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Prognostic value of the C-reactive protein-to-albumin ratio in patients with infective endocarditis

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Abstract. – OBJECTIVE: Infective endocarditis (IE) is a life-threatening disease that causes various complications and mortality. The C-reactive protein-to-albumin ratio (CAR) has been reported as a novel prognostic marker in inflammatory and cardiovascular diseases. We retrospectively investigated whether there is a relationship between admission CAR values and prognosis in patients with IE.

PATIENTS AND METHODS: The study population was classified into 2 groups: patients with a primary clinical outcome (n = 64) and those without (n = 132). The primary clinical outcome consisted of the need for intensive care unit treatment and in-hospital mortality. For all patients, serum CAR levels at hospital admission were calculated.

RESULTS: In this study, 196 patients with a definite diagnosis of IE during a 5-year period were included. The mean age of the total patients was 52.7 ± 14.9 years (67% male, mean age 51.9 ± 15.0 years; 33% female, mean age 54.3 ± 14.4 years, respectively). Serum CAR values were associated with prognosis in IE patients. According to Cox regression analysis, admission CAR value remained an independent predictor of mortality ($p < 0.05$). In receiver operating curve analysis, a cutoff value of CAR > 20.24 predicted primary clinical outcome with a sensitivity of 82.4% and specificity of 70.3% ($p < 0.001$).

CONCLUSIONS: For the first time, the present study showed that in IE, admission CAR could be a useful predictor of poor prognosis, including hospital death.

Key Words:
C-reactive protein-to-albumin ratio, Infective endocarditis, Mortality.

Abbreviations

IE: Infective endocarditis, CAR: C-reactive protein-to-albumin ratio, NLR: neutrophil-lymphocyte ratio, PLR: platelet-lymphocyte ratio, SII: systemic immune inflammation index, CRP: C-reactive protein, CAD: coronary artery disease, ICU: intensive care unit, CBC: complete blood count, TEE: transesophageal echocardiography.

Introduction

The term "infective endocarditis" (IE) is used to describe an infection of cardiac valves (native or prosthetic) or intracardiac structures associated with bacteremia[1]. It commonly affects elderly patients with chronic diseases, artificial cardiac devices, or prosthetic valves[1]. On clinical presentation, the patient may exhibit severe infectious disease such as septic shock and multiorgan failure. Due to its impact on cardiac functions and embolic complications, the morbidity and mortality remain high in IE[1,2].

The patients' clinical characteristics, infecting microorganism, and development of complications can determine the prognosis in IE[2]. Systemic inflammation plays an important role in the pathogenesis of IE[1]. Therefore, systemic inflammatory biomarkers can be associated with poor outcomes in IE cases. Early identification of high-risk patients is crucial for predicting optimal timing of surgery, improving treatment modality, and preventing complications and even mortality.

Many studies[3,4] have focused on new, easily available, and inexpensive inflammatory parameters in the cardiovascular field. In this regard, various inflammatory biomarkers including neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have been studied in IE. A new marker, known as the systemic immune inflammation index (SII), which is a combination of NLR and platelet counts, represents the inflammatory and immune response in patients[5]. Moreover, the C-reactive protein-to-albumin ratio (CAR), a novel indicator of inflammatory response, has recently been shown to be an important marker for evaluating and monitoring inflammatory conditions[6]. The CAR could be a more sensitive marker for inflammatory states than serum C-reactive protein (CRP) or albumin alone[6].

Several previous studies[7,8] have established the prognostic value of the CAR in patients with var-

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ious inflammatory diseases, such as sepsis, cancer, acute pancreatitis, or coronary artery disease (CAD).

However, the relationship between the CAR and clinical outcomes in patients with IE is not yet clear. The aim of this study was to investigate whether serum CAR levels at admission are associated with prognosis and mortality in patients with IE. To the best of our knowledge, the prognostic value of the CAR in IE patients has not been previously investigated.

Patients and Methods

Study Population

Patients diagnosed with definite IE according to the modified Duke criteria were collected from the Istanbul University Medical Faculty from 2016 to 2021 in this retrospective study. The present study protocol was reviewed and approved by Local Ethics Committee of Istanbul University, Faculty of Medicine (Approval no.: 1080290). Patients with severe chronic inflammatory disease, autoimmune disease, hematological disease, malignancy, severe chronic kidney disease (estimated glomerular filtration rate [eGFR] < 30 mL/minute/1.73 m^2), or chronic liver disease, patients receiving corticosteroids or immunosuppressive therapy, and patients with missing laboratory data were excluded from the study.

