

Prognostic nutritional index as a marker of mortality: an observational cohort study of patients undergoing cardiac surgery

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Nutritional problem of the patient is a valuable situation in patients undergoing surgery. In this study, we aimed to investigate the relationship between prognostic nutritional index (PNI) and postoperative in-mortality in patients undergoing cardiac surgery. 1003 patients undergoing on-pump cardiac surgery in our hospital between January 2016–January 2020 were included in this study retrospectively. Patients were divided into two groups based on in-hospital mortality, as survivors (Group I, $n = 934$) and non-survivors (Group II, $n = 69$). Their preoperative nutritional status was determined using the PNI. Compared to survivors, non-survivors were found to have a significantly higher mean age (62.5 ± 10.8 vs. 67.45 ± 10.1 , $P < 0.001$) and significantly lower mean preoperative ejection fraction (51.6 ± 0.3 vs. 44.5 ± 1.2 , $P < 0.001$). And combined cardiac surgery rate was significantly higher in non-survivors ($P = 0.009$). Also non-survivors had a significantly lower mean PNI compared to survivors (44.76 ± 7.63 vs. 48.34 ± 6.71 , $P < 0.001$). Multivariate analysis Model 1 revealed that age (Odds ratio (OR): 1.756; 95% confidence interval (CI): 1.250–3.790, $P = 0.029$), intra-aortic balloon pump usage (OR: 2.252, 95% CI: 1.885–6.194, $P < 0.001$), combined cardiac surgery (OR: 0.542, 95% CI: 0.428–0.690, $P = 0.041$) and the PNI (OR: 0.639, 95% CI: 0.552–0.874, $P = 0.021$) were independent predictors of mortality. In Model 2, age > 70 (OR: 2.437, 95% CI: 1.983–5.390, $P = 0.005$), LVEF $< 35\%$ (OR: 1.945, 95% CI: 1.586–3.492, $P = 0.012$), IABP usage (OR: 1.365, 95% CI: 1.109–2.196, $P = 0.001$) and PNI (OR: 0.538, 95% CI: 0.492–0.791, $P = 0.033$) were determined as independent predictors for mortality. In on-pump cardiac surgery, postoperative mortality is significantly associated with preoperative low PNI, and PNI can be a useful and suitable parameter for preoperative risk evaluation.

Keywords

Prognostic nutritional index; Nutritional status; Cardiac surgery; Cardiopulmonary bypass; Malnutrition; Risk factors

1. Introduction

Technological advances and new surgical methods have so far been insufficient to lower the high risk of mortality and morbidity in patients undergoing cardiac surgery [1–3]. Mortality and morbidity rates are caused by multiple factors, including left ventricular dysfunction, preoperative anemia,

chronic renal failure, coronary artery diameter, advanced age, and socioeconomic status [4–9]. The risk involved with cardiac surgery can currently be estimated using certain risk estimation algorithms, the most common of which are the Society of Thoracic Surgeons (STS) score and the Euroscore [10, 11]. Despite being quite comprehensive, neither of these systems consider patients' clinical nutritional status. This factor has been found to be associated with risk in gastrointestinal system and malignancy surgery [12, 13]. Patients undergoing malignancy surgery can currently be tested for nutritional status by a variety of tests, like the Mini Nutritional Assessment, Malnutrition Universal Screening Tool, Subjective Global Assessment, and Short Nutritional Assessment Questionnaire. Of these, the most common one is the prognostic nutritional index (PNI), developed by Buzby *et al.* [12] in 1980 and simplified by Onodera *et al.* [14]. The PNI is measured based on serum albumin concentration and peripheral blood lymphocyte count. In a recent study, it has been shown that low PNI affected surgical outcomes in hemodialysis-dependent patients undergoing cardiac surgery [15]. Therefore, the current study aimed to evaluate PNI findings for predicting in-hospital mortality and morbidity in patients undergoing cardiac surgery.

2. Materials and methods

The study protocol was approved by the Ethics Committee at Bursa Postgraduate Training and Research Hospital (2011-KAEK-25 2020/03-11). No informed consent was required as per the retrospective design.

