indicators such as white blood cell count (WBC), C-reactive protein (CRP), procalcitonin, and erythrocyte sedimentation rate (ESR) are used to assess the severity of inflammation. Thus, readily accessible and inexpensive inflammatory indicators, such as peripheral blood cell ratios, have drawn the attention of medical researchers.

Numerous biomarkers including the platelet lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), systemic immune-inflammation index ($SII = \text{platelet count} \times \text{neutrophil count} / \text{lymphocyte count}$) have been assessed as a promising indicator of adverse outcomes in various infectious, inflammatory, and immune-related disorders. The prognostic nutritional index (PNI), based on serum albumin and lymphocyte concentrations, is a new inflammation-based risk score that predicts outcomes in various patient populations. Despite their increasing use in other clinical settings, it remains unclear how these indices can meaningfully influence risk-based clinical decisions in IE. Clarifying this could enhance early prognostic assessment using simple and cost-effective tools.

This study aimed to investigate the influence of characteristics and indexes (NLR, PNI, and SII) evaluated at admission on the mortality prediction of IE patients. The findings are expected to significantly increase the understanding and management of IE, contributing to the medical community.

Materials and Methods

Patients who were treated and followed up consecutively with the diagnosis of infective endocarditis at Bakırköy Dr. Sadi Konuk Training and Research Hospital between May 2014 and May 2024 were retrospectively evaluated to identify risk factors for mortality. Infective endocarditis was diagnosed by the infectious disease specialist according to the Modified Duke criteria² and confirmed by the cardiology specialist. Patients who were HIV positive, under the age of 18, or had no criteria for the definitive diagnosis of endocarditis, were excluded from the study. Only patients with complete data for all laboratory variables required for the analysis were included.

Patients who survived were compared with those who died of endocarditis during hospital stay in terms of risk factors for mortality. Clinical information (including demographic characteristics, laboratory findings, comorbidities, prosthetic valve, blood culture results, echocardiography findings, the presence of urinary and central venous catheters, hospitalization and intensive care unit stays within the last 3 months, clinical outcomes, complications, and surgical interventions) was retrieved retrospectively from the hospital's information operating system.

Demographic Data included gender, age, presence of echocardiography findings, fever, having microbiological evidence, native or prosthetic valve endocarditis; comorbidities (predisposing heart disease, diabetes mellitus, hypertension, coronary artery disease, chronic renal failure, chronic obstructive pulmonary disease, congestive heart failure, immunosuppressive therapy), intravenous (iv) drug use, previous history of endocarditis, surgical intervention; complications (Embolic Phenomenon, Cardiac Complication, Neurological Complications, Affected heart valve); laboratory data including leukocyte counts, hemoglobin values, lymphocyte counts, platelet counts, CRP, ESR, procalcitonin, albumin, ALT, AST, and total cholesterol values were compared between survivor and non-survivor patients.

Chronic pulmonary dysfunction was defined as $FEV1/FVC < 70\%$ predicted, renal dysfunction was defined as $GFR < 60 \text{ mL/min/1.73 m}^2$ or serum creatinine $> 1.5 \text{ mg/dL}$, "predisposing heart disease" was clarified as including prior history of valvular or congenital heart disease, or presence of prosthetic valves.

Three sets of blood cultures were collected at 30-minute intervals without waiting for a febrile period. Each set contained one aerobic and one anaerobic bottle, inoculated with 10 mL of blood per bottle. Two sets of control blood cultures were repeated every 48 hours after the initiation of therapy until sterile blood cultures. Blood samples were cultured in BACTEC (Beckton Dickinson, USA). Identification was performed using both conventional methods and automated systems, Phoenix BD (Becton Dickinson, USA) until 2020 and VITEK 2 Compact (bioMérieux, France) thereafter. Antimicrobial Susceptibility Testing was evaluated according to the standards set by EUCAST (European

Committee on Antimicrobial Susceptibility Testing). The time for the last blood culture positivity refers to the number of days from hospital admission to the last positive blood culture result.

