ORIGINAL ARTICLE

# Prognostic nutritional index predicts mortality in infective endocarditis

## Prognostik nutrisyonel indeks enfektif endokardit hastalarında mortaliteyi öngördürür

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## ABSTRACT

***Objective:*** The prognostic nutritional index (PNI), based on serum albumin and lymphocyte concentration, is an inflammation-based nutritional score that has been shown to be a prognostic determinant in several populations. The aim of this study was to investigate the impact of PNI on mortality in patients with infective endocarditis (IE).

***Methods:*** A total of 131 patients with IE were enrolled in this retrospective study. The patients were divided into 2 groups based on in-hospital mortality. The PNI value of the patients was evaluated, as well as baseline clinical and demographical variables.

***Results:*** Among the study group, 29 patients died in-hospital during the median follow-up of 37 days. The PNI was found to be lower in cases of mortality (35.90±6.96; 31.09±5.88; p=0.001). ROC curve analysis also demonstrated that the PNI had a good predictive value for in-hospital mortality with a cut-off value of 35.6 (Area under the curve: 0.691; 95% confidence interval [CI]: 0.589–0.794; p=0.002). In multivariate logistic regression analysis, advanced age (Odds ratio [OR]: 1.078; 95% CI: 1.017–1.143; p=0.012), PNI (OR: 0.911; 95% CI: 0.835–0.993; p=0.034), and leaflet perforation (OR: 5.557; 95% CI: 1.357–22.765; p=0.017) were found to be independent predictors of mortality. Kaplan-Meier survival analysis revealed that long-term survival was found to be significantly decreased in patients with a lower PNI (Log rank: p=0.008).

***Conclusion:*** The PNI result was associated with an increased in-hospital mortality rate in patients with IE. The PNI value, advanced age, and cardiac valve perforation as a complication of IE were found to be independent predictors of mortality.

## ÖZET

***Amaç:*** Serum albümin ve lenfosit konsantrasyonlarını baz alan prognostik nutrisyonel indeks (PNİ) çeşitli hasta popülasyonlarında prognozu gösteren yeni bir enflamasyon temelli risk skorudur. Çalışmamızda enfektif endokardit (EE) hastalarında PNİ'nin mortalite üzerine etkisini incelemeyi amaçladık.

***Yöntemler:*** Geriye dönük çalışmamıza 131 hasta alındı. Hastaların bazal demografik ve klinik verilerinin yanı sıra PNİ seviyeleri ölçüldü. Hastalar hastane içi mortalite gelişen ve gelişmeyenler olarak iki gruba ayrıldı.

***Bulgular:*** Ortalama 37 günlük takip süresinde 29 hasta hastane içerisinde hayatını kaybetti. Mortalite olan hastalarda PNİ seviyesi daha düşük bulundu (35.90±6.96; 31.09±5.88, p=0.001). ROC eğrisi analizinde 35.6 eşik değeri ile PNİ iyi bir hastane içi mortalite prediktörü olarak saptandı (Eğri altında kalan alan: 0.691, %95 güven aralığı [GA]: 0.589–0.794, p=0.002). Çok değişkenli lojistik regresyon analizinde ileri yaş (Odds oranı [OO]=1.078; %95 GA=1.017–1.143; p=0.012), PNİ (OO=0.911; %95 GA=0.835–0.993; p=0.034) ve perforasyon (OO=5.557; %95 GA=1.357–22.765; p=0.017) mortalitenin bağımsız öngördürücüleri olarak saptandı. Ayrıca, Kaplan-Meier sağkalım analizinde düşük PNİ seviyesi olan hastalarda uzun dönem hayatta kalış süreleri daha düşük bulundu (Log rank: p=0.008).

***Sonuç:*** PNİ seviyesi EE hastalarında artmış hastane içi mortalite ile ilişkili saptandı. İleri yaş, PNİ ve kalp kapağı perforasyonu mortalitenin bağımsız ön gördürücüleri olarak saptandı.

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Infective endocarditis (IE) is still an important, life-threatening cardiac disease. The incidence rate is 2 to 8 cases per 100,000 per year.[1–3] The clinical spectrum of the disease varies; it is a complex, multi-organ, infectious disease, which affects the prognosis of the patient. Despite early diagnosis and more intensive treatment modalities, the morbidity and mortality rates of IE remain high. It has been reported to be responsible for nearly 10% to 24% of short-term mortality in hospitalized IE patients.[1–4] Due to the complex and heterogeneous nature of IE, the ability to predict high-risk patients in to order to improve prognosis is of great interest. New prognostic markers of IE are needed.