Primary Outcome Definition

The primary clinical outcome was defined as meeting at least one of the following conditions: (1) in-hospital mortality and/or (2) the need for intensive care unit (ICU) treatment.

Study Design

The study population was classified into two groups according to primary clinical outcomes: 64 patients who had a primary clinical outcome (admitted to the ICU or died) and 132 patients without. Patients with hypotension (systolic blood pressure < 90 mmHg) and signs of peripheral hypoperfusion and multiorgan failure with sepsis or septic shock were admitted to the ICU.

The patients' comorbidities, including age, gender, hypertension, diabetes mellitus, CAD, chronic renal disease, and smoking, were evaluated. Data about comorbidities, predisposing valvular diseases, the presence of prosthetic valves and intracardiac devices, blood culture results, echocardiographic findings, vegetation size, laboratory parameters, and severe complications due to IE were carefully reviewed and collected from the hospital electronic medical records.

Blood cultures were collected from at least three sets for each patient before starting antibiotics. Cultures were obtained from different venous sites with at least 1-hour intervals between the first and last samples drawn. Excised materials, including any valves, vegetation, infected prostheses, or emboli during surgery, were submitted for culture. The antibiotic regimen was given based on the American Heart Association guidelines[9].

All hematologic and biochemical data were recorded. The complete blood count (CBC), CRP, albumin, and serum biochemistry were all assessed at admission and periodically recorded during the hospital course. The CBC analyses were conducted using the LH780 Hematology Analyzer (Beckman Coulter, Inc., Brea, CA, USA), and a Cobas 8000 (Roche Diagnostics, Mannheim, Germany) was used to measure serum CRP and albumin levels. The CAR was calculated as the ratio of serum CRP level to serum albumin level at admission. The SII was measured as follows: SII = platelet × neutrophil/lymphocyte counts at admission. The NLR and PLR were directly obtained from the CBC at admission.

Transthoracic echocardiography was performed for all patients within 24 hours of admission. Additionally, transesophageal echocardiography (TEE) was performed as indicated within 72 hours by an experienced cardiologist blinded to the patients' data. For the vegetation size, the maximum length was chosen. Severe heart failure, peripheral septic embolism, and uncontrolled infection were the main indications for surgery.

Statistical Analysis

All statistical analyses were performed using the SPSS 26.0 for Windows (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov test was used to analyze the normality of the data. Continuous data are expressed as mean ± standard deviation (SD), and categorical data are expressed as percentages. A Chi-square test was used to assess the differences in categorical variables between the groups. A Student's *t*-test or the Mann-Whitney U test was used to compare unpaired samples as needed. For the parameters SII, NLR, and CAR, receiver operating curves (ROCs) were obtained, and optimal values with the greatest total sensitivity and specificity in the prediction of a primary outcome were selected. Cumulative survival curves were derived according to the Ka-

plan-Meier survival method. A Cox regression analysis was used to identify the predictors of mortality and estimate hazard ratios (HRs), 95% confidence intervals (CIs), and *p*-values. Significance was assumed at a two-sided $p < 0.05$.

Results

A total of 196 cases with a definite diagnosis of IE were retrospectively reviewed for a 5-year period. The mean age of the total study population was 52.7 ± 14.9 years (67% male, mean age 51.9 ± 15.0 years; 33% female, mean age 54.3 ± 14.4 years, respectively). The median duration of hospitalization was 33 days (range 0-173 days). Twenty-five (12.8%) patients had prosthetic valve endocarditis, and 14 (7.1%) had vegetation on an intracardiac device. Valves affected by vegetation were an aortic valve in 79 patients (40.3%) and a mitral valve in 65 (33.2%). The median vegetation size was 11 mm (range 2-36 mm). Degenerative valvular disease was the most frequent predisposing valvular disease, followed by rheumatic heart disease, bicuspid aorta, mitral valve prolapses, and congenital heart disease. Surgical therapy was performed in 51 patients (26%). *Staphylococcus species, Streptococcus*, and *Enterococcus* were the most frequent isolated microorganisms.

In our study, the patients were divided into 2 groups based on primary clinical outcomes. The baseline clinical characteristics, echocardiographic and laboratory findings, and microbiological data of the patients with and without a primary clinical outcome are presented in Table I.