Cardiology physicians examined patients suspected of IE with transthoracic and multiplane transesophageal echocardiography at admission or with patient consultation. Echocardiographic data included routine parameters and the presence of vegetation and abscesses.

We calculated the Prognostic Nutritional Index (PNI) as follows: $PNI = (10 \times \text{serum albumin [g/dL]}) + (0.005 \times \text{lymphocytes}/\mu\text{L})$ and the Systemic Immune Inflammation Index (SII) as follows: $SII = (\text{platelet count} \times \text{neutrophil count})/\text{lymphocyte count at admission}$.^{5,6}

Indications for surgery were severe heart failure, severe valve dysfunction, prosthetic valve infection, invasion beyond the valve leaflets, recurrent systemic embolization, large mobile vegetations, or persistent sepsis despite adequate antibiotic therapy for more than 5–7 days.⁷ In our hospital, cardiologists and cardiovascular surgeons collaborate to make surgical decisions regarding IE based on the established guidelines but specific to the patient.¹

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were expressed as numbers and percentages. The chi-squared test was used to compare categorical variables. Statistical analyses were performed using SPSS version 26.0 (IBM Corporation, Armonk, NY, USA). Differences with $p < 0.05$ were considered to be statistically significant. The distribution of variables was evaluated using the Shapiro–Wilk and Kolmogorov–Smirnov tests. Non-parametric tests (Mann–Whitney *U*-test and chi-squared test) were applied to data that were not normally distributed. Variables included in the multivariate analysis (multivariate regression analysis) were selected based on statistical significance in the univariate analysis ($p < 0.05$) and their clinical relevance, as supported by the literature. Given the limited number of mortality events in our cohort, the number of variables was restricted to minimize the risk of overfitting. This approach aimed to maintain a balance between statistical significance and clinical plausibility while respecting the event-per-variable principle.

Results

In this study, seventy-eight patients diagnosed with definite IE, 47 (60%) male and 31 (40%) female, were retrospectively analyzed. The mean age of men, women, and all patients was 56.25 ± 17.86 , 57.18 ± 21.2 years, and 56.3 ± 17.76 years, respectively.

The most common comorbidity was hypertension ($n = 30$, 38.5%), followed by coronary artery disease ($n = 26$, 33.3%) and diabetes mellitus ($n = 22$, 28.2%). Fifteen patients (19.2%) had chronic kidney failure. Fifty-eight patients were hospitalized and/or in intensive care in the last three months. Forty-nine patients had urinary catheters, and 41 patients had central venous catheters. A history of hospitalization at intensive care in the last 3 months was found to be in 58 (74%) patients overall and 32 (78%) of the deceased patients. In our study population, 4 of the patients had a prior history of infective endocarditis and 3 patients reported intravenous drug use.

Mortality rates were 52.5% ($n:41$). Notably, the mean age of non-survivor patients was significantly higher than the mean age of survivor patients (64.21 ± 2.42 years vs 47.59 ± 2.63 years, $p < 0.001$; Table 1). Among the non-survivors, surgery was not performed in 6 patients due to high operative risk and in 7 patients due to early-onset cerebrovascular events following diagnosis.

When the demographic characteristics of survivors and non-survivors were compared, the statistically significant findings were age, embolic phenomenon ($p:0.013$), cardiac complication ($p:0.031$), and neurological complication ($p:0.003$) (Table 1).

To undergo cardiac surgery was found to be significant between survivor (22 of 37 patients) and non-survivor patients (15 of 41 patients), statistically ($p = 0.043$).

The mean time for the last blood culture positivity in 47 patients was 13 ± 8.9 days, as that mean time was 10 days in survivor patients and 13 days in non-survivor patients.