**Abbreviations:**

| | |
|---|---|
| *CI* | *Confidence interval* |
| *IE* | *Infective endocarditis* |
| *OR* | *Odds ratio* |
| *PNI* | *Prognostic nutritional index* |
| *ROC* | *Receiver operating characteristic* |
| *STEMI* | *ST-segment elevated myocardial infarction* |
| *TEE* | *Transesophageal echocardiography* |

Nutritional status is one of the most important prognostic determinants in several populations.[5–8] The prevalence of malnutrition varies from 12% to 75% in hospitalized patients. The prognostic nutritional index (PNI), based on serum albumin and lymphocyte concentration, is an inflammation-based nutritional score. It was first described to evaluate the perioperative immunonutritional status and surgical risk in gastrointestinal surgery patients.[5] The PNI has also been reported to be useful in assessing malnutrition and predicting clinical outcomes in patients with cardiovascular diseases, such as coronary artery disease, heart failure, and pulmonary embolism.[6–9] However, to the best of our knowledge, it has not previously been studied in IE. The aim of this study was to investigate the impact of the PNI on mortality in patients with IE.

## METHODS

### Study population

This retrospective study was conducted at a single tertiary center using data from 2010 to 2019. A total of 198 patients were screened and patients younger than 18 years of age, those with multiple hospital admissions, diagnosed as IE after major cardiac surgery during hospitalization, and patients without admission serum albumin and/or lymphocyte level information were excluded from the study. Additionally, patients with other causes of increased inflammatory markers, such as trauma, major surgery, malignancy, systemic steroid therapy, chronic inflammatory disease, end-stage renal disease, and end-stage hepatic disease were also excluded from the study. In all, 131 patients with definite IE according to the Duke criteria were included in the study. The study was approved by the local ethics committee.

### Biochemical analysis and nutritional status evaluation

Baseline demographic and clinical variables of the study population were recorded from details in the hospital database. The biochemical analysis data collected included the complete blood count and levels of serum creatinine, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, serum electrolytes, serum albumin, and C-reactive protein assessed at the hospital admission. The PNI was calculated as an indicator of nutritional status using the formula: PNI = 10 x serum albumin (g/dL) + 0.005 x total lymphocyte count (per $mm^3$). Additionally, a body mass index was calculated using the formula: body mass index = body weight / $(\text{body height})^2$. The finding of blood culture positivity and the associated microorganism was also recorded.

### Clinical follow-up

Transthoracic echocardiography and/or transesophageal echocardiography (TEE) was performed on all of the patients using a Vivid 5 (GE Healthcare, Inc. Chicago, IL, USA) or an Epiq 7 (Koninklijke Philips N.V., Amsterdam, Netherlands) ultrasound device. The presence of a vegetation, the valve type, impairment of left ventricular function, and intracardiac complications of IE, such as perivalvular abscess, perforation of leaflet, paravalvular regurgitation, and new dehiscence of a prosthetic valve were evaluated and the results were noted. Electrocardiographic findings other than sinus rhythm were also determined from the records. Clinical complications of acute heart failure, acute renal failure, septic shock, peripheral emboli, need for surgery, and death were recorded. Previous research demonstrated baseline demographic and clinical parameters of patients with IE in this center.[10] In this study, the mortality rate of patients with IE for as long as 1 year was revealed. In that study, the patients were divided into 2 groups: survival (group 1) and mortality (group 2) during the index hospitalization. The variables were compared between groups.

### Statistical analysis

Statistical analysis was performed using the IBM SPSS Statistics for Windows, Version 21.0 software (IBM Corp., Armonk, NY, USA). The data were expressed as n (%) for categorical variables. The Pearson chi-square and Fisher exact tests were performed for categorical variables. After normal distribution was analyzed with the Kolmogorov-Smirnov test, the data were expressed as median ($25^{th}$ and $75^{th}$ percentiles) for variables without a normal distribution and mean±SD for variables with normal distribution. Student's t-test was used for comparing quantitative variables with normal distribution, and the Mann-Whitney U test was used for comparing quantitative variables without normal distribution. Univariate and multivariate logistic regression analyses were used to determine the independent predictors of in-hospital mortality. Receiver operating characteristic (ROC) curve analysis was conducted to determine the optimal PNI value to indicate mortality in terms of both sensitivity and specificity. The survival curve for 1 year using the PNI was analyzed using the Kaplan-Meier method, and statistical assessment was performed using the log-rank test. A p value <0.05 was considered statistically significant.

## RESULTS

A total of 131 patients with defined IE were included in this study. Of these 131 patients, 43 patients (32.8%) were female and the median age was 60 years (45–68). In all, 74 patients had mitral valve vegetation, 55 had aortic valve vegetation, 6 had tricuspid valve vegetation, and 7 had intra-cardiac device vegetation. Among the study group, 29 patients died during hospitalization and formed group 2, while the 101 surviving patients made up group 1. The baseline demographic, laboratory, and clinical variables of the groups are demonstrated in Tables 1 and 2. While the mean age [58 (41–65); 68 (60–73) years; p<0.001] was higher in group 2, the hospitalization time [41 (25–47); 27 (13–42) days; p=0.013] was higher in group 1. The incidence of hypertension [25.5% (26); 44.8% (13); p=0.044], chronic renal failure [10.8% (11); 31.0% (9); p=0.012], dyspnea [51.0% (52); 72.4% (21); p=0.040], and baseline atrial fibrillation [16.7% (17); 37.9% (11); p=0.014] was higher in group 2 when compared with group 1.