Patients with a primary outcome were much older than those without. No significant differences were observed in gender, comorbidities, predisposing valvular disease, vegetation size, and blood culture results between the 2 groups ($p > 0.05$).

Primary Clinical Outcomes

During hospitalization, 53 (27%) patients died, and 34 (17.3%) patients were admitted to the ICU. Ultimately, 64 patients (32.7%) had the primary composite endpoint (Table I).

In the present study, acute renal failure occurred in 20.4% of patients, congestive heart failure in 8.7%, and septic embolism in 24.5% as a complication. The paravalvular complications seen on TEE were aortic root abscess in 12 patients (6.1%), mitral chordae rupture in 13 patients (6.6%), perforation in 3 patients (1.5%), aortic pseudoaneurysm in 3 patients (1.5%), and prosthetic valve dehiscence in 2 patients (1%).

In our study, patients with a primary clinical outcome had significantly higher CAR levels at admission compared with those without (40.4 [0.2-166.9] *vs.* 17.9 [0.4-141.6], respectively; $p < 0.001$) (Table I, Figure 1A).

In the Cox regression analysis, acute renal failure and CAR levels were found to be independent predictors of mortality (HR = 3.605, 95% CI 1.397-9.305, $p = 0.008$; HR = 1.015, 95% CI 1.002-1.028, $p = 0.02$, respectively) (Table II).

The ROC analysis showed that a cutoff value of > 20.24 for CAR levels at admission predicted primary clinical outcome with 82.4% sensitivity and 70.3% specificity (AUC = 0.838, 95% CI 0.734-0.941, $p < 0.001$) (Figure 1B).

According to the Kaplan-Meier survival analysis, the total survival rate was 72.9%. The survival rate was found to be significantly lower in patients with acute renal failure than in those without ($p = 0.025$; Figure 2A).

Discussion

To the best of our knowledge, this is the first study to evaluate the relationship between serum CAR and prognosis in patients with IE. Our study showed that higher CAR levels were associated with poor clinical outcomes in IE patients. In the present study, we found that CAR was an independent predictor of mortality. Values above 20.24 for admission CAR predicted primary clinical outcome with a sensitivity of 82.4% and specificity of 70.3%. We suggest that admission CAR values could serve as a new biomarker to predict a poor clinical outcome in high-risk IE patients.

Despite advanced medical therapy and improvement in diagnosis, IE is still a serious clinical condition with a high mortality and morbidity rate[10,11]. The in-hospital mortality rate of patients with IE can vary from 15% to 30%[10,11]. Complications including septic embolism, periannular extension of the infection, valvular dysfunction, development of heart failure, and renal failure can cause a poor prognosis in IE[12,13]. Another study[1] reported the prosthetic valve infection, heart failure, mitral valve vegetation, and paravalvular complications to be associated with in-hospital mortality. Surgical therapy is recommended in the presence of severe complications due to IE[13]. Although rheumatic heart disease is the most common underlying valvular condition in developing

Table I. Baseline clinical characteristics, and laboratory findings of the patients with and without primary clinical outcome.

