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Importance of prognostic nutritional index in on-pump coronary artery bypass graft surgery

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ABSTRACT

Objectives: A simple and appropriate risk index is still required to show the patient's nutritional status undergoing coronary artery bypass graft (CABG) surgery. This study aimed to evaluate the Prognostic Nutritional Index (PNI) value as a predictor of in-hospital mortality in patients undergoing CABG surgery.

Methods: In this study, we scanned the medical data of 742 patients' who underwent on-pump CABG surgery retrospectively. Patients' were divided into two groups based on the PNI cut-off value (high-risk group, PNI < 45.85, n = 230; low-risk group, PNI ≥ 45.85, n = 512).

Results: To analyze the factors affecting in-hospital mortality in the postoperative period, univariate and multivariate logistic regression analysis was performed. In univariate analysis, advanced age (Odds ratio (OR): 1.219, 95% confidence interval (CI): 1.194-2.669, $p < 0.001$), left ventricular ejection fraction (LVEF) (OR: 3.471, 95% CI: 2.854-6.927, $p < 0.001$), total perfusion time (OR: 0.876, 95% CI: 0.690-0.954, $p = 0.012$), intra-aortic balloon pump (IABP) use (OR: 2.148, 95% CI: 1.394-2.889, p = 0.002), preoperative high creatinine (OR: 1.229, 95% CI: 1.066-2.118, $p = 0.019$), low lymphocyte count (OR: 0.879, 95% CI: 0.789-0.945, $p = 0.017$), low albumin (OR: 1.682, 95% CI: 1.433-2.765, $p = 0.003$), high C-reactive protein (CRP) (OR: 1.0.790, 95% CI: 0.678-0.927, $p = 0.042$) and low PNI (OR: 1.290, 95% CI: 1.119-1.654, $p < 0.001$) were correlated with the postoperative mortality. In multivariate logistic regression analysis, advanced age (OR: 1.145, 95% CI: 1.110-1.938, $p = 0.017$), LVEF (OR: 2.916, 95% CI: 1.768-4.928, $p < 0.001$), IABP use (OR: 1.880, 95% CI: 1.350-2.554, $p = 0.032$) and PNI (OR: 0.932, 95% CI: 0.889-0.978, $p = 0.004$) were independent predictors of mortality.

Conclusions: In on-pump CABG surgery, postoperative mortality is associated with low preoperative PNI, and can be a useful and suitable parameter for preoperative risk evaluation.

Keywords: Prognostic nutritional index, nutritional status, CABG surgery, cardiopulmonary bypass, risk factors

Coronary artery disease (CAD) is lead to death and disability throughout the world [1]. Coronary artery bypass graft (CABG) surgery is one of the most important treatment methods of CAD. Although new developments in the treatment of CAD have reduced mortality rates, the perioperative and hospital mortality and morbidity rates of patients remain high [2-4]. In CABG surgery, the mortality and mortality rates of patients are affected by many factors [5, 6]. A simple and appropriate risk index is still required to show the

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patient's nutritional status undergoing CABG surgery.

Clinical nutritional status is an indirect indicator of patient resistance. This relationship has been demonstrated in patients undergoing gastrointestinal system and malignancy surgery [7, 8]. Various methods such as Mini Nutrition Assessment, Malnutrition Universal Screening Tool and Subjective Global Assessment have been developed to determine the nutritional status of patients undergoing malignancy surgery. The Prognostic Nutritional Index (PNI) is the most widely used method for determining nutritional status, and low PNI has been shown as a predictor of postoperative mortality and morbidity in malignant diseases [9, 10]. The PNI, which was simplified by Onodera *et al*. [11], was calculated based on the serum albumin concentration and lymphocyte count. Some comprehensive studies evaluate the effects of preoperative nutritional factors on coronary artery surgery outcomes and vascular diseases [12, 13]. However, the importance of PNI in CABG surgery is not yet clear.