### Laboratory assessment and PNI measurement

While the mean PNI was 35.90±6.96 in the surviving patients, it was 31.09±5.88 in the cases of mortality (p=0.001) (Fig. 1). In addition, the thrombocyte count (264.7±101.2; 219.0±102.9 × 103/$mm^3$; p=0.034), calcium level [8.6 (8.2–9.0); 8.1 (7.8–8.5) mg/dL; p<0.001] and albumin level (3.59±0.70; 3.11±0.59 g/dL; p=0.001) were also significantly lower in group 2 than in group 1. In contrast, the red cell distribution width [15.1% (13.5–16.6); 16.2% (15.0–17.6); p=0.013], blood urea nitrogen level [17 (13–29); 29 (21–39) mg/dL; p<0.001] and creatinine level [0.92 (0.70–1.20); 1.19 (0.90–1.79) mg/dL; p=0.003] were higher in group 2. Systolic pulmonary artery pressure [40 (25–45); 45 (35–60) mmHg; p=0.004] was also higher in the mortality group, and the TEE examination results revealed that the incidence of perforation [11.1% (11); 30.8% (8); p=0.019] was higher in group 2 patients. There was a higher incidence of blood culture positivity [46.1 (47); 72.4 (21); p=0.012] in the mortality group. Methicillin-sensitive *Staphylococcus aureus* and methicillin-resistant coagulase-negative staphylococci endocarditis [2.9% (3) vs 17.2% (5); 11.8% (12) vs 31.0% (9), respectively; p=0.014] were more common in group 2.

### Clinical features

The surgical operation rate [78.4% (80); 58.6% (17); p=0.032] was significantly lower in group 2. Although there were more complications, such as heart failure,

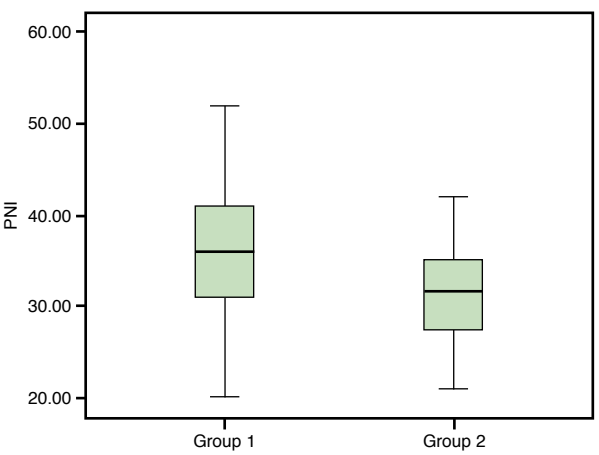


**Figure 1.** Comparison of prognostic nutritional index values of patients who did and did not survive. Patients with in-hospital mortality (group 2) had lower PNI values compared with patients who survived (group 1). PNI: Prognostic nutritional index.

renal failure, cerebrovascular accident, and peripheral emboli in group 2, only the higher incidence of septic shock [1.0% (1); 10.3% (3); p=0.034] was statistically significant (Table 2).