	Total Patients (n=196)	Patients-without primary-clinical outcome (n=132)	Patients-with primary-clinical outcome (n=64)	*p*-value
Clinical characteristics				
Age, (years)	52.72 ± 14.9	50.6 ± 13.1	56.56 ± 17	0.013*
Gender Male, n (%) Female, n (%)	131 (66.8%) 65 (33.2%)	93 (47.4%) 39 (19.9%)	38 (19.4%) 26 (13.3%)	0.122
Hospitalization time, (days)	33 (0-173)	28 (0-173)	26 (0-166)	0.620
Comorbidities				
HT, n (%)	44 (22.4%)	26 (13.3%)	18 (9.2%)	0.352
DM, n (%)	26 (13.3%)	15 (7.7%)	11 (5.6%)	0.407
Coronary artery disease, n (%)	20 (10.2%)	10 (5.1%)	10 (5.1%)	0.138
Heart failure, n (%)	86 (43.9%)	50 (25.5%)	36 (18.4%)	0.058
Chronic renal disease, n (%)	23 (11.7%)	11 (5.6%)	12 (6.1%)	0.066
Smoking, n (%)	40 (20.4%)	24 (12.2%)	16 (8.2%)	0.630
Alcohol use, n (%)	5 (2.6%)	3 (1.5%)	2 (1%)	0.882
Laboratory findings				
Creatinine (mg/dl)	1.44 ± 0.8	1.9 ± 1.4	1.23 ± 0.6	0.389
AST (U/I)	29 (14-168)	14.5 (14-15)	30 (23-168)	0.390
ALT (U/I)	25 (3-87)	7 (3-11)	36 (6-87)	0.146
LDH (U/I)	323 ± 66.8	344.5 ± 77.1	319.8 ± 76.8	0.244
CRP at admission (mg/L)	63 (0.9-614)	56 (1-614)	96 (0.9-304)	0.067
CRP peak (mg/L)	232.5 (87-454)	161 (87-235)	230 (101-454)	0.021*
Ferritin (ng/ml)	381 (28-4,517)	444.3 (28-4,000)	289.4 (45-4,517)	0.620
Hs-TnT peak (pg/ml)	135.5(22.1-323)	44.43 (31.35-57.5)	168 (22.1-323)	0.009*
Pro-BNP peak (pg/ml)	22,440 (1,145-35,000)	13,235 (1,145-25,326)	19,880 (2,740-35,000)	0.004*
Albumin (g/dl)	2.85 ± 0.8	3.41 ± 1.4	2.67 ± 0.6	<0.001*
Hgb (gr/dl)	9.62 ± 1.6	11.6 ± 1	8.87 ± 1.3	0.181
WBC (10^3/µl)	8.73 ± 2.9	7.13 ± 1.2	8.3 ± 2.6	0.787
Neutrophile (10^3/µl)	6.98 ± 2.5	5.26 ± 0.5	6.67 ± 1.7	0.198
Lymphocyte (10^3/µl)	1.25 ± 0.8	1.42 ± 1.4	0.96 ± 0.6	0.760
Platelet (10^3/µl)	203.7 ± 100.8	136.8 ± 23.8	152 ± 11.6	0.106
NLR	4.2 (0.2-58.5)	3.9 (0.2-58.5)	4.6 (0.8-11.3)	0.339
PLR	141.9 (5.3-686.7)	136.7 (5.3-686.7)	189.8 (9.5-335.5)	0.461
SII	744.8 (7.3-6,180)	744.8 (7.3-6,180)	759.9 (40-2,415)	0.617
CRP/albumin	21.1 (0.2-166.9)	17.9 (0.4-141.6)	40.4 (0.2-166.9)	<0.001*
Etiology for infective endocarditis				
Rheumatic heart disease, n (%)	31 (15.8%)	20 (10.2%)	11 (5.6%)	0.714
Mitral valve prolapses, n (%)	18 (9.2%)	14 (7.1%)	4 (2%)	0.322
Bicuspid aortic valve, n (%)	26 (13.3%)	19 (9.7%)	7 (3.6%)	0.503
Degenerative valve disease, n (%)	65 (33.2%)	40 (20.4%)	25 (12.8%)	0.222
Congenital heart disease, n (%)	13 (6.6%)	11 (5.6%)	2 (1%)	0.169
Vegetation on cardiac device (ICD/PM), n (%)	14 (7.1%)	10 (5.1%)	4 (2%)	0.735
Vegetation on catheter, n (%)	7 (3.6%)	5 (2.6%)	2 (1%)	0.815
Native valve endocarditis, n (%)	150 (76.5%)	104 (53.1%)	46 (23.5%)	0.284
Prosthetic valve endocarditis, n (%)	25 (12.8%)	13 (6.6%)	12 (6.1%)	0.080
Affected valve				
Aortic valve, n (%)	79 (40.3%)	53 (27%)	26 (13.3%)	0.949
Mitral valve, n (%)	65 (33.2%)	39 (19.9%)	36 (18.4%)	0.122
Aortic and mitral valve, n (%)	13 (6.6%)	10 (5.1%)	3 (1.5%)	0.446
Other valves, n (%)	39 (19.9%)	30 (15.3%)	9 (4.6%)	0.154

Continued

Table I *(Continued)*. Baseline clinical characteristics, and laboratory findings of the patients with and without primary clinical outcome.