Staphylococcus aureus bacteremia was found in 17 (21.7%) patients. The rates of methicillin-resistant *S. aureus* (MRSA) were 52.9%. Other pathogens were coagulase-negative staphylococci (12.8%), enterococci (11.5%), and

Table 1 Demographic Data of Survivor and Non-Survivor Patients

Variables		Survivor (n:37)		Non-Survivor (n:41)		p-value
		N	%	N	%	
Gender	Men	20	54.1	27	65.9	0.288
	Women	17	45.9	14	34.1	
Age		47.59 ± 2.63		64.21 ± 2.42		<0.001
Presence of echocardiography finding		37	47.4	41	52.6	1
Blood culture yielding	Negative	13	35.1	18	43.9	0.429
	Positive	24	64.9	23	56.1	
Fever (≥ 38°C)	No	17	45.9	14	34.1	0.288
	Yes	20	54.1	27	65.9	
Predisposing Heart Disease	No	30	81.1	26	63.4	0.083
	Yes	7	18.9	15	36.6	
Vascular phenomenon	No	30	81.1	27	65.9	0.130
	Yes	7	18.9	14	34.1	
Immunological Phenomenon	No	36	97.3	40	97.6	1
	Yes	1	2.7	1	2.4	
Microbiological Evidence	No	13	35.1	18	43.9	0.429
	Yes	24	64.9	23	56.1	
Affected heart valve	Mitral	20	54.1	28	68.3	0.336
	Tricuspid	6	16.2	3	7.3	
	Aort	11	29.7	19	46.3	
Native Valve Endocarditis	Yes	30	81.1	33	80.5	0.947
Prostatic valve endocarditis	Yes	6	16.2	9	22	0.521
Embolic Phenomenon	No	18	48.6	9	22	0.013
	Yes	19	51.4	32	78	
Cardiac Complication	No	30	81.1	24	58.5	0.031
	Yes	7	18.9	17	41.5	
Neurological Complications	No	26	70.3	15	36.6	0.003
	Yes	11	29.7	26	63.4	
Diabetes mellitus	No	29	78.4	27	65.9	0.220
	Yes	8	21.6	14	34.1	
Hypertension	No	26	70.3	22	53.7	0.132
	Yes	11	29.7	19	46.3	

(Continued)

Table 1 (Continued).

Variables		Survivor (n:37)		Non-Survivor (n:41)		p-value
		N	%	N	%	
Coronary artery disease	No	27	73	25	61	0.262
	Yes	10	27	16	39	
Chronic renal failure	No	31	83.8	32	78	0.521
	Yes	6	16.2	9	22	
Chronic obstructive pulmonary disease	No	34	91.9	38	92.7	0.896
	Yes	3	8.1	3	7.3	
Congestive heart failure	No	33	89.2	35	85.4	0.740
	Yes	4	10.8	6	14.6	
Immunosuppressive therapy	No	34	91.9	37	90.2	1
	Yes	3	8.1	4	9.8	
Surgical Intervention	No	15	40.5	26	63.4	0.043
	Yes	22	59.5	15	36.6	
Intravenous drug use	No	34	91.9	41	100	0.102
	Yes	3	8.1	0	0	
Previous history of endocarditis	No	35	94.5	39	95.1	1
	Yes	2	5.5	2	4.9	

streptococci (5%), respectively. Other identified agents included Gram-negative bacteria and Candida species. Blood culture did not yield in 39.7% of patients. Blood cultures yielded in 56.1% of the deceased patients.

The neutrophil count was significantly higher in patients who died than in those who survived (8090 ± 953 vs 15077 ± 1719 , $p < 0.001$; [Table 2](#)). NLR index significantly differed between survivor and non-survivor patients; this index was higher in non-survivor patients ($p < 0.001$). Lower PNI ($p = 0.012$) and higher SII ($p = 0.002$) rates were found to be significant between patients who died and those who survived, respectively, in univariate analysis ([Table 2](#)).