This study aims to determine of the value of PNI as a predictor of in-hospital mortality and morbidity in patients undergoing on-pump CABG surgery.

METHODS

A total of 742 patients were included in this retrospective study that underwent on-pump CABG surgery at our institute between January 2016 and January 2020. In order to avoid the possible effects of the COVID-19 pandemic, the study was terminated in January 2020, when no pandemic patients were detected in our country yet. The research was approved by the institutional ethics committee of the Bursa Yuksek Ihtisas Training and Research Hospital. The study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practices.

Demographic characteristic and clinical outcomes of the patients were retrospectively collected by searching our hospital database. Other data, body mass index (BMI), cross-clamp (X-clamp) time, cardiopulmonary bypass (CPB) time, preoperative left ventricular ejection fraction (LVEF), intra-aortic balloon pump (IABP) usage, intensive care unit (ICU) stays, postoperative hospital-acquired infection and stroke were noted. We defined six types of infections after cardiac surgery as hospital-acquired infections based on O'Keefe *et al*. [14]. These included urinary tract infections, pneumonia, harvest site infections, superficial sternal wound infections, deep sternal wound infections, and sepsis. We also noted that stroke events after surgery.

Blood parameter analysis

Peripheral blood samples taken on the first day of hospitalization for all patients were noted. The complete blood cell count analysis was performed using automatic blood analyzer (Beckmann Coulter LH 780) and biochemical analyzes were performed using automatic biochemical analyzer (Cobas 6000, Manheim).

Calculation of PNI

The preoperative nutritional status of the patients was assessed using the PNI classification. PNI was calculated according to the formula: 10 × serum albumin + 0.005 × total lymphocyte count [13]. To determine the optimal cut-off value for PNI, a method described by Budczies *et al*. [15] was used.

Surgical Technique

All operations were performed under general anaesthesia with a median sternotomy. Standard CPB was used in mild hypothermia (32°C) with aorta-venous two-stage cannulation. Cardioplegic arrest was achieved. Cardiopulmonary bypass was provided by roller pumps at a flow rate of 2-2.4 L/min/m^2 and a membrane oxygenator (Maquet, Getinge Group, Rastatt, Germany). Arterial filters were used in all operations. All distal anastomoses were performed under aortic cross-clamp (ACC), while proximal anastomoses were performed using the partial clamp technique. All patients received warm potassium-free blood cardioplegia before the ACC was removed. All patients were transferred to the cardiovascular surgery intensive care unit after the operation.

Statistical Analysis

Continuous data were expressed as the mean ± standard deviation. Categorical data were expressed as the number and percentage. Continuous variables were analyzed with Student's t-test (for normally distributed data) or Mann-Whitney U test (for non-normally distributed data). The difference in categorical variables was tested using the chi-squared test. Univariate and multivariate logistic regression analysis were performed to determine potential risk factors for postoperative mortality. The predictive value of PNI for mortality was determined with Receiver Operating Characteristic (ROC) curve analysis and Area Under Curve (AUC) was calculated. All statistical analyses were performed using the SPSS package for Windows version 21 (SPSS Inc., Chicago, IL, USA). A p value of < 0.05 was accepted statistically significant.

RESULTS

The overall study consisted of 742 patients. In-hospital mortality occurred in 43 (5.4%) patients. The mean and median levels of the PNI were 49.92-7.44 and 49.81 (45.58-54.27). The cut-off point was set at 45.85. When the cut-off point was 45.85, the specificity was 58%, the sensitivity was 70.7% satisfactory, and patients were divided into two groups according to this cut-off point (high-risk group; PNI < 45.85, n = 230; low-risk group; PNI ≥ 45.85, n = 512).

