

A Novel Independent Survival Predictor in Pulmonary Embolism: Prognostic Nutritional Index

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Abstract

The prognostic impact of nutritional status in patients with pulmonary embolism (PE) is poorly understood. A well-accepted nutritional status parameter, prognostic nutritional index (PNI), which was first demonstrated to be valuable in patients with cancer and gastrointestinal surgery, was introduced to patients with PE. Our aim was to evaluate the predictive value of PNI in outcomes of patients with PE. We evaluated the in-hospital and long-term (53.8 ± 5.4 months) prognostic impact of PNI on 251 patients with PE. During a median follow-up of 53.8 ± 5.4 months, 27 (11.6%) patients died in hospital course and 31 (13.4%) died in out-of-hospital course. The patients with lower PNI had significantly higher in-hospital and long-term mortality. The Cox proportional hazard analyses showed that PNI was associated with an increased risk of all-cause death for both unadjusted model and adjusted for all covariates. Our study demonstrated that PNI, calculated based on serum albumin level and lymphocyte count, is an independent prognostic factor for mortality in patients with PE.

Keywords

pulmonary embolism, prognostic nutritional index, mortality

Introduction

Venous thromboembolism, which covers pulmonary embolism (PE), is the third most common cardiovascular disease following acute myocardial infarction and stroke.¹ Pulmonary embolism is a life-threatening disease, and adjusted PE hospitalization rate is 302/100 000 in the United States, even higher in black patients.¹ The long-term mortality of PE is effected by many factors including age, comorbidities, type and time of treatment, right ventricular dilatation, right ventricular ejection fraction, tricuspid valve insufficiency, and pulmonary hypertension (HT).² Many prognostic factors and laboratory biomarkers have been put forward to correlate long-term survival in PE. Creatinine kinase isoenzyme-MB and N-terminal pro-B-type natriuretic peptide were reported as prognostic laboratory biomarkers in PE.³ In addition, recent operation or fracture, shock during hospitalization, and mechanical ventilation were also defined as prognostic factors.⁴ The recent PE guideline insistently suggests Pulmonary Embolism Severity Index (PESI) to estimate long-term survival.⁵ Despite many valuable prognostic factors, PE still requires a cheap and reliable index revealing patient's nutritional status. Several studies demonstrated correlation between a single nutritional indicator such as albumin and poor outcomes in patients with cancer.⁶ Whereas to determine nutritional status more complex and in

detail, prognostic nutritional index (PNI) has been postulated.⁷ The PNI was first established to assess perioperative immunonutritional status and surgical risk in patients undergoing gastrointestinal surgery.⁸ We introduce this simple risk index to patients with PE, which was first adapted and examined in patients with malnutrition. The PNI, which reflects albumin concentration and lymphocyte count, is a newly established inflammation-based nutritional score.⁹ Inexpensive and simple blood biomarkers are required to determine these 2 parameters.¹⁰ Nevertheless, several nutritional indices such as controlling nutritional status and geriatric nutritional index have

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been reported to have prognostic value in patients with congestive heart failure and cancer.¹⁰ Among nutritional indices, PNI is the most well-accepted index whose value has been documented many times in the literature. The aim of our retrospective observational study was to evaluate the impact of admission PNI on outcome of patients with PE at a median follow-up of 53.8 ± 5.4 months.

Materials and Methods

Patient and Study Design

Between May 2009 and July 2011, 291 consecutive confirmed patients with PE, who were admitted to Dr Siyami Ersek Cardiovascular and Thoracic Surgery Training and Research Hospital, were evaluated retrospectively. A total of 29 patients who did not have albumin measurement or lymphocyte count during the hospitalization were excluded. An additional 11 patients were excluded from the study secondary to missing data after hospitalization. Pulmonary multislice computed tomography (CT) angiography (SOM-ATOM Sensation 64; Siemens, Erlangen, Germany) was used to diagnose PE.

The study population was divided into tertiles according to their admission PNI starting with the lowest PNI. The PNI was calculated using the following formula: $10 \times \text{serum albumin value (g/dL)} + 0.005 \times \text{total lymphocyte count in the peripheral blood (per mm}^3\text{)}$. The optimal cutoff value for the continuous PNI was calculated by applying a receiver operating curve (ROC) analysis to test all possible cutoffs that would predict the in-hospital survival. A PNI of 38 was identified through an ROC analysis as an optimal cutoff value to predict the in-hospital survival (Figure 1).