**Table 1. Demographic and laboratory variables of patients according to survival**

| | All patients | Survivors (Group 1) (n=102) | Mortality (Group 2) (n=29) | *p* |
|---|---|---|---|---|
| Age (years) | 60 (45–68) | 58 (41–65) | 68 (60–73) | <0.001 |
| Gender (female), n (%) | 43 (32.8) | 34 (33.3) | 9 (31.0) | 0.816 |
| Hospitalization time (days) | 37 (24–47) | 41 (25–47) | 27 (13–42) | 0.013 |
| Diabetes mellitus, n (%) | 21 (16.0) | 15 (14.7) | 6 (20.7) | 0.303 |
| Hypertension, n (%) | 39 (29.8) | 26 (25.5) | 13 (44.8) | 0.044 |
| Coronary artery disease, n (%) | 32 (24.4) | 23 (22.5) | 9 (31.0) | 0.348 |
| Congestive heart failure, n (%) | 19 (14.5) | 14 (13.7) | 5 (17.2) | 0.415 |
| Atrial fibrillation, n (%) | 17 (13.0) | 11 (10.8) | 6 (20.7) | 0.139 |
| CPM-ICD implantation history, n (%) | 12 (9.2) | 10 (9.8) | 2 (6.9) | 0.478 |
| Chronic renal failure, n (%) | 20 (15.3) | 11 (10.8) | 9 (31.0) | 0.012 |
| COPD, n (%) | 6 (4.6) | 3 (2.9) | 3 (10.3) | 0.122 |
| Angina, n (%) | 36 (27.5) | 27 (26.5) | 9 (31.0) | 0.627 |
| Dyspnea, n (%) | 73 (55.7) | 52 (51.0) | 21 (72.4) | 0 040 |
| Syncope, n (%) | 8 (6.1) | 4 (3.9) | 4 (13.8) | 0.072 |
| Fever, n (%) | 89 (67.9) | 71 (69.6) | 18 (62.1) | 0.443 |
| Cerebrovascular disease, n (%) | 18 (13.7) | 15 (14.7) | 3 (10.3) | 0.399 |
| Electrocardiographic evaluation, n (%) | | | | |
| Atrioventricular block | 2 (1.5) | 1 (1.0) | 1 (3.4) | 0.395 |
| Atrial fibrillation | 28 (21.4) | 17 (16.7) | 11 (37.9) | 0.014 |
| Hemoglobin (g/dL) | 10.6±1.96 | 10.76±2.0 | 10.31±1.85 | 0.280 |
| Leukocyte $\times 10^3/mm^3$ | 10.4 (8.2–14.1) | 10.34 (8.28–13.8) | 12.6 (8.46–17.18) | 0.165 |
| Neutrophil ($10^9$/L) | 8.1 (5.5–11.4) | 8.03 (5.48–10.11) | 10.46 (6.36–12.63) | 0.092 |
| Lymphocyte ($10^9$/L) | 1.58 (1.08–2.08) | 1.60 (1.17–2.08) | 1.46 (1.02–1.92) | 0.387 |
| Monocyte ($10^9$/L) | 0.78±0.33 | 0.77±0.31 | 0.86±0.41 | 0.215 |
| Thrombocyte ($\times 10^3/mm^3$) | 254.5±102.9 | 264.7±101.2 | 219.0±102.9 | 0.034 |
| Mean platelet volume (fL) | 9.59±1.70 | 9.5±1.6 | 9.8±2.1 | 0.520 |
| C-reactive protein (mg/L) | 82 (32–130) | 70.5 (32.0–127.0) | 107 (52.0–160.0) | 0.120 |
| Red cell distribution width (%) | 15.4 (13.6–17.1) | 15.1 (13.5–16.6) | 16.2 (15.0–17.6) | 0.013 |
| Blood urea nitrogen (mg/dL) | 20 (14–30) | 17 (13–29) | 29 (21–39) | <0.001 |
| Creatinine (mg/dL) | 1.0 (0.72–1.30) | 0.92 (0.70–1.20) | 1.19 (0.90–1.79) | 0.003 |
| Sodium (mmol/L) | 135.2±4.40 | 135.6±4.4 | 134.1±4.2 | 0.123 |
| Potassium (mmol/L) | 4.22±0.61 | 4.2±0.6 | 4.2±0.7 | 0.742 |
| Calcium (mg/dL) | 8.5 (8.1–9.0) | 8.6 (8.2–9.0) | 8.1 (7.8–8.5) | <0.001 |
| Alanine aminotransferase (U/L) | 18 (12–29) | 17 (12–29) | 20 (15–28) | 0.317 |
| Aspartate aminotransferase (U/L) | 22 (16–35) | 21 (16–31) | 30 (14–44) | 0.191 |
| Albumin (g/dL) | 3.48±0.70 | 3.59±0.70 | 3.11±0.59 | 0.001 |
| Body mass index ($kg/m^2$) | 23.5 (21.8–24.6) | 23.5 (21.9–24.6) | 23.4 (21.5–23.5) | 0.052 |
| Prognostic nutritional index value | 34.83±7.00 | 35.90±6.96 | 31.09±5.88 | 0.001 |

COPD: Chronic obstructive pulmonary disease; CPM: Cardiac pacemaker; ICD: Intra-cardiac defibrillation.