The low-risk group and the high-risk group patients were compared, and there was a significant difference in age (low- risk group: 66 ± 0.75 vs. high-risk group: 62.62 ± 0.43, p = 0.001). The BMI was similar between the groups (26.97 ± 0.19 vs. 26.51 ± 0.13; p = 0.179). Preoperative LVEF was statistically lower in the high-risk group (49.67 ± 0.62 vs. 51.20 ± 0.43; p = 0.018). There was no difference between two groups in terms of hypertension, DM and COPD rates. Comparisons of the groups regarding the laboratory data revealed that the high-risk group had significantly lower hemoglobin and albumin levels (p = 0.001). Preoperative serum creatinine levels were differences between groups and the high-risk group had significantly higher creatinine levels (1.25 ± 0.08 vs. 0.94 ± 0.02; p = 0.001). Comparison of demographic features and basic blood values of patients in groups are demonstrated in Table 1.

Operative X-clamp time (p = 0.661), CPB time (p = 0.143) was similar between the groups, but IABP usage (p = 0.001), and ICU stay (p = 0.011) significantly higher in the high-risk group. Since the infection was broadly categorized in our study, we compared hospital-acquired infection between groups.

Table 1. Comparison of demographic features and basic blood values of patients in groups

Features	High-risk group	Low-risk group	*p* values
Male, n (%)	185 (80.5)	409 (79.9)	0.527
Age (year)	66 ± 0.75	62.62 ± 0.43	**0.001**
Preoperative LVEF (%)	49.67 ± 0.62	51.20 ± 0.43	**0.018**
BMI (m^2/kg)	26.97 ± 0.19	26.51 ± 0.13	0.179
Hypertension, n (%)	132 (57.3)	277 (54.1)	0.108
Diabetes mellitus, n (%)	48 (20.8)	93 (18.1)	0.227
COPD, n (%)	42 (18.2)	79 (15.4)	0.090
Hemoglobin (gr/dL)	12.15 ± 0.14	13.66 ± 0.08	**0.001**
WBC ($x10^3$)	9.36 ± 0.26	9.22 ± 0.11	0.431
Neu ($x10^3$)	7.11 ± 0.22	6.05 ± 0.07	**0.001**
Lym ($x10^3$)	1.42 ± 0.04	2.32 ± 0.04	**0.001**
Platelets ($x10^3$)	240.24 ± 0.54	247.30 ± 2.96	**0.011**
CRP (mg/L)	22.17 ± 2.19	9.31 ± 0.71	**0.001**
Cre (mg/dL)	1.25 ± 0.08	0.94 ± 0.02	**0.001**
Total protein (g/dl)	6.47 ± 0.04	7.07 ± 0.03	**0.001**
Albumin (g/dL)	3.39 ± 0.03	4.04 ± 0.02	**0.001**

Data are shown as mean±standard deviation or n (%). WBC = White blood cell, CRP = C-reactive protein, Cre = Creatinine, Neu = Neutrophil, Lym = Lymphocyte, LVEF = Left ventricular ejection fraction, BMI = Body Mass Index

Table 2. Operative and postoperative features of patients

Characteristic	High-risk group	Low-risk group	*p* values
X-clamp time (min)	66.41 ± 1.58	64.32 ± 0.9	0.661
CPB time (min)	95.20 ± 2.05	90.54 ± 1.22	0.143
IABP usage, n (%)	29 (12.6%)	24 (4.6)	**0.001**
ICU stay (days)	3.71 ± 0.16	3.09 ± 0.13	**0.011**
Mortality, n (%)	25 (10.8)	18 (3.5)	**< 0.001**
Morbidity			
Hospital-acquired infection, n (%)	59 (25.6)	62 (12.1)	**0.001**
Stroke, n (%)	26 (3.7)	36 (7)	0.052

Data are shown as mean ± standard deviation or n (%). X- clamp = Cross clamp, CPB = Cardiopulmonary bypass, IABP = Intra-aortic balloon pump, ICU = Intensive care unit

There was a significantly higher tendency of hospital-acquired infection in the high-risk group (59; 25.6% vs. 62; 12.1%; *p* = 0.001). Postoperative stroke was similar between the groups (26; 11.3% vs. 36; 7%; *p* = 0.052) (Table 2).