	Total Patients (n=196)	Patients-without primary-clinical outcome (n=132)	Patients-with primary-clinical outcome (n=64)	*p*-value
Vegetation size (mm)	11 (2-36)	10.5 (3-35)	11 (2-36)	0.958
Blood culture				
Staph. Aureus MRSA, n (%)	13 (6.6%)	8 (4.1%)	5 (2.6%)	0.644
Staph. Aureus MSSA, n (%)	18 (9.2%)	11 (5.6%)	7 (3.6%)	0.554
Coagulase negative staph., n (%)	12 (6.1%)	8 (4.1%)	4 (2%)	0.959
Streptococcus, n (%)	21 (10.7%)	16 (8.2%)	5 (2.6%)	0.360
Enterococcus, n (%)	19 (9.7%)	14 (7.1%)	5 (2.6%)	0.535
Enterobacter, n (%)	3 (1.5%)	1 (0.5%)	2 (1%)	0.249
Brucella, n (%)	4 (2%)	3 (1.5%)	1 (0.5%)	0.742
Candida spp., n (%)	6 (3.1%)	2 (1%)	4 (2%)	0.090
Coxiella, n (%)	2 (1%)	1 (0.5%)	1 (0.5%)	0.548
HACEK, n (%)	2 (1%)	2 (1%)	0 (0%)	0.322
Others, n (%)	15 (7.7%)	8 (4.1%)	7 (3.6%)	0.228
Surgery, n (%)	51 (26%)	31 (15.8%)	20 (10.2%)	0.467
Transthoracic echocardiographic findings				
LVEF, (%)	60.67 ± 9.9	62.75 ± 7.4	57.44 ± 12.3	0.017*
RV, (mm)	26.39 ± 4.1	26.79 ± 4.2	25.78 ± 3.9	0.766
LA, (mm)	40.3 ± 6.7	40.21 ± 7.6	40.44 ± 6.2	0.074
sPAP, (mmHg)	39.3 ± 11.2	39.5 ± 11.4	39 ± 12.2	0.327

HT: hypertension; DM: diabetes mellitus; AST: aspartate transaminase, ALT: alanine transaminase; LDH: lactate dehydrogenase; CRP: C-reactive protein; Hs-TnT: high-sensitivity troponin T; Pro-BNP: prohormone B-type natriuretic peptide; Hgb: hemoglobin; WBC: white blood cell; NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; SII: systemic immune inflammation index; ICD: implantable cardioverter defibrillator; PM: pace maker; MRSA: methicillin resistant *staphylococcus aureus*; MSSA: methicillin sensitive *staphylococcus aureus*; LVEF: left ventricular ejection fraction; RV: right ventricle; LA: left atrium; sPAP: systolic pulmonary artery pressure.

countries, degenerative valvular lesions have become the most frequent predisposing valvular diseases in developed countries. Additionally, vegetation size and causative microorganisms have been identified as predictors of unfavorable outcomes and mortality[1,10].

In our study, 76.5% patients had native valve endocarditis. Consistent with the literature, degenerative valve lesions were the most frequent predisposing valvular disease. The overall in-hospital mortality rate was 27%, similar to previous studies[14,15], and 17.3% needed ICU treatment due to septic shock and multiorgan failure. The complications of heart failure, acute renal failure, and septic peripheric embolism occurred in 17 (9%), 40 (20%), and 48 (25%) patients, respectively. The most common paravalvular complications were mitral chordae rupture (6.6%) and abscess (6.1%). Surgery was required in 51 patients due to complications. In the present study, patients with acute renal failure which was also found to be a strong independent

Table II. Cox regression analysis as a predictor of mortality

Parameter	HR	95% CI	*p*-value
Age	1.022	0.991-1.055	0.165
Acute renal failure	3.605	1.397-9.305	0.008*
Posterior wall thickness	0.798	0.623-1.021	0.072
CAR	1.015	1.002-1028	0.020*

CAR: C-reactive protein-to-albumin ratio.
* $p<0.05$.

predictor of mortality, had a significantly lower survival rate in comparison to patients with septic embolism and heart failure according to Kaplan-Meier survival analysis.