**Table 2. Clinical variables of patients according to survival**

| | All patients | Survivors (Group 1) (n=102) | Mortality (Group 2) (n=29) | *p* |
|---|---|---|---|---|
| Mitral valve, n (%) | | | | |
| Native | 98 (74.8) | 75 (73.5) | 23 (79.3) | 0.527 |
| Prosthesis | 33 (25.2) | 27 (26.5) | 6 (20.7) | |
| Aortic valve, n (%) | | | | |
| Native | 106 (80.9) | 84 (82.4) | 22 (75.9) | 0.433 |
| Prosthesis | 25 (19.1) | 18 (17.6) | 7 (24.1) | |
| sPAP (mmHg) | 40 (30–50) | 40 (25–45) | 45 (35–60) | 0.004 |
| Ejection fraction (%) | 60 (50–60) | 60 (50–60) | 55 (45–60) | 0.121 |
| TEE evaluation, n (%) | | | | |
| Aortic vegetation | 55 (42.0) | 41 (41.4) | 14 (53.8) | 0.256 |
| Mitral vegetation | 74 (56.5) | 60 (60.6) | 14 (53.8) | 0.533 |
| Tricuspid vegetation | 6 (4.6) | 5 (5.1) | 1 (3.8) | 0.635 |
| Intracardiac device vegetation | 7 (5.3) | 5 (5.1) | 2 (7.7) | 0.448 |
| Abscess | 18 (13.7) | 13 (13.1) | 5 (19.2) | 0.306 |
| Fistula | 4 (3.1) | 2 (2.0) | 2 (7.7) | 0.191 |
| Perforation | 19 (14.5) | 11 (11.1) | 8 (30.8) | 0.019 |
| Pseudoaneurysm | 6 (4.6) | 4 (4.0) | 2 (7.7) | 0.365 |
| Paravalvular leakage | 14 (10.7) | 11 (11.1) | 3 (11.5) | 0.592 |
| Prosthetic valve dehiscence | 10 (7.6) | 6 (6.1) | 4 (15.4) | 0.126 |
| Vegetation size (mm) | | | | |
| Aortic valve | 12.3±6.72 | 11.62±6.30 | 14.50±7.68 | 0.140 |
| Mitral valve | 12.7±7.55 | 13.04±8.16 | 11.38±4.18 | 0.259 |
| Septic emboli, n (%) | 2 (1.5) | 2 (2.0) | 0 (0) | 0.614 |
| Blood culture positivity, n (%) | 68 (51.9) | 47 (46.1) | 21 (72.4) | 0.012 |
| Microorganism, n (%) | | | | |
| *Streptococci* | 7 (5.3) | 6 (5.9) | 1 (3.4) | |
| *Brucella* | 1 (0.8) | 1 (1.0) | 0 (0) | |
| *Candida* | 2 (1.5) | 1 (1.0) | 1 (3.4) | |
| *Corynebacterium striatum* | 1 (0.8) | 1 (1.0) | 0 (0) | |
| *Escherichia coli* | 1 (0.8) | 0 (0) | 1 (3.4) | |
| *Enterococcus faecalis* | 8 (6.1) | 8 (7.8) | 0 (0) | |
| Gram-positive | 2 (1.5) | 1 (1.0) | 1 (3.4) | |
| *Staphylococcus aureus* | 12 (9.2) | 6 (5.9) | 6 (20.7) | 0.014 |
| Methicillin-resistant *S. aureus* | 4 (3.1) | 3 (2.9) | 1 (3.4) | |
| Methicillin-susceptible *S. aureus* | 8 (6.1) | 3 (2.9) | 5 (17.2)* | |
| Coagulase negative staphylococcus | 32 (24.4) | 21 (20.6) | 11 (37.9) | |
| MRCNS | 21 (16.0) | 12 (11.8) | 9 (31.0)* | |
| MSCNS | 11 (8.4) | 9 (8.8) | 2 (6.9) | |
| *Serratia marcescens* | 1 (0.8) | 1 (1.0) | 0 (0) | |
| *Stenotrophomonas maltophilia* | 2 (1.5) | 1 (1.0) | 1 (3.4) | |
| Surgery, % (n) | 97 (74.0) | 80 (78.4) | 17 (58.6) | 0.032 |

**Table 2. Clinical variables of patients according to survival *(cont.)***

| | All patients | Survivors (Group 1) (n=102) | Mortality (Group 2) (n=29) | *p* |
|---|---|---|---|---|
| Clinical complications, % (n) | | | | |
| Heart failure | 7 (5.3) | 4 (3.9) | 3 (10.3) | 0.182 |
| Renal failure | 15 (11.5) | 9 (8.8) | 6 (20.7) | 0.080 |
| CVA | 6 (4.6) | 4 (3.9) | 2 (6.9) | 0.398 |
| Intracerebral hemorrhage | 4 (3.1) | 4 (3.9) | 0 (0) | 0.363 |
| Peripheral emboli | 4 (3.1) | 3 (2.9) | 1 (3.4) | 0.637 |
| Osteomyelitis | 1 (0.8) | 0 (0) | 1 (3.4) | 0.221 |
| Rhythm disturbances | 9 (6.9) | 8 (7.8) | 1 (3.4) | 0.366 |
| Septic shock | 4 (3.1) | 1 (1.0) | 3 (10.3) | 0.034 |
| Pericarditis-myocarditis | 1 (0.8) | 1 (1.0) | 0 (0) | 0.779 |

CVA: Cerebrovascular accident; MRCNS: Methicillin-resistant coagulase-negative staphylococci; MRSA: Methicillin-resistant *Staphylococcus aureus*; MSCNS: Methicillin-sensitive coagulase-negative staphylococci; MSSA: Methicillin-sensitive *Staphylococcus aureus*; sPAP: Systolic pulmonary artery pressure; RDW: Red cell distribution width; TEE: Transesophageal echocardiography.

## PNI and mortality evaluation

In all, 131 patients with IE were followed-up for up to 1 year. There was no death observed after discharge from the hospital. Twenty-nine patients died during hospitalization with a median follow-up of 37 days. The length of hospitalization was 4 to 201 days in group 1 while it was 2 to 184 days in group 2. ROC curve analysis was conducted to determine the optimal PNI cut-off value to indicate in-hospital mortality. The highest combined sensitivity and specificity values crossed the curve at 35.6 (sensitivity: 51%; specificity: 80%). The area under the curve was 0.691 (95% CI: 0.589–0.794; p=0.002) (Fig. 2). The entire study group was divided into 2 groups according to the PNI value. A Kaplan-Meier survival analysis also revealed that long-term survival was found to be significantly decreased in patients with a lower PNI (Log rank: p=0.008) (Fig. 3). Logistic regression was conducted and significant variables found in the univariate analysis were entered into multiple logistic regression (Table 3). The multivariate logistic regression analysis indicated that advanced age (OR: 1.078; 95% CI: 1.017–1.143; p=0.012), PNI (OR: 0.911; 95% CI: 0.835–0.993; p=0.034), and perforation (OR: 5.557; 95% CI: 1.357–22.765; p=0.017) were found to be independent predictors of mortality.