To analyze the factors affecting in-hospital mortality in the postoperative period, univariate and multivariate logistic regression analysis was performed (Table 3). In univariate analysis, advanced age (OR [odds ratio]: 1.219, 95% CI [confidence interval]: 1.194-2.669, *p* < 0.001), LVEF (OR: 3.471, 95% CI: 2.854-6.927, *p* < 0.001), total perfusion time (OR: 0.876, 95% CI: 0.690-0.954, *p* = 0.012), IABP use (OR: 2.148, 95% CI: 1.394-2.889, p = 0.002), preoperative high creatinine (OR: 1.229, 95% CI: 1.066-2.118, *p* = 0.019), low lymphocyte count (OR: 0.879, 95% CI: 0.789-0.945, *p* = 0.017), low albumin (OR: 1.682, 95% CI: 1.433-2.765, *p* = 0.003), high CRP (OR: 0.790, 95% CI: 0.678-0.927, *p* = 0.042) and low PNI (OR: 1.290, 95% CI: 1.119-1.654, *p* < 0.001) were correlated with the postoperative mortality. In multivariate logistic regression analysis, advanced age (OR: 1.145, 95% CI: 1.110-1.938, *p* = 0.017), LVEF (OR: 2.916, 95% CI: 1.768-4.928, *p* < 0.001), IABP

Table 3. Logistic regression analysis to identify factors affecting postoperative mortality

Variables	Univariate analysis			Multivariate analysis		
	p value	Exp (B) Odds Ratio	95% CI Lower-Upper	*p* value	Exp (B) Odds Ratio	95% CI Lower-Upper
Age	**< 0.001**	1.219	1.194- 2.669	**0.017**	1.145	1.110- 1.938
Hypertension	0.221	1.317	0.975- 1.786	--	--	--
COPD	0.190	0.895	0.667- 1.110	--	--	--
LVEF	**< 0.001**	3.471	2.854- 6.927	**< 0.001**	2.916	1.768- 4.928
Total perfusion time	**0.012**	0.876	0.690- 0.954	0.345	0.790	0.690- 1.134
IABP use	**0.002**	2.148	1.394- 2.889	0.032	1.880	1.350- 2.554
Creatinin	**0.019**	1.229	1.066- 2.118	0.314	1.110	0.890- 1.440
Lymphocyte count	**0.017**	0.879	0.789- 0.945	--	--	--
Albumin	**0.003**	1.682	1.433- 2.765	--	--	--
CRP	**0.042**	0.790	0.678- 0.927	0.410	0.914	0.776- 1.190
PNI	**< 0.001**	1.290	1.119- 1.654	**0.004**	0.932	0.889- 0.978

COPD = Chronic obstructive pulmonary disease, LVEF = Left ventricular ejection fraction, IABP = Intraaortic balloon pump, CRP = C reactive protein, PNI = Prognostic nutritional index