In this regard, rapid identification of high-risk patients could offer an opportunity to improve prognosis. Inflammation plays a central role in the IE process. Serum CRP, a prototype inflammation marker, is a positive acute phase protein that rises in both acute and chronic inflammation[8,16]. Serum CRP levels have been commonly used for the determination and monitoring of various inflammatory conditions[6,17]. On the other hand, albumin is a negative acute phase protein, and its serum levels decrease during inflammation[17]. Albumin has potential roles in the body, such as anti-inflammatory, antioxidant, and antiplatelet aggregation properties[18]. In previous studies, serum albumin levels

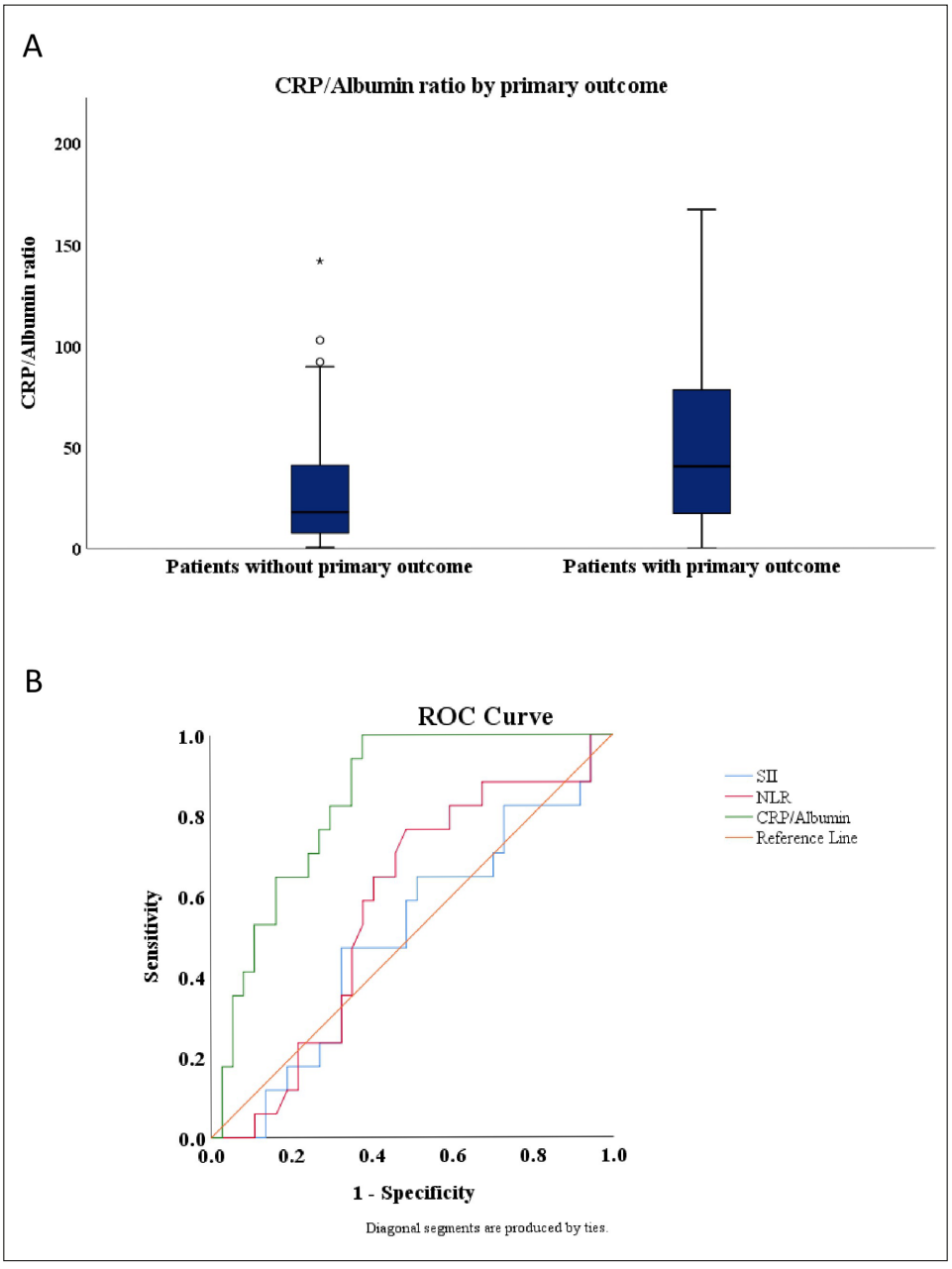

Figure 1. ***A***, Serum C-reactive protein to albumin ratio values according to primary clinical outcome of the patients with infective endocarditis. **B**, The receiver operating characteristics (ROC) curve analysis for predicting primary clinical outcome by CAR compared with NLR and SII at Hospital admission.