Clinical complications and the underlying mechanisms of death of both the low and high PNI groups are demonstrated in Table 4. The incidence of renal failure [16.4% (12); 5.2% (3); p=0.044] and mortality [31.5% (23); 10.3% (6); p=0.004] were found to be higher in patients with a lower PNI value.

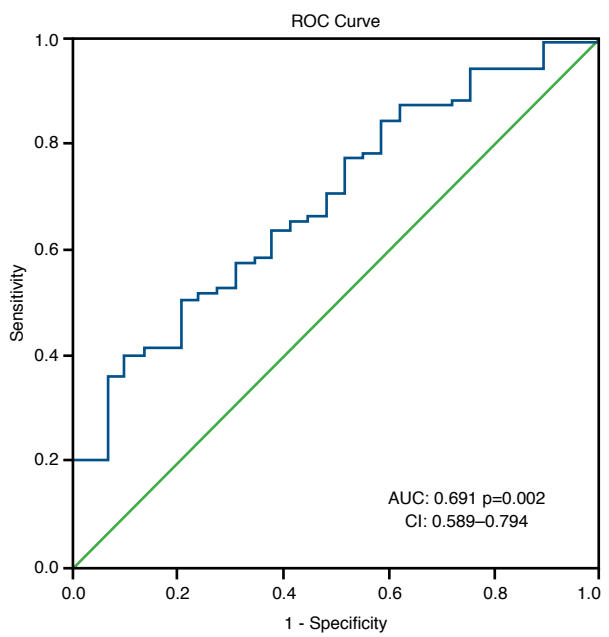


**Figure 2.** Receiver-operating characteristic curve indicating the discriminative ability of the prognostic nutritional index. ROC analysis was conducted to determine the optimal PNI cut-off value to indicate in-hospital mortality. The highest combined sensitivity and specificity values crossed the curve at 35.6 (sensitivity: 51%; specificity: 80%). The area under the curve (AUC) was 0.691 (95% confidence interval [CI]: 0.589–0.794; p=0.002). PNI: Prognostic nutritional index; ROC: Receiver operating characteristic.

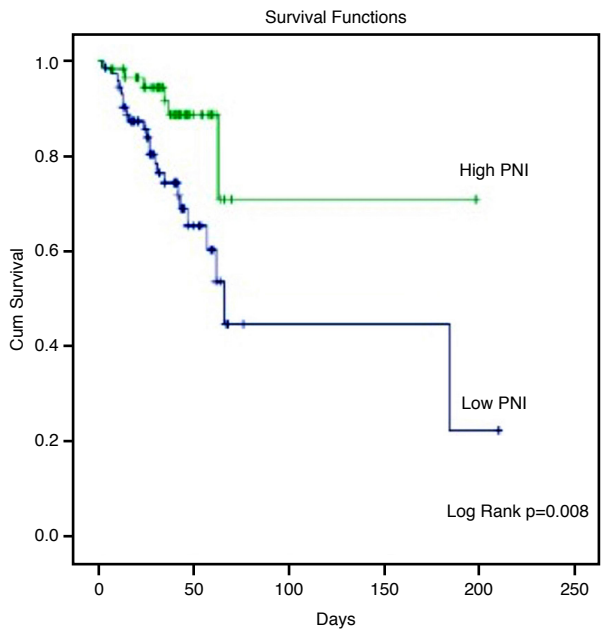


**Figure 3.** Kaplan-Meier survival curve for low and high prognostic nutritional index groups. In-hospital mortality occurred more often in patients with a lower PNI. PNI: Prognostic nutritional index.

## DISCUSSION

To the best of our knowledge, this is the first study to demonstrate an association between PNI and in-hospital mortality in patients with IE. Additionally, PNI, advanced age and perforation as a complication of IE were found to be independent predictors of mortality.

Nutritional status is accepted as an indicator of general health status, including immune competence, protein turnover, and physical condition. Malnutrition is a very important health problem due to the association with a poorer prognosis in several populations.[11] It is associated with decreased immune system function, impairment of respiratory function, poor wound healing, fluid retention, and cachexia.[12–14] As an immunonutritional screening tool, the PNI reflects serum albumin concentration and lymphocyte count; however, it has also been reported to predict adverse clinical outcomes in cardiovascular disease.[6–9] Albumin, synthesized by the hepatocyte, is the most abundant plasma protein. It is a good indicator of nutritional status in addition to its role of influencing osmotic pressure and has anti-oxidant and anti-inflammatory properties.[15] Albumin is also an acute phase responder protein; synthesis of albumin is reduced during the inflammatory process due to decreased hepatic synthesis, increased leakage into the interstitial space, and catabolism.[16] Hypoalbuminemia as a result of increased inflammation is a strong predictor of mortality in cardiovascular disease.[17] In 1706 patients with ST-segment elevated myocardial infarction (STEMI), hypoalbuminemia was associated with a 2.98 times greater mortality and a 2.96 times greater heart failure rate.[17] In a study by Bonilla-Palomas et al.,[18] 362 patients with heart failure were screened and hypoalbuminemia was found to be associated with a 2.9 times greater hospital mortality rate. Lymphocytes also have an important role in the immune system