1003 patients undergoing on-pump cardiac surgery in our hospital between January 2016–January 2020 were included in this study retrospectively. The research was stopped before any COVID-19 case was reported in Turkey to eliminate the effects of the pandemic. Patients' demographic characteristics, medical records, laboratory findings, and clinical outcomes were obtained retrospectively from the clinical database of the institution. Surgical procedures included

coronary artery bypass grafting (CABG), aortic valve replacement (AVR), mitral valve replacement (MVR), and combined procedures (Table 1). Patients were divided into two groups based on in-hospital mortality, as survivors (Group I, n = 934) and non-survivors (Group II, n = 69).

Table 1. Surgical procedures of the patients.

Surgical procedure	Group I (n = 934)	Group II (n = 69)
CABG, n (%)	699 (74.8%)	43 (62.3%)
CABG + AVR, n (%)	26 (2.8)	5 (7.2%)
CABG + MVR, n (%)	25 (2.7%)	5 (7.2%)
CABG + AVR + MVR, n (%)	4 (0.4%)	0
AVR, n (%)	59 (6.3%)	8 (11.6%)
MVR, n (%)	100 (10.7%)	6 (8.7%)
AVR + MVR, n (%)	21 (2.2%)	2 (2.9%)

CABG, Coronary artery bypass grafting; AVR, Aortic valve replacement; MVR, Mitral valve replacement.

2.1 Blood parameter analysis

Peripheral blood samples were obtained from all patients on the first day of hospitalization. Complete blood cell count was analyzed using a Beckmann Coulter LH 780 Hematology analyzer. Biochemical measurements were done using a Roche diagnostic Cobas 6000 analyzer (Manheim).

2.2 Calculation of PNI

The prognostic nutritional index (PNI) was used to evaluate preoperative nutritional status, calculated by the following formula [14]:

$$10 \times \text{serum albumin} + 0.005 \times \text{total lymphocyte count}.$$

Other recorded data included body mass index (BMI), preoperative left ventricular ejection fraction (LVEF), cross-clamp (X-clamp) time, cardiopulmonary bypass (CPB) time, use of intra-aortic balloon pump (IABP), length stay in the intensive care unit (ICU), hospital-acquired infections, and stroke.

Also, postoperative stroke and infection events (surgical site, septicemia, or pneumonia) were recorded. Early stroke cases after an asymptomatic interval were mostly defined as stroke 'on waking' or 'after extubation'.

2.3 Statistical analysis

Continuous variables are given as mean \pm standard deviation, while categorical variables are given as number and percentage. Group comparisons in terms of symptom severity were made using Student's *t*-test for data with normal distribution and the Mann-Whitney U test for data with non-normal distribution. The Chi-squared test was used to determine differences in terms of categorical variables. Multivariate binary logistic regression analysis was used to analyze the predictors of mortality. In Model 1, age and LVEF were used as continuous parameters. In Model 2, age >70 years and LVEF $<35\%$ were used as categorical parameters. The receiver operating characteristic (ROC) curve analysis was performed to identify the predictive value PNI for postoperative

mortality and the area under the curve (AUC) was calculated. All statistical analyses were performed using the SPSS package for Windows version 21 (SPSS Inc., Chicago, IL, USA). Level of statistical significance was set at $P < 0.05$ for all analyses.

3. Results

The research sample consisted of 1003 patients, 69 of whom (6.87%) resulted in in-hospital mortality. Isolated CABG surgery was performed in 742 (73.9%) patients, CABG with valve surgery was performed in 65 (6.4%) patients and isolated valve surgery was performed in 173 (17.2%) patients. Details of surgical procedures were shown in Table 1. Demographic features and preoperative blood parameters of the patients were presented in Table 2. Compared to survivors, non-survivors were found to have a significantly higher mean age (62.5 ± 10.8 vs. 67.45 ± 10.1 , $P < 0.001$) and significantly lower mean Preoperative LVEF (51.6 ± 0.3 vs. 44.5 ± 1.2 , $P < 0.001$). Rates of hypertension, sex, and diabetes mellitus did not differ significantly between the two groups (Table 2). Considering laboratory findings, non-survivors were found to have significantly lower hemoglobin and albumin levels ($P = 0.001$) and significantly higher preoperative serum creatinine levels (1.0 ± 0.02 vs. 1.3 ± 0.1 , $P = 0.01$). Moreover, non-survivors had a significantly lower mean PNI compared to survivors (44.76 ± 7.63 vs. 48.34 ± 6.71 , $P < 0.001$).

