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Original article

Relationship between the prognostic nutritional index and long-term clinical outcomes in patients with stable coronary artery disease

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ABSTRACT

Background: Malnutrition has recently been reported to correlate with prognosis in patients with heart failure. However, the prognostic significance of nutritional status in patients with stable coronary artery disease (CAD) is unknown. The present study sought to examine the association between nutritional status assessed by the prognostic nutritional index (PNI) and cardiovascular outcomes in patients with stable CAD.

Methods: A total of 1988 patients with stable CAD who underwent elective percutaneous coronary intervention (PCI) between 2000 and 2011 were examined. The PNI was calculated as 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (per mm^3). Patients were assigned to tertiles based on their PNI. The incidence of major adverse cardiac events (MACE), including all-cause death and non-fatal myocardial infarction, was evaluated.

Results: The median PNI was 48.9 (interquartile range: 45.5–52.1). During the median follow-up of 7.5 years, Kaplan–Meier analysis showed that patients with lower PNI tertiles had higher rates of MACE (PNI <46.7: 35.5%; 46.7–50.8: 22.3%; >50.8: 16.0%; log-rank $p < 0.0001$). After adjusting for other risk factors, the PNI was independently associated with MACE (hazard ratio 2.05 per 10 PNI decrease, 95% confidence interval: 1.66–2.54, $p < 0.0001$). Adding the PNI to a baseline model with established risk factors improved the *C*-index ($p = 0.03$), net reclassification improvement ($p = 0.03$), and integrated discrimination improvement ($p = 0.0001$).

Conclusions: The PNI was significantly associated with long-term cardiovascular outcomes in patients with stable CAD. Assessing PNI may be useful for risk stratification of CAD patients undergoing elective PCI.

Introduction

Cardiovascular disease is the leading cause of mortality and disability worldwide. Although evidence-based management of cardiovascular disease has improved outcomes, cardiovascular disease remains one of the major issues worldwide [1]. Therefore, identification of residual risk of cardiovascular disease and early risk stratification is important for more effective tailoring of risk-reduction strategies [2,3].

Malnutrition has been reported to be associated with worse clinical outcomes in patients with cancer, renal failure, and heart failure [4–6]. Thus, nutritional information could be important for risk stratification in patients with these diseases. However, it is not easy to assess nutritional status, because there are several elements of malnutrition. The prognostic nutritional index (PNI), calculated from the serum albumin concentration and the total

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lymphocyte count, has been used to predict the risk of complications after gastrointestinal surgery [7,8]. The PNI is easy to calculate and a good predictor for patients with malignant diseases [9–11]. Recently, some reports have shown associations between PNI values and clinical outcomes in patients with heart failure or ST-segment elevation myocardial infarction (MI) [12,13]. However, the prognostic significance of the PNI in patients with stable coronary artery disease (CAD) has not been fully investigated. Therefore, the aim of the present study was to evaluate the prognostic value of nutritional status using the PNI in patients with stable angina following elective percutaneous coronary intervention (PCI).

Methods

Patients and data collection

Data from a single-center, observational study of consecutive patients who underwent elective PCI for the first time at our institution from January 2000 to December 2011 were analyzed. Patients missing serum albumin levels and total lymphocyte counts and patients with known malignancy or active inflammatory disease were excluded from the study. The baseline PNI was calculated as 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (per mm^3) [7]. Patients were divided into tertiles according to the pre-procedural PNI (<46.7, 46.7–50.8, >50.8).

Demographic data and information about coronary risk factors, medications, revascularization procedure-related factors, and comorbidities were prospectively collected and analyzed. Blood samples were collected in the early morning after overnight fasting, and blood pressure (BP) was measured on admission. Patients with BP >140/90 mmHg or those receiving antihypertensive drugs were regarded as hypertensive. Dyslipidemia was defined as low-density lipoprotein cholesterol (LDL-C) ≥140 mg/dL, high-density lipoprotein cholesterol (HDL-C) ≤40 mg/dL, triglycerides ≥150 mg/dL, or current treatment with statins and/or lipid-lowering agents [14]. Diabetes mellitus was defined as either hemoglobin A1c ≥6.5% or medication with insulin or oral hypoglycemic drugs. Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate <60 ml/min/1.73 m^2 as calculated using the modification of the diet in renal disease equation modified with a Japanese coefficient using baseline serum creatinine [15]. A current smoker was defined as a person who smoked at the time of PCI or who had stopped smoking within 1 year before PCI. Left ventricular ejection fraction (LVEF) was assessed using left ventricular angiography or echocardiography before PCI. All patients had symptoms of effort angina, documented myocardial ischemia, or both.