**Table 3. Univariate and multivariate logistic regression analysis of independent predictors of mortality**

| | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | Odds ratio | 95% CI (Lower-Upper) | *p* | Odds ratio | 95% CI (Lowe-Upper) | *p* |
| Age | 1.071 | 1.029–1.114 | 0.001 | 1.078 | 1.017–1.143 | 0.012 |
| Hypertension | 0.421 | 0.179–0.992 | 0.048 | 1.434 | 0.421–4.890 | 0.564 |
| Chronic renal failure | 3.723 | 1.362–10.172 | 0.010 | 2.360 | 0.640–8.694 | 0.197 |
| Atrial fibrillation | 3.056 | 1.226–7.615 | 0.017 | 1.939 | 0.571–6.584 | 0.288 |
| PNI | 0.895 | 0.835–0.959 | 0.002 | 0.911 | 0.835–0.993 | 0.034 |
| Perforation | 3.556 | 1.254–10.083 | 0.017 | 5.557 | 1.357–22.765 | 0.017 |
| Prosthetic valve | 1.013 | 0.433–2.369 | 0.976 | 1.169 | 0.348–3.925 | 0.800 |
| Heart failure | 0.354 | 0.074–1.680 | 0.191 | 1.162 | 0.069–19.490 | 0.917 |
| Staphylococcus | 4.174 | 1.233–14.133 | 0.022 | 6.187 | 0.946–40.454 | 0.057 |
| Septic shock | 11.654 | 1.164–116.686 | 0.037 | 11.846 | 0.503–278.718 | 0.125 |

PNI: Prognostic nutritional index.

**Table 4. Demographic and clinical variables of patients with low and high PNI**

| | Patients with PNI <35.6 (n=73) | Patients with PNI >35.6 (n=58) | *p* |
|---|---|---|---|
| Age (years) | 60 (46–69) | 60 (45–66) | 0.786 |
| Gender (female), n (%) | 20 (27.4) | 23 (39.7) | 0.138 |
| Heart failure, n (%) | 6 (8.2) | 1 (1.7) | 0.103 |
| Renal failure, n (%) | 12 (16.4) | 3 (5.2) | 0.044 |
| Cerebrovascular accident, n (%) | 2 (2.7) | 4 (6.9) | 0.238 |
| Intracerebral hemorrhage, n (%) | 1 (1.4) | 3 (5.2) | 0.228 |
| Peripheral emboli, n (%) | 1 (1.4) | 3 (5.2) | 0.228 |
| Osteomyelitis, n (%) | 1 (1.4) | 0 (0) | 0.557 |
| Rhythm disturbances, n (%) | 3 (4.1) | 6 (10.3) | 0.146 |
| Septic shock, n (%) | 4 (5.5) | 0 (0) | 0.093 |
| Pericarditis-myocarditis, n (%) | 1 (1.4) | 0 (0) | 0.557 |
| Death, n (%) | 23 (31.5) | 6 (10.3) | 0.004 |

PNI: Prognostic nutritional index.

and are affected by inflammation. Under inflammatory conditions, increased cortisol and catecholamine levels, increased apoptosis, and margination and redistribution of lymphocytes to lymphatic organs result in reduced lymphocyte levels.[19,20] Bian et al.[21] demonstrated that lymphopenia was associated with major adverse cardiac events in coronary artery disease patients. Marçula et al.[22] revealed that the lymphocyte count can predict prognosis in heart failure. Moreover, in a study including 121 patients with IE, it was demonstrated that lymphopenia could be related to mortality.[23] In IE, these parameters change due to increased inflammation. Supporting these findings, in our study, hypoalbuminemia was demonstrated to be more frequent in IE patients with in-hospital mortality. We also found that IE patients with in-hospital mortality had a lower lymphocyte level compared with surviving patients. However, this difference was not statistically significant in our study.