Table 2. Demographic features and preoperative blood parameters of the patients.

Variables	Group I (n = 934)	Group II (n = 69)	P value
Male sex, n (%)	709 (70.7%)	46 (66.7%)	0.21
Age (years)	62.5 ± 10.8	67.4 ± 10.1	<0.001
Hypertension, n (%)	417 (44.6%)	35 (50.7%)	0.176
Diabetes mellitus, n (%)	259 (27.7%)	20 (28.9%)	0.410
Preoperative LVEF (%)	51.6 ± 0.3	44.5 ± 1.2	<0.001
BMI (m^2/kg)	26.70 ± 2.87	26.54 ± 2.60	0.660
Hemoglobin (g/dL)	13.1 ± 0.06	12.2 ± 0.25	0.001
WBC ($\times 10^3/\text{uL}$)	9.2 ± 0.1	10.5 ± 0.5	0.006
Neutrophil ($\times 10^3/\text{uL}$)	6.2 ± 0.08	7.8 ± 0.4	0.001
Lymphocyte ($\times 10^3/\text{uL}$)	1.986 ± 0.02	1.8 ± 0.1	0.14
Platelets ($\times 10^3/\text{uL}$)	244 ± 2.4	226 ± 10.4	0.10
CRP (mg/L)	14.2 ± 0.8	22.5 ± 5.3	0.12
Creatinine (mg/dL)	1.0 ± 0.02	1.3 ± 0.1	0.01
Total Protein (g/dL)	6.9 ± 0.06	6.6 ± 0.1	0.009
Albumin (g/dL)	3.8 ± 0.01	3.57 ± 0.06	0.001
PNI	48.34 ± 6.71	44.76 ± 7.63	<0.001

WBC, White blood cell; CRP, C-reactive protein; LVEF, Left ventricular ejection fraction; BMI, Body mass index; PNI, Prognostic nutritional index.

Operative and postoperative features of the patients were presented in Table 3. Non-survivors were determined to have a significantly higher rate of hospital-acquired infections (44, 63.8% vs. 151, 16.2%, $P < 0.001$) and postoperative

Table 3. Operative and postoperative features of the patients.

Characteristics	Group I (n = 934)	Group II (n = 69)	P value
X-clamp time (min)	70.7 ± 0.9	83.8 ± 4.4	<0.001
CPB time (min)	97.3 ± 1.1	121.2 ± 5.6	<0.001
Combined cardiac surgery, n (%)	76 (8.1%)	12 (17.3%)	0.009
IABP usage, n (%)	48 (5.1%)	30 (43.5%)	<0.001
ICU stay (days)	3.1 ± 0.1	8.7 ± 1.1	<0.001
Morbidity:			
-Hospital-acquired infection	151 (16.2%)	44 (63.8%)	<0.001
-Stroke (early/delayed)	35 (3.7%)	62 (89.9%)	<0.001

X- clamp, Cross clamp; CPB, Cardiopulmonary bypass; IABP, Intraaortic balloon pump; ICU, Intensive care unit.

Table 4. Multivariate logistic regression analysis to identify factors affecting postoperative mortality.