Analysis of Patient Data

A clinical history of risk factors, such as age, sex, HT, diabetes mellitus (DM), hyperlipidemia, and chronic lung and kidney disease, was determined from the hospital's medical database. Echocardiographic and pulmonary CT angiography findings were also obtained from the same database. Echocardiogram was performed using a Vivid 7 system (GE Vingmed Ultrasound AS, Horten, Norway) in 96% of patients at first 48 hours in the coronary care unit, and left ventricular ejection fraction was calculated by using the Simpson method.¹¹ The pulmonary arterial peak systolic pressure was calculated using the simplified Bernoulli equation.¹² The occurrences of in-hospital and long-term events were evaluated by a trained study coordinator. The estimated glomerular filtration rate was calculated by using CKD-EPI equation. Blood values obtained from venous blood samples at hospital admission were recorded from the medical reports. White blood cell (WBC) count, hemoglobin level, and lymphocyte count were measured as part of the automated complete blood count using a Coulter LH 780 Hematology Analyzer (Beckman Coulter Ireland, Inc, Galway, Ireland). Biochemical measurements were performed using Siemens Healthcare Diagnostic Products kits and calibrators (Marburg, Germany). Creatinine kinase isoenzyme-MB levels

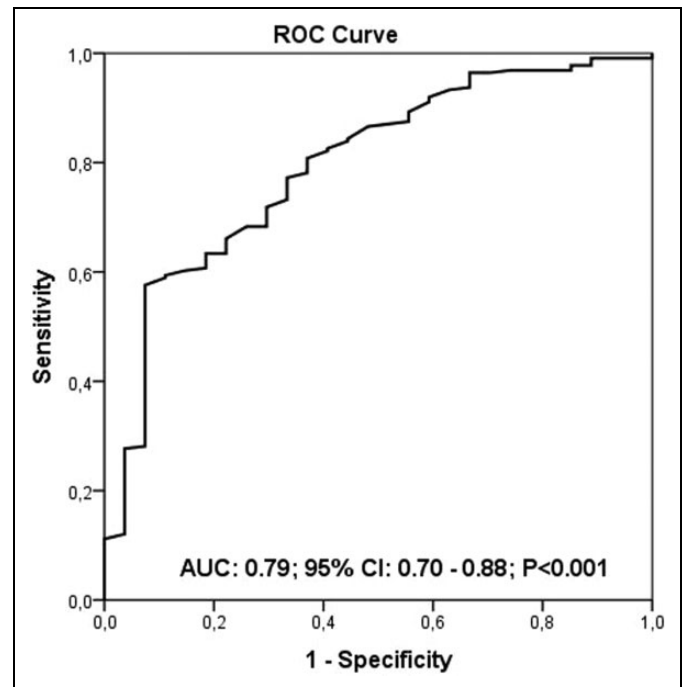


Figure 1. The prognostic nutritional index (PNI) level of 38 was identified as an effective cutoff point for in-hospital survival rate (area under the curve = 0.79; 95% confidence interval: 0.70-0.88, $P < .001$), and it had a sensitivity of 53% and specificity of 93%.

were measured using an immune-inhibition method (Architect C 8000; Abbott Inc). The drugs were administered during the hospitalization according to the European Society of Cardiology Guidelines.¹³

Definitions

The primary end points were the incidence of in-hospital and long-term mortality. In-hospital mortality was defined as death from any cause during hospitalization. Long-term mortality was defined as death from any cause after discharge. Hypertension was defined as systolic pressure greater than 140 mm Hg or diastolic pressure greater than 90 mm Hg. Diabetes mellitus was defined as the use of insulin or antidiabetic agents in the patient's medical history or a fasting glucose level greater than 126 mg/dL. Hyperlipidemia was defined as serum total cholesterol ≥ 240 mg/dL, serum triglyceride ≥ 200 mg/dL, low-density lipoprotein cholesterol ≥ 130 mg/dL, and previously diagnosed hyperlipidemia. Heart failure was defined as having typical symptoms (breathlessness, fatigue, and ankle swelling) and signs (elevated jugular venous pressure and pulmonary crackles) resulting from an abnormality of cardiac function.¹⁴ Shock was defined as systolic pressure less than 90 mm Hg or systolic pressure drop greater than or equal to 40 mmHg for more than 15 minutes without new-onset arrhythmia, hypovolemia, or sepsis.¹³ Major bleeding was defined as a decline in the hemoglobin level of 20 g/L or more or transfusion of 2 or more units of red cells. Altered mental status was defined as signs of disorientation, lethargy, stupor, or coma. Syncope was defined as a transient, self-limited loss of consciousness due to

transient global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery.¹⁵

Follow-Up

All follow-up data were obtained from hospital records or by interviewing (directly or by telephone) patients, their families, or their personal physicians. The primary end point was death. Recurrent PE, major and minor bleeding, use of fresh frozen plasma, and history of international normalized ratio greater than 5 were noted. Patients without cancer were all prescribed and followed up with warfarin treatment for 3 months following their acute PE. Patients with cancer were followed up with enoxaparin treatment for 3 months.