The PNI was originally described as an immunonutritional status indicator based on the serum albumin level and lymphocyte count. This nutritional index is widely used for risk prediction in patients with malnutrition, systemic inflammation, and malignancy. Buzby et al.[5] first demonstrated that the PNI could be a valuable measure to assess the nutritional status and surgical risk in patients undergoing gastrointestinal surgery. In other studies, the PNI level has been strongly associated with prognosis in cardiovascular diseases.[6–9] In a prospective study of 388 consecutive patients with heart failure conducted by Narumi et al.[6] the malnutrition prevalence was 60% to 69% and a lower PNI was associated with cardiovascular events, such as death and rehospitalization during a mean follow-up period of 28.4 months. The impact of PNI on in-hospital and long-term mortality in 1823 patients with STEMI was evaluated. Patients with a lower PNI value had a 7.9 times greater in-hospital and 6.4 times greater long-term (3 years) mortality compared with patients with a higher PNI. The PNI has also been studied in patients with stable coronary artery disease undergoing elective percutaneous coronary intervention. The PNI was significantly associated with long-term major adverse cardiovascular events during the median follow-up of 7.5 years.[9] The PNI was also found to be an independent predictor of mortality in patients undergoing coronary artery bypass grafting surgery.[24] Furthermore, the PNI has been shown to have a predictive value on prognosis in patients with pulmonary embolism. Hayıroğlu et al.[7] demonstrated an association between PNI and mortality in pulmonary embolism with a median follow-up of 53.8 months. The PNI is associated with adverse outcomes in all increased inflammatory cardiovascular diseases. However, to the best of our knowledge, an association between the PNI value and prognosis in infective endocarditis has been demonstrated for the first time in our study. IE patients with in-hospital

mortality had a lower PNI value than the patients who survived. It confirms that the suppressive effect of the elevated inflammatory process on PNI may be a simple and effective method for predicting mortality. Hypoalbuminemia and lymphopenia were more common in the patients who did not survive. The PNI was the only independent predictor of mortality among these parameters. It also supports the concept that the PNI is a more sensitive parameter than albumin or lymphocyte levels alone.

Additionally, complications due to IE, such as heart failure, renal failure, and septic shock were demonstrated to be more frequent in patients with a lower PNI in our study. In previous studies, it has been shown that lymphopenia and hypoalbuminemia were independent risk factors for acute kidney injury.[25,26] A lower PNI reflects poorer nutritional status, which leads to a decay in the intravascular osmotic pressure that is primarily created by albumin and can result in increased acute kidney injury. Dolapoglu et al.[27] found that a low PNI was related to acute kidney injury in patients undergoing coronary bypass surgery. Our results also supported an increased incidence of acute renal failure in patients with a lower PNI value. Although the mentioned complications could be associated with a lower PNI, only the incidence of renal failure after IE was higher with statistical significance. It may be explained by the relatively small sample size of the study. On the other hand, these clinical events could be the underlying mechanisms of increased mortality rates in IE patients with lower PNI.

Patient characteristics and some clinical factors can be associated with prognosis in IE. In a previous study, advanced age was found to be related with increased in-hospital and 1-year mortality rates in IE.[28] An age of ≥70 years had a 1.98 times increased in-hospital mortality rate and a 1.90 times increased 1-year mortality rate. Our study findings demonstrated that advanced age was associated with increased in-hospital mortality in IE as well as being an independent predictor of mortality. Microorganisms are also important to prognosis. Several studies revealed that the outcome of patients with Staphylococcus aureus-related IE was poorer compared with other bacterial endocarditis patients. Sunder et al.[28] demonstrated that IE linked to *Staphylococcus aureus* had a 2.01 times greater in-hospital mortality rate and Marques et al.[29] observed that *Staphylococcus aureus* etiology was found to be related with a 6.47 times greater in-hospital mortality rate in IE. Our results demonstrated an increased mortality rate in patients with staphylococci endocarditis. Additionally, it was previously found that patients with renal failure had a poorer prognosis in IE.[30] This was also supported by our study. However, advanced age was the only independent predictor of mortality among the clinical parameters examined, which may be related to the small sample size of our study.

Septic shock is a life-threatening complication of IE. Several studies have demonstrated a poorer prognosis in IE due to septic shock.[30,31] Tuğcu et al.[31] found that septic shock was associated with death in 68 patients with IE during hospitalization. Similarly, we determined that septic shock was more common in patients with in-hospital mortality compared with surviving patients. It is well known that IE can be associated with periannular complications, and it can also be associated with increased mortality rates. García-Granja et al.[30] demonstrated that a periannular complication was an independent predictor of mortality in patients with IE. Perforation is one of the most important periannular complications of IE. Our results indicated an association between perforation and in-hospital mortality in IE. In addition, the surgical requirement of complications linked to IE can be a predictor of poor prognosis. Nonetheless, cardiac surgery in selected patients at the appropriate time may decrease mortality rates. Supporting this, Marques et al.[29] demonstrated that cardiac surgery was a protective factor against mortality in IE. This may be a reason for the higher surgical operation rate among survivors in our study population. However, large-scale studies are needed to investigate further.

## Conclusion

The PNI was associated with an increased in-hospital mortality rate in patients with IE. The PNI, advanced age, and perforation as a complication of IE were found to be independent predictors of mortality. Additionally, IE patients with a lower PNI had a higher incidence of acute kidney injury during hospitalization.

## Study limitations

The main limitation of this study is the relatively small sample size. Lack of data about long-term clinical events due to the retrospective nature of the study

is another limitation. A lack of analysis of the nutritional status of patients before hospitalization is an additional limitation.

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*Keywords:* Albumin; infective endocarditis; in-hospital mortality; lymphocyte; prognosis; prognostic nutritional index.

*Anahtar sözcükler:* Albümin; enfektif endokardit; hastane içi mortalite; lenfosit; prognoz; prognostik nutrisyonel indeks.