ROC analysis revealed that the neutrophil/lymphocyte ratio (NLR), systemic inflammatory index (SII), and prognostic nutritional index (PNI) were statistically significant in predicting mortality. When the cut-off value for NLR was set at 11.1, sensitivity was 56.1% and specificity was 43.9% (AUC: 0.756; $p < 0.001$). When the cut-off value for SII was set at 2819.6 sensitivity was 51.2% and specificity was 41.5% (AUC: 0.699; $p = 0.001$). When the PLR value was set at 56.1% sensitivity and 43.9% specificity, no statistical significance was found (AUC: 0.434, $p = 0.311$, Cut-Off = 138.6). When the PNI cut-off was set at 29.5, the sensitivity was 58.5% and the specificity was 41.5% (AUC: 0.335; $p = 0.009$).

When evaluated according to cut-off values ([Table 3](#)), NLR, PNI, and SII affected mortality in the univariate analysis ($p = 0.009$, $p = 0.015$, $p = 0.015$, respectively). On the other hand, no significant difference was found between the groups according to the cut-off value determined for PLR ($p = 0.953$). [Table 4](#) shows the factors affecting mortality, according to ROC analysis.

Table 2 Laboratory Parameters in Survivors and Non-Survivors

Variables	Survivor	Non-Survivor	p-value
ESR (mean)	60.5 ± 30.7	64 ± 33.5	0.895
WBC (cell/ μ L) (mean)	14305.2 ± 2135	16893.5 ± 2028	0.310
Hb (g/dL) (mean)	8.5 ± 0.5	9.7 ± 0.49	0.087
Neu (cell/ μ L) (mean)	8090 ± 953	15077 ± 1719	<0.001
Lymph (cell/ μ L) (mean)	1284.21 ± 166.92	1085.5 ± 174.6	0.055
Plt (cell/ μ L) (mean)	195057 ± 24932	228571 ± 31516	0.996
CRP (mg/dL) (mean)	132.78 ± 24.31	157.35 ± 27.38	0.365
Procalcitonin (ng/mL) (mean)	30.5 ± 8.4	36.07 ± 13.6	0.553
BUN (mg/dL) (median)	34	53.5	0.148
Creatinin (mg/dL) (median)	13	17	0.602
ALT (U/L) (median)	17	17.5	0.984
AST (U/L) (median)	23	20.5	0.678
Albumin (g/dl) (mean)	2.86 ± 0.1	2.53 ± 0.13	0.053
Total cholesterol (mg/dL) (mean)	151.26 ± 11.09	152.71 ± 7.51	0.952
NLR (median)	5.23	11.26	<0.001
PLR (mean)	257.7 ± 41.5	302.3 ± 103.1	0.315
PNI (mean)	35.1 ± 1.42	30.78 ± 1.55	0.012
SII (median)	1494.64	2823.35	0.002

Note: SII: (Systemic immune inflammation index) platelet count $\times$ neutrophils/lymphocytes, PNI: (Prognostic nutritional index) $10 \times$ serum albumin (g/dl) + $0.005 \times$ total lymphocyte count.

Abbreviations: WBC, White blood cell; Hb, hemoglobin; Neu, neutrophil; lymph, lymphocyte; Plt, platelet; BUN, blood urea nitrogen; ALT, alanine aminotransaminase; AST, aspartate aminotransferase; CRP, c reactive protein; ESR, erythrocyte sedimentation rate; BUN, blood urea nitrogen; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio.

Table 3 ROC Analysis of Inflammatory Indices for Predicting Mortality

Variables	Cut-Off	p-value	Sensitivity (%)	Specificity (%)	AUC
NLR	11.1	<0.001	56.1	43.9	0.756
PLR	138.6	0.311	56.1	43.9	0.434
PNI	29.5	0.009	58.5	41.5	0.335
SII	2819.6	0.001	51.2	48.8	0.699

According to the results of multivariate analysis (Table 5), low PNI levels were significantly and independently associated with mortality ($p = 0.014$; HR: 0.092; 95% CI: 0.016–0.617). The risk of mortality was significantly lower in patients who underwent surgery ($p = 0.004$; HR: 0.093; 95% CI: 0.019–0.467). Cardiac complications significantly increased the risk of mortality ($p = 0.024$; HR: 6.505; 95% CI: 1.286–32.898). Additionally, older age increases the risk of mortality ($p = 0.001$; HR: 1.073; 95% CI: 1.027–1.120).