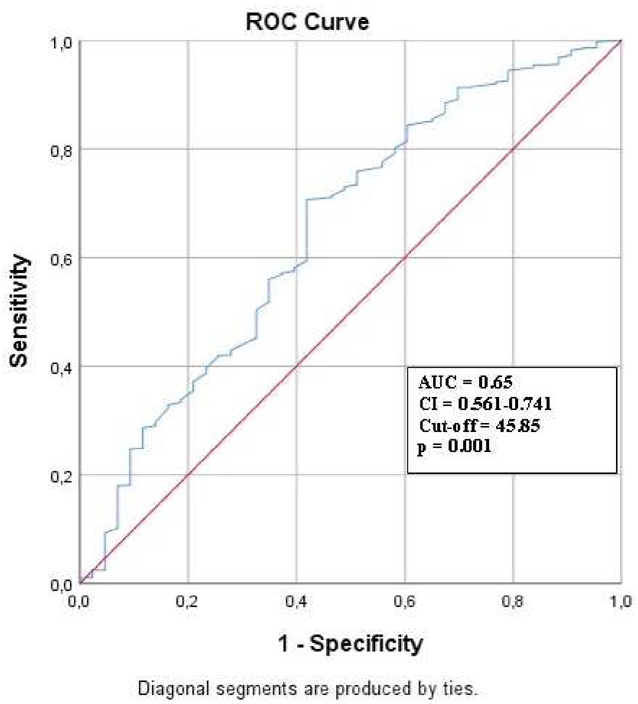

Fig. 1. Data figure of the area under the curve (AUC), confidence interval (CI), and cut-off values in receiver-operating characteristic (ROC) curve analysis for prognostic nutritional index.

use (OR: 1.880, 95% CI: 1.350-2.554, $p = 0.032$) and PNI (OR: 0.932, 95% CI: 0.889-0.978, $p = 0.004$) were independent predictors of mortality.

In the receiver-operating characteristic analysis, PNI lower than 45.85 predicted in-hospital mortality with 70.7% sensitivity and 58% specificity [area under the curve: 0.651, 95% confidence interval: 0.561-0.741; $p = 0.001$] (Fig. 1). In-hospital outcomes were significantly worse in low-risk group (Fig. 2).

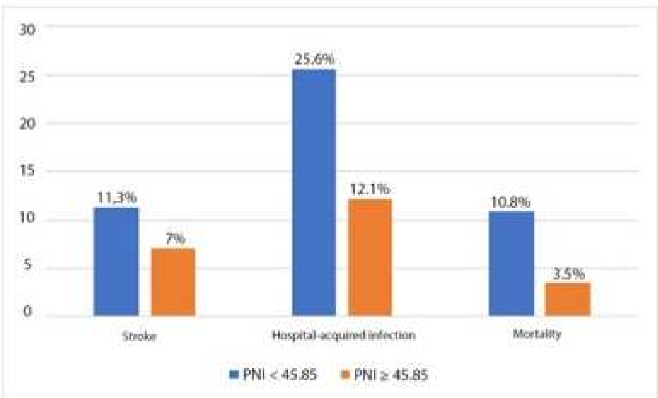

Fig. 2. In-hospital outcomes were significantly worse when the PNI was lower.

DISCUSSION

CABG surgery is one of the most important treatment methods of CAD. Operation success is related to individual risk factors as well as technical skills. In this current study, we showed that PNI value, which is an important indicator of malnutrition status, is an independent predictor of postoperative mortality in addition to known risk factors such as age and low LVEF value.

Patients with poor nutritional status before cardiac surgery have been higher postoperative morbidity and mortality rates [16]. In the literature some studies have demonstrated the importance of energy and protein metabolism in the early period after heart surgery and documented significant post-operative consumption of macronutrients and micronutrients [16, 18]. Sufficient nutritional therapy has been proposed to improve patient outcomes by maintaining energy metabolism and promoting improved wound healing after surgery [19]. Lomivorotov *et al*. found that depending on the used nutrition screening tool, the percentage of malnourished cardiac surgery patients before surgery ranged between 4.6-19.1% [18]. The present findings point to high malnutrition rates in cardiac patients, and it is very important to consider the nutritional profiles of these patients before surgery and simultaneously, and to draw more attention to the concept of individual diet for pre-operative optimization in these patients [20, 22]. Therefore, preoperative evaluation of nutritional status in patients at high risk of developing postoperative complications may guide to consider postoperative nutritional interventions. Studies evaluating the relationship of BMI, albumin, and prealbumin levels have demonstrated that they are independent predictors of mortality and morbidity after coronary artery and valve surgery [23, 24].