Multivariate analysis			
Variables (Model 1)	P value	Exp (B) Odds Ratio	95% CI Lower-Upper
Age, years	0.029	1.756	1.250–3.790
Preoperative LVEF, %	0.058	1.251	0.812–1.878
X-clamp time, minutes	0.114	1.432	0.916–1.880
CPB time, minutes	0.012	1.378	1.110–3.894
IABP usage, n	<0.001	2.252	1.885–6.194
Combined cardiac surgery, n	0.041	0.542	0.428–0.690
WBC, ($\times 10^3$ /uL)	0.198	1.116	0.779–1.226
PNI	0.021	0.639	0.552–0.874
Variables (Model 2)	P value	Exp (B) Odds Ratio	95% CI Lower-Upper
Age >70 years, n	0.005	2.437	1.983–5.390
Preoperative LVEF <35%, n	0.012	1.945	1.586–3.492
CPB time, minutes	0.325	1.233	0.966–1.493
IABP usage, n	0.001	1.365	1.109–2.196
Combined cardiac surgery, n	0.139	1.459	0.994–1.796
PNI	0.033	0.538	0.492–0.791

In Model 2 we use age and left ventricular ejection fraction as categorical variables. LVEF, Left ventricular ejection fraction; CPB, Cardiopulmonary bypass; WBC, White blood cell; PNI, Prognostic nutritional index.

stroke (62, 89.9% vs. 35, 3.7%, $P < 0.001$). Combined cardiac surgery rate was significantly higher in non-survivors ($P = 0.009$). Again, non-survivors had significantly higher X-clamp time, CPB time, IABP use, and length of ICU stay ($P < 0.001$ for all).

The multivariate logistic regression analysis was utilized to evaluate the parameters in predicting mortality showed that age (Odds ratio (OR): 1.756; 95% confidence interval (CI): 1.250–3.790, $P = 0.029$), intra-aortic balloon pump usage (OR: 2.252, 95% CI: 1.885–6.194, $P < 0.001$), combined cardiac surgery (OR: 0.542, 95% CI: 0.428–0.690, $P = 0.041$) and the PNI (OR: 0.639, 95% CI: 0.552–0.874, $P = 0.021$) were independent predictors for mortality in Model 1. In Model 2, age >70 (OR: 2.437, 95% CI: 1.983–5.390, $P = 0.005$), LVEF <35% (OR: 1.945, 95% CI: 1.586–3.492, $P = 0.012$), IABP usage (OR: 1.365, 95% CI: 1.109–2.196, $P = 0.001$) and PNI (OR: 0.538, 95% CI: 0.492–0.791, $P = 0.033$) were determined as independent predictors for mortality (Table 4).

Receiver-operating characteristic (ROC) curve analysis revealed that the cut-off value for PNI was 42.6 with 82% sensitivity and 42.6% specificity (AUC: 0.64, 95% CI: 0.572–0.714, $P = 0.001$) (Fig. 1).

4. Discussion

The European Society for Clinical Nutrition and Metabolism defines malnutrition as a condition resulting from lack of nutritional intake, which leads to changes in body composition and cell mass and physical and mental dysfunction. Also, an indicator for poor prognosis, cardiac cachexia is known to induce neuroendocrine and immunological dysfunction [16, 17].

Malnutrition is often correlated with humoral and cellular immune dysfunction, changes in inflammatory response, impaired wound healing, and increased mortality in malignant tumors and is well-known to be affected by postoperative complications, length of hospital stay, and quality of life [18]. Recent research has highlighted the adverse effects of long-term calorie and protein deficiency on surgical outcomes in critically ill cases [19].

PNI is measured based on serum albumin concentration and peripheral blood lymphocyte count and is considered a good indicator for disease severity in patients undergoing cardiac surgery. Recent studies on cardiovascular diseases have reported lower PNI values to be significantly correlated with higher rates of mortality [20–23]. PNI does not require