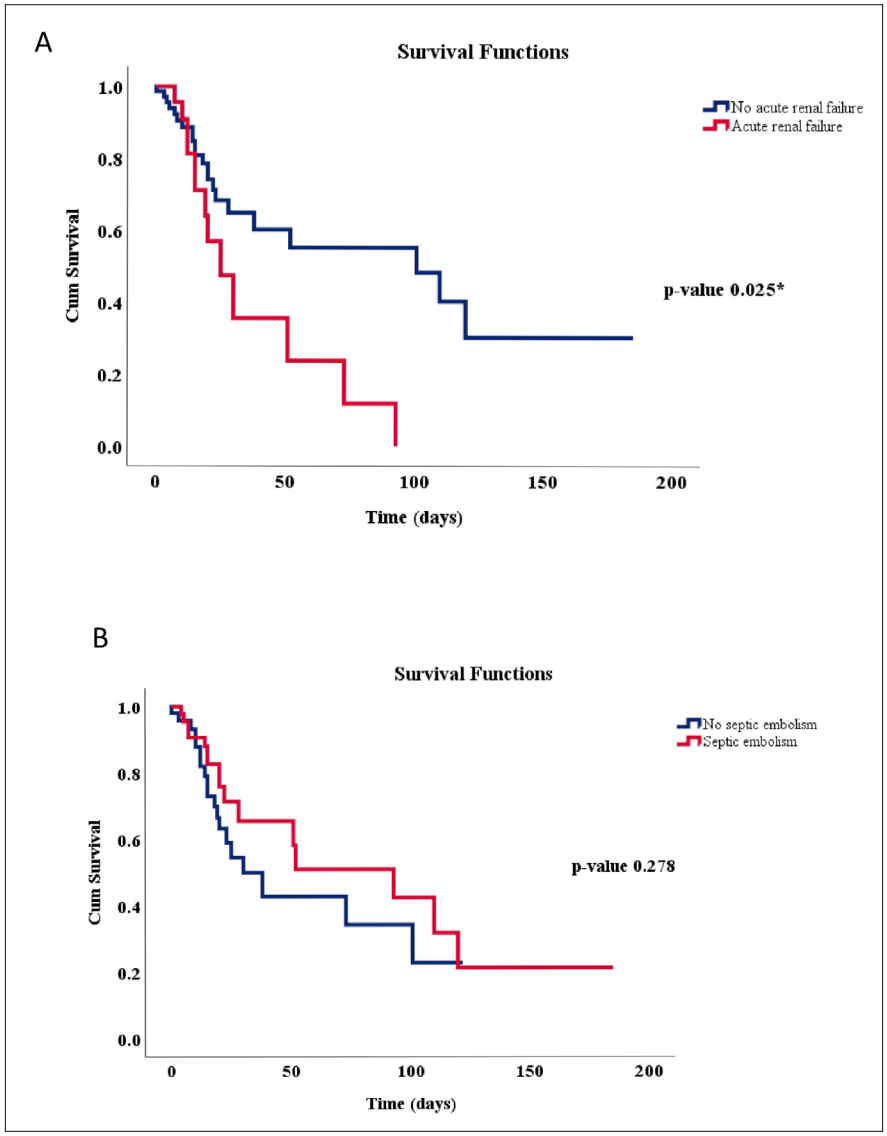

Figure 2. A, Kaplan-Meier survival analysis according to acute renal failure in patients with infective endocarditis. **B**, Kaplan-Meier survival analysis according to septic peripheral embolism in patients with infective endocarditis.

were found to be associated with inflammation severity, as well as mortality[17,18].

Although CRP is a valuable inflammatory marker in establishing the diagnosis of IE, data about its prognostic implications are lacking. It is of great importance to identify the IE patients needing more aggressive treatment at the time of admission. In this regard, there is a need for easily measurable and available inflammatory markers at hospital admission. Therefore, we investigated the utility of the CAR for the determination of prognosis and mortality in IE patients.

Serum CAR is a novel defined combined inflammatory index of CRP and albumin[8]. Many studies have shown the prognostic significance of CAR in various inflammatory diseases, including cancer, sepsis, acute pancreatitis, or ulcerative colitis[7,8,16,19]. Moreover, Lucijanić et al[20] found higher CAR values to be associated with worse clinical outcomes and higher mortality in patients with the 2019 novel coronavirus disease (COVID-19). They showed that survival was improved with lower CAR values[20]. In another study, Kunutsor et al[6] showed serum CAR levels to be associated with increased risk of community-acquired pneumonia. Again, CAR was found to be a more sensitive marker than the CRP level in predicting mortality in patients with sepsis[17].