Table 4 Analysis of Factors Affecting Mortality

Variables		Mortality				p-value
		Survivors		Non-Survivors		
NLR	<11.1	27	73	18	43.9	0.009
	>11.1	10	27	23	56.1	
PLR	<138.6	16	43.2	18	43.9	0.953
	>138.6	21	56.8	23	56.1	
PNI	<29.5	6	16.2	17	41.5	0.015
	>29.5	31	83.8	24	58.5	
SII	<2819.6	28	75.7	20	48.8	0.015
	>2819.6	9	24.3	21	51.2	

Table 5 Multivariate Analysis for Mortality

	p-value	HR	95% CI	
			Lower	Upper
NLR	0.937	0.923	0.126	6.738
PNI	0.014	0.092	0.016	0.617
SII	0.477	2.014	0.293	13.858
Embolic phenomenon	0.388	2.244	0.358	14.051
Operational intervention	0.004	0.093	0.019	0.467
Cardiac complication	0.024	6.505	1.286	32.898
Neurological complication	0.204	3.124	0.539	18.116
Age	0.001	1.073	1.027	1.120

Discussion

Mortality rates in cases of infectious endocarditis can vary significantly, depending on the characteristics of the patient, with rates reaching as high as 30%.⁸ The elevated mortality rate observed in our study (52.5%) could likely be the result of the increased median age of participants and the greater prevalence of comorbid conditions. Culture negativity may also have led to a delay in diagnosis in patients who did not survive; however, late presentation, comorbidities causing clinical deterioration, comorbidities preventing patients having surgery due to high risk may have all contributed to the high mortality in our study.

In our study, age was identified as an independent risk factor for mortality ($p = 0.001$; HR: 1.073; 95% CI: 1.027–1.120). Previous studies have also found a high prevalence of IE among hospitalized elderly patients.³ Older individuals with IE have significantly higher long-term mortality rates compared to other age groups.³ Mortality may have been found to be higher because comorbid conditions are more common in the elderly population.

Neurological (ischemic stroke, transient ischemic attack (TIA), and cerebral embolism),⁹ cardiac¹⁰ (coronary embolism, new-onset arrhythmias secondary to embolic involvement, or embolic myocardial infarction), and embolic events¹⁰ are known contributors to increased mortality in infective endocarditis. In our study, these complications were significantly more common among non-survivors ($p < 0.05$) as reported in other articles.^{9,10} These complications are known

to occur as a result of infectious endocarditis and they significantly affect patient mortality. Among them, cardiac complications emerged as an independent predictor of mortality in multivariate analysis ($p = 0.024$; HR: 6.505), underscoring their prognostic importance. Neurological and embolic complications, while associated with mortality in univariate analysis, did not retain statistical significance after adjustment in multivariate analysis, possibly due to sample size limitations or their collinearity with other variables. Nevertheless, early recognition and management of these complications remain essential for improving patient outcomes.

Cardiac surgery, when indicated early and performed in a timely manner, may provide a survival benefit despite its associated risks and potential complications. However, the decision to proceed with surgery must balance the risks and benefits for these high-risk patients. In our study, undergoing surgical intervention was significantly associated with decreased mortality in both univariate and multivariate analyses. Importantly, it was identified as an independent protective factor ($p = 0.004$; HR: 0.093; 95% CI: 0.019–0.467). Among the non-survivor patients, there were 7 patients who were considered to have high operative risk due to comorbid conditions and 6 patients with early-onset cerebrovascular events following diagnosis could not be operated. High-risk comorbidities and conditions that prevent patients having surgery may have also contributed to high mortality rates in our study. These findings are consistent with previous meta-analyses showing that early and appropriate surgical management can reduce both short- and long-term mortality rates.¹¹ It emphasizes the critical importance of surgical options in improving survival outcomes.¹¹ Close monitoring of the cardiac functions of these patients and decision-making for surgery will be beneficial in terms of timely intervention, which will constitute an important step in reducing mortality.