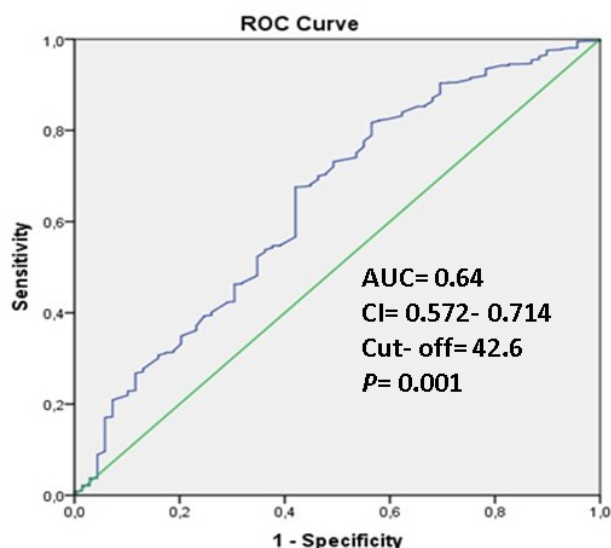


Fig. 1. Data figure of the area under the curve (AUC), confidence interval (CI), and cut-off values in receiver-operating characteristic (ROC) curve analysis for prognostic nutritional index.

any special equipment, is time-efficient, and easy to perform during routine clinical practice. Also, surgical outcomes are known to be affected by preoperative nutritional status beside other factors like technical skills. Still, despite having a well-proven prognostic value in abdominal and gastrointestinal surgery, PNI has yet to be studied comprehensively for its effect in cardiac surgery.

Keskin *et al.* [24] reported a significant correlation between PNI score and both in-hospital and long-term mortality in patients undergoing CABG. Hayashi *et al.* [25] found that higher PNI scores were correlated with lower mechanical ventilation duration, ICU stay, and infection rate. The authors reported lower PNI scores to be among independent predictors for mortality in their multivariate analysis. Lee *et al.* [26] evaluated the use of PNI scores in adult patients undergoing cardiac surgery for the first time. They determined that lower PNI could independently predict early mortality and morbidity, and was correlated with longer mechanical ventilation duration and ICU stay.

Considering the increasing number of high-risk patients admitted to elective cardiac surgery, the Enhanced Recovery after Surgery and preoperative rehabilitation protocols suggest nutritional management practices like serum albumin and nutritional supplementation in cases with low preoperative albumin [27].

Based on the findings obtained here, PNI scores were significantly lower in non-survivors. Receiver-operating characteristic (ROC) curve analysis revealed that the cut-off value for PNI was 42.6 with 82% sensitivity and 42.6% specificity. Thus, it can be used preoperatively to help estimate surgical outcomes and choose correct strategies. Accordingly, for optimum care, patients with a low PNI score may require preoperative intervention by a cardio-metabolic

team, including a cardiologist, an internal medicine specialist, a dietician, a cardiovascular surgeon, and possibly other physicians. This team may also reconsider the current surgery plans in this patient group.

The female population is known to be exposed to different risk factors than males [28]. They have a higher likelihood to go through lifestyle changes and develop visceral obesity after menopause [29]. Some previous studies have reported the female sex to be a factor for poor cardiac surgery outcomes, while others have remarked no difference between sexes [30]. In parallel with the latter, we found no significant correlation between our study groups in terms of sex.

5. Limitations of the study

The findings obtained in this research may have been affected by a number of limitations. First, the research was conducted as a retrospective single-center study. Second, although PNI was found to be as an independent predictor for mortality, the ROC analysis revealed a low AUC value. Third, we did not evaluate preoperative nutritional supplementation for its effect on postoperative mortality and morbidity in patients with low PNI scores. Further research can focus on the effects of preoperative nutrition management by a cardio-metabolic team in these patients.

6. Conclusions

Preoperative PNI value was found to be significantly associated with in-hospital mortality rates after cardiac surgery. We believe that patients with low PNI value can benefit from preoperative nutritional management by a cardio-metabolic team that includes specialists from various fields of health-care.

Author contributions

AG and OAO contributed to the conception and design of the study; ME, SAS, IBS and AS collected data; AG and OAO analysed the data; AG, OAO, ME, SAS, IBS and AS wrote and revised the manuscript. AG and OAO contributed equally.

Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by Bursa Yuksek Ihtisas Training and Research Hospital Ethics Committee (2011-KAEK-25 2020/03-11). The informed consent requirement was renounced due to the retrospective nature of the study.

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Conflict of interest

The authors declare no conflict of interest.

Data availability statement

The data presented in this study are available on request from the corresponding author.

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