Serum CAR has been studied not only in inflammatory disease but also in cardiovascular disorders[21,22]. For example, Kelesoglu et al[18] showed a strong positive relationship between CAR levels and poor coronary collaterals in patients with stable CAD. Sogut et al[7] found CAR levels to be independent predictors of mortality in patients with acute myocardial infarction.

In the present study, CAR levels were significantly higher in IE patients with a primary clinical outcome than in those without. The increased CAR levels remained an independent predictor of in-hospital mortality. We found that the cutoff value for admission CAR was 20.24, which predicts a primary clinical outcome consisting of hospital death and ICU admission, with a sensitivity of 82.4% and specificity of 70.3%. We suggest that low serum albumin and high CRP levels might have a synergistic effect on the development of poor prognosis in IE patients.

We also evaluated the relationship between some new inflammatory biomarkers (NLR, PLR, SII) and prognosis. NLR is indicative of an impaired cell-mediated immunity associated with systemic inflammation. PLR and NLR have been found to be independent predictors of unfavorable clinical outcomes in many cardiovascular and inflammatory diseases[4,23,24,25].

Several important functions of platelets have been identified in the pathogenesis of inflammatory diseases. In this regard, Zencir et al[26] found PLR to be independently associated with in-hospital mortality in IE patients. Meshaal et al[3] found that a higher NLR at admission was significantly associated with increased risk of hospital death in IE patients. However, we could not show significant associations between PLR and NLR values and mortality in IE patients.

Recently, some authors[5] have investigated the prognostic importance of a novel inflammation marker known as SII. Higher SII levels were suggested to be a prognostic marker in some malignancies, heart failure, and CAD. In a recent study, Agus et al[12] showed SII to be an independent predictor of in-hospital mortality in IE patients. Contrary to their results, the SII showed no significant association with mortality in our study.

Therefore, we can speculate that higher CAR values at the time of hospital admission could be a more sensitive marker than the other inflammatory biomarkers for predicting patients at high risk of mortality.

As a result, early identification of patients at high risk for mortality could provide important clues for making clinical decisions, improving treatment approaches, and performing early surgery intervention. Serum admission CAR values could be useful for prognostic implications in IE patients. No available studies have investigated the prognostic significance of serum admission CAR levels in patients with IE.

Although sample size of our study is relatively small, it may be suggested that our study made an important contribution to clinical practice about IE with emphasizing the significance of admission CAR, a novel indicator of inflammation, in the prediction of poor prognosis and mortality in high-risk patients.

Limitations

The present study has some limitations. First, it has a retrospective design, and it was a single-center study. Second, we used serum NLR, PLR, SII and CAR levels to indicate inflammation; however, it would be better if we had evaluated proinflammatory cytokines and interleukins. Larger, prospective studies will be needed to confirm our findings.

Conclusions

Adding admission CAR values to established prognostic parameters could provide more valuable prognostic information in IE patients at high-risk for mortality and could improve patients' clinical management.

Conflict of Interest

The authors declare that they have no conflict of interests.

Availability of Data

The data and materials generated/analyzed in the present study are available from the corresponding author upon request.

Ethics Approval

This research was carried out with the permission of Istanbul University, Istanbul Faculty of Medicine, Local Ethics Committee, dated 08/07/2022 and numbered 1080290.

Informed Consent

Not applicable.

Authors' Contributions

D. Baykiz is the principal author of this study, and designed the study with resources acquisition, data collection and processing data, data analysis and interpretation, writing-original draft preparation, and editing. D. Baykiz, and Z. Bugra: conceived the idea for the article, framing the hypothesis, D. Baykiz, E. A. Govdeli, and Z. Bugra: designed the methods to generate results, A. Elitok, B. Umman, and Z. Bugra: supervision of the project and the manuscript, E.A. Govdeli, Z. G. Demirtakan, and D. Baykiz: resources acquisition, Z. G. Demirtakan, and E.A. Govdeli: materials and referring patients, E.A. Govdeli, Z. G. Demirtakan, and D. Baykiz: data collection and processing data, D. Baykiz, B. Umman, and A. Elitok: data analysis and interpretation, E.A. Govdeli, and D. Baykiz: writing-original draft preparation, A. Elitok, B. Umman, and Z. Bugra: critical review and editing. All authors have read and approved the paper.

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