The rate of methicillin resistance among *S. aureus* (MRSA) was 52.9%. We can explain this high rate by our high rate of patients with a history of hospitalization in intensive care.

The variability in the clinical presentation of IE causes a clinical challenge. Early risk stratification and effective management are important to reduce the morbidity and mortality of IE. Therefore, simple blood tests may be useful in assessing prognosis and identifying patients at higher risk for poor outcomes. In general, in patients who have difficulty in their daily activities, who have accompanying cardiac complaints, elevated sedimentation rate, anemia, leukocyte count, elevated procalcitonin, NLR, and PLR, it will be beneficial to use these tests in prognostic evaluation.

In the medical literature, high-risk patient groups in critically ill populations such as cancer, sepsis, polytrauma, acute ischemic stroke, and acute coronary syndrome has been an important research area. For this reason, various measurements were evaluated. These vary in complexity and range from simple biomarkers based on a single measurement to more complex indices that measure ratios to complex modeling and algorithms that combine multiple methods.

One of these ratios, NLR, as a cost-effective and easily accessible inflammatory marker, has emerged as an indicator of poor prognosis in infectious diseases. NLR indicates impaired cell-mediated immunity associated with systemic inflammation, and studies focus on its role in predicting outcomes as a simple prognostic marker.^{12,13} The predictive value of NLR is important in many malignancies, central nervous system events and infectious and cardiovascular diseases.^{14–17}

Some studies have investigated the relationship between NLR and IE.^{12,13} Similarly, in our study, NLR levels were significantly higher in non-survivors ($p < 0.001$), and its predictive value was supported by ROC analysis (AUC: 0.756). However, NLR did not remain an independent predictor in multivariate analysis, possibly due to confounding factors such as age or comorbidities. While exact threshold values remain to be standardized, NLR may still contribute to early prognostic assessment when interpreted alongside other clinical and laboratory findings.

Many publications show the relationship between nutrition immunity and mortality in infection. Evaluation and support of nutrition are important, and various nutritional indices have been reported, especially to evaluate malignancy and intensive care patients.^{18–20}

PNI calculation allows us to assess a patient's nutritional status quickly, providing an easy and practical assessment. In our study, lower PNI values were significantly associated with increased mortality ($p = 0.012$), and PNI was found as an independent predictor of mortality in multivariate analysis ($p = 0.014$; HR: 0.092; 95% CI: 0.016–0.617). Previous studies have identified $PNI < 35$ as a marker of severe malnutrition.^{5,6,20} Our ROC analysis demonstrated a cut-off value of 29.5 for PNI, with a sensitivity of 58.5%, specificity of 41.5%, and an AUC of 0.335. Although the discriminative ability was limited, the multivariate findings support PNI's prognostic relevance beyond its ROC performance.

These results underline the importance of baseline nutritional status in influencing outcomes in infective endocarditis.

SII consists of the neutrophil, lymphocyte, and platelet count. It is a novel marker for presenting patients' inflammatory and immune responses. Previous studies have confirmed that increased SII may represent the impaired balance of inflammatory and immunologic status in patients with infection.^{21–25} In our study, SII values were significantly higher among non-survivors ($p = 0.002$), and ROC analysis identified a cut-off value of 2819, with a sensitivity of 51.2%, specificity of 48.8%, and an AUC of 0.699, indicating a moderate predictive capacity for mortality. Similarly, SII was reported to be useful in predicting in-hospital mortality in patients with IE in recent studies.²⁶ One proposed hypothesis is that vegetation initiation and expansion are due to complex interactions between pathogens and blood cells, including platelets, neutrophils, and other immune cells.²⁷ Increased neutrophil counts in endothelial dysfunction and neutrophils, together with platelets, play an active role in the formation of atherosclerosis.²⁷ SII acts as a marker by simultaneously considering the inflammation and immune status in the host and thus may have the potential to predict IEs.²⁷ However, SII did not retain statistical significance in our study in multivariate analysis ($p = 0.477$), suggesting that its prognostic utility may be confounded by other factors such as age or nutritional status. While not an independent predictor in our model, SII may still offer valuable insight into patient prognosis when interpreted in conjunction with other clinical and laboratory parameters, particularly in settings where rapid risk stratification is needed.