Written, informed consent was obtained from all patients before undergoing PCI. This study was performed in accordance with the Declaration of Helsinki and with the approval of our institutional review board.

Primary endpoints

The primary outcome was major adverse cardiac events (MACE), defined as a composite of all-cause death and non-fatal MI. Clinical follow-up comprised analyses of office visit charts and responses to questionnaires sent to patients or their families and telephone contact. Mortality data were collected from the medical records of patients who died or who were treated at our institution, and details and causes of death were obtained from other hospitals to which patients had been admitted. Cardiac death was defined as death from CAD, cardiogenic shock, or sudden death. MI was defined as evidence of myocardial necrosis in a clinical setting consistent with myocardial ischemia. The last observation analyzed in this study was September 30, 2014.

Statistical analysis

Quantitative data are expressed as means ± standard deviation, and categorical variables are presented as frequencies. Continuous variables were compared across groups using one-way analysis of variance or the Kruskal–Wallis test. The chi-squared test was used for categorical variables. Simple linear regression analysis was used for the PNI and biochemical and clinical measurements. Pearson's correlation coefficients were used to examine relationships between the PNI and other variables. Unadjusted cumulative event rates were estimated using Kaplan–Meier curves and compared across groups using the log-rank test. Effects of PNI values on clinical outcomes after PCI were determined using multivariate Cox proportional hazard regression analysis. Model 1 was adjusted for age and sex. Model 2 was adjusted for the variables in model 1 plus established risk factors such as body mass index (BMI), CKD, current smoker, diabetes mellitus, dyslipidemia, hypertension, LVEF, multivessel coronary disease, and statin use on admission. PNI values were included in the multivariate modeling, and hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated.

To assess whether the accuracy of predicting adverse cardiac events would improve after adding PNI values to a baseline model with established risk factors (i.e. age, BMI, CKD, current smoking, diabetes mellitus, dyslipidemia, hypertension, LVEF, multivessel coronary disease, and use of statins), the *C*-index, net reclassification improvement (NRI), and integrated discrimination improvement (IDI) were calculated. Differences were considered significant at $p < 0.05$. Statistical analyses were carried out using JMP version 12.0 (SAS Institute, Cary, NC, USA) and R version 3.2.3 (http://www.R-project.org/; R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline and procedural characteristics

Of the 2092 patients who underwent elective PCI, pre-procedural PNI data were available for 1988 patients (95.0%). For these patients, the median and mean PNI values were 48.9 (IQR: 45.4, 52.1) and 48.5 ± 5.7, respectively. Fig. 1 shows the distribution of the PNI. Clinical and procedural characteristics of these patients are shown in Table 1. Patients in the lowest PNI tertile were significantly older and had a higher prevalence of CKD and multi-vessel coronary disease, as well as lower BMI, triglycerides, LDL-C, and LVEF, and a higher concentration of high-sensitivity

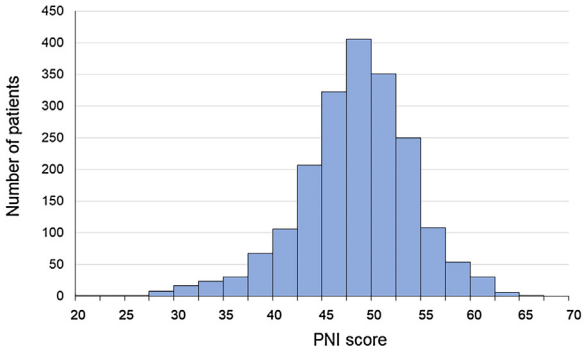

Fig. 1. Distribution of PNI values. The median PNI value is 48.9 (IQR: 45.4, 52.1). PNI, prognostic nutritional index; IQR, interquartile range.

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