The PNI, calculated based on the serum albumin concentration and lymphocyte count of peripheral blood was designed by Buzby *et al*. [7] in 1980 and simplified by Onodera *et al*. [11] in 1984. Lymphocytes are significant part of the immune system, and the prognostic role of lymphocyte count has been previously investigated in cardiovascular diseases [25, 27]. Lymphopenia is an important mortality predictor in patients undergoing CABG surgery [28]. Albumin is a serum protein that is a good indicator of a patient's nutritional status, and it makes up the majority of the serum total protein and is mainly responsible for the serum osmotic pressure. Also albumin has antioxidant and anti-inflammatory properties in scavenging reactive oxygen radicals and limiting their production [29]. In particular, postoperative hypoalbuminemia is an independent risk factor for postoperative outcome in patients undergoing CABG surgery [30].

PNI was originally designed to determine immunonutrition status and has been widely used to assess surgical risk, particularly in patients with malignancy and gastrointestinal operations [7, 8, 31]. Several studies have reported that lower PNI levels are significantly associated with higher mortality in patients with cardiovascular disease [32]. PNI can be used to predict patients' outcomes before cardiac surgery and to choose an appropriate surgical strategy. Given all these data, the management of patients with low PNI may require a "Cardio-metabolic Team" approach to optimized patient care prior to surgery. In the cardio-metabolic team consisting of cardiologist, internal medicine, dietician, cardiovascular surgeon and needed additional branches. It is clear that pre-operative metabolic optimal support is particularly important in this low- and middle-income patient. On the other hand, in patients with low PNI, cardiac surgery plan can be re-evaluated by the cardio-metabolic team. Less invasive surgery may be appropriate if possible. There are various studies in the literature investigating the effect of PNI value on clinical outcomes after cardiac operations. In a study conducted by Lee *et al*. [33], the prognostic role of PNI value in predicting early clinical outcomes after cardiac surgery was investigated. In this study, the authors divided the patients into two groups according to the value they determined as cut-off (46.13). At the end of the study, early mortality rates were found to be higher in the group with low PNI values. In addition, the mean length of stay on mechanical ventilation and length of stay in the intensive care unit were found to be significantly higher in this group [33]. In our study patients' were seperated into two groups based on the PNI cut-off value (high-risk group, PNI $<$ 45.85; low-risk group, PNI $\geq$ 45.85). There was a significantly higher tendency of hospital-acquired infection in the high-risk group (59; 25.6% vs. 62; 12.1%; $p = 0.001$) and postoperative stroke was similar between the groups (26; 11.3% vs. 36; 7%; $p = 0.052$). In multivariate analysis PNI value was found as an independent predictor of postoperative mortality.

An increasing number of elderly people are accepted for elective CABG surgery. When low preoperative PNI is detected in elderly patients undergoing elective coronary artery surgery, postoperative methods such as serum albumin supplementation, dietary maintenance or nutritional support should be considered to improve the nutritional status of patients [34].

Our research demonstrated that a low PNI value affects postoperative mortality and morbidity. There was significantly different a higher tendency for postoperative hospital-acquired infection in the high-risk group. PNI may be used to predict patients' outcomes before coronary artery surgery and select an adequate surgical strategy. In the case of patients with a low PNI, less invasive surgery may be suitable if possible.

Limitations

Our study does not include the effects of preoperative nutritional support on postoperative mortality and morbidity in patients with low PNI values. The fact that this is a single-center study with a retrospective design is the most important limitation. Further studies are needed to show the results of preoperative nutritional support in elective cases.

CONCLUSION

Preoperative low PNI level was statistically significantly associated with postoperative mortality and morbidity in cardiac surgery. According to the results we obtained in our study, we firmly believe that PNI is a useful and suitable parameter for preoperative assessment of nutritional status and should be regarded in managing the indication and strategy in on-pump CABG surgery.

Authors' Contribution

Study Conception: AG; Study Design: AG; Supervision: AG; Funding: AG; Materials: AG; Data Collection and/or Processing: AG; Statistical Analysis and/or Data Interpretation: AG; Literature Review: AG; Manuscript Preparation: AG and Critical Review: AG.

Conflict of interest

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