The platelet-to-lymphocyte ratio (PLR) has been investigated as a potential prognostic marker in various inflammatory and infectious conditions.¹⁵ However, in our study, PLR was not significantly associated with in-hospital mortality in either univariate analysis ($p = 0.953$) or ROC analysis (AUC: 0.434; $p = 0.311$). These findings suggest that PLR may have limited value compared to other indices such as NLR, PNI, and SII.

Although composite clinical scoring systems such as AEPEI,²⁸ EndoSCORE,²⁹ or De Feo³⁰ are available for prognostic assessment in infective endocarditis, they require multiple clinical and laboratory inputs and are not routinely implemented in all centers. In contrast, the indices evaluated in our study (NLR, PNI, and SII) are simple, cost-effective, and readily available from routine admission tests, making them practical complementary tools for early risk stratification.

Limitations

Several limitations of this study should be acknowledged. First, it was conducted as a single-center retrospective study. Second, the relatively small sample size ($n = 78$) may have reduced the statistical power to detect associations between all potential risk factors and mortality. Despite the extended 10-year study period, our sample size is a significant limitation and may affect the generalizability of the findings. Additionally, while we performed univariate and multivariate analyses, the adjustment for potential confounding factors such as comorbidities, disease severity, and treatment timing was limited due to the small sample size. Third, while we analyzed the prognostic value of NLR, PNI, and SII, the lack of established threshold values for these indices in infective endocarditis limits their clinical applicability. As this was an observational study, causal relationships cannot be established, and unmeasured confounding factors may have influenced the findings. Another important limitation of this study is the potential variability in diagnostic and therapeutic practices over the 10-year period. Although all patients were treated according to contemporary standards at the time of admission, clinical protocols and treatment availability may have evolved throughout the study period, potentially influencing outcomes.

The high mortality rate (52.5%), which is higher than generally reported in the literature, may reflect the characteristics of our patient population, including older age and a higher prevalence of comorbidities. Comorbidities not only cause clinical deterioration but also pose a high surgical risk, preventing patients from having surgery. Future prospective, multicenter studies with larger sample sizes and standardized biomarker cut-off values are needed to validate our findings and determine the optimal use of these indices in clinical practice.

Conclusion

Identifying reliable prognostic markers for infective endocarditis is extremely valuable, and it is important to increase the number of studies and gather information on this subject.

Parameters such as NLR, PNI, and SII emerge as easily calculable and cost-effective measurements. Nevertheless, a common feature among these biomarkers is their limited independent predictive performance for a given condition. To our knowledge, this is among the first studies to evaluate all three inflammation-based indices together in patients with infective endocarditis, providing a more comprehensive and comparative perspective on their prognostic utility.

Additional studies on infective endocarditis patients should be conducted to obtain more definitive results. However, these indices provide insight into prognosis by aggregating data from multiple factors and help clinicians make critical decisions.

Ethical Statement

All procedures were performed by the ethical standards outlined in the Declaration of Helsinki.

The name of the approving ethics committee was “Clinical Research Ethics Committee of University of Health Sciences, Bakırköy Dr. Sadi Konuk Training and Research Hospital”. The Protocol Number of the ethical approval was 2024/302, Decision Date: October 7, 2024. Approving institution was the same with the authors’ institution.

Informed Consent Statement

Informed consent was waived due to the retrospective design of the study. The waiver was obtained by the Clinical Research Ethics Committee of University of Health Sciences, Bakırköy Dr. Sadi Konuk Training and Research Hospital.

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Disclosure

The authors do not have any conflict of interest in the study.

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