Statistical Analysis

In a first step, the study population was divided into tertiles according to admission PNI. Three groups were formed accordingly: one with 84 patients (tertile 1), other with 84 patients (tertile 2), and the last with 83 patients (tertile 3). In a second step, baseline characteristics were compared among these 3 groups. Quantitative variables were expressed as mean \pm SD. Kolmogorov-Smirnov test was used for testing normality. All continuous variables showed skewed distributions and compared using the Mann-Whitney *U* test. Categorical variables were expressed as number and percentages and Pearson χ^2 or Fisher exact test was used to evaluate the differences. Logistic regression was used to assess the independent relationship between PNI and in-hospital mortality. After follow-up periods of 53.8 ± 5.4 months, the median survival times of 3 groups were compared using the Kaplan-Meier survival method. Overall survival was calculated from the day of diagnosis to the day of death. Differences between the groups were analyzed by the log-rank test. Univariate analysis and multivariate analysis with Cox proportional hazard regression were used to identify predictors of 53.8 ± 5.4 months of mortality. Three Cox multivariable models were used: model I, unadjusted; model II, age and sex adjusted; and model III, fully adjusted. The variables covariated in model III were demographics (age, sex); first measurement of systolic blood pressure and heart rate; first measurement during hospitalization of the following laboratory values (admission glomerular filtration rate calculated by CKD-EPI, blood urea nitrogen, WBC count, hematocrit, platelet count); creatine kinase-MB, troponin I, D-dimer, and brain-type natriuretic peptide; comorbidities (diabetes, chronic kidney disease, HT, stroke, heart failure, cancer, chronic lung disease, and atrial dysrhythmia), and medications (use of oral contraceptives, warfarin, and steroid). Analyses were performed using Statistical Package for Social Sciences software, version 20.0 (SPSS; IBM, Armonk, New York).

Results

Baseline Characteristics

Baseline characteristics, categorized by admission PNI, are listed in Table 1. A total of 251 patients (mean age

64 ± 15 years; men 46%) with PE were included. The patients in tertile 1 had higher age compared with other tertiles ($P = .091$). The 3 groups were similar in terms of HT, DM, hyperlipidemia, previous myocardial infarction, previous PCI, previous coronary artery bypass graft, chronic kidney disease, heart failure, chronic lung disease, cerebrovascular disease, prior PE, cancer, use of oral contraceptives, steroids, and warfarin. Whereas, tertile 1 had significantly higher PESI score ($P < .001$). All types of admission symptoms were similar between groups. Considering admission electrocardiography sinus tachycardia, right bundle branch block, T-wave inversion, atrial dysrhythmia, and S1Q3T3 were detected statistically similarly in all tertiles. Table 2 summarizes laboratory and echocardiography findings of the patients. Albumin, lymphocyte, and blood urea nitrogen were significantly lower in tertile 1 ($P < .001$). Whereas other laboratory parameters such as troponin, D-dimer, creatinine kinase-MB, brain-type natriuretic peptide, WBCs, and neutrophils were similar between groups. All of the echocardiographic parameters were statistically similar between tertiles. The mean PNI of patients with and without cancer was 39.1 and 38.1, respectively.

In-Hospital and Long-Term Outcomes

Table 3 summarizes the in-hospital and long-term clinical outcomes. In-hospital mortality was significantly higher in tertile 1 compared to other tertiles (22.6%, 7.2%, and 2.4%, respectively, $P < .001$). Patients in tertile 1 group also had a higher incidence, asystole, hypotension, and cardiogenic shock. All-cause mortality was significantly higher in tertile 1 in long-term follow-up (26.2%, 12.8%, and 4.9%, $P < .001$). The PNI level of 38 was identified as an effective cutoff point for in-hospital survival rate (area under curve = 0.79; 95% confidence interval [CI]: 0.70-0.88, $P < .001$), and it had a sensitivity of 53% and specificity of 93% (Figure 1). The patients were followed up for a mean period of 53.8 ± 5.4 months. The 5-year Kaplan-Meier overall survivals for the 3 groups were 84.3% and 97.9%, respectively. The Kaplan-Meier cumulative survival curve is shown in Figure 2. The 5-year Kaplan-Meier survivals for T1, T2, and T3 were 77.4%, 92.9%, and 97.6%, respectively.

Table 4 lists unadjusted and adjusted logistic regression for in-hospital events (mortality and major adverse cardiac events) and Cox proportional regression analysis for long-term mortality categorized by tertiles. The in-hospital mortality of tertile 1 had 8.1 times higher mortality rates (95% CI: 2.1-27.1) than tertile 3, which had lower rates and was used as the reference. The long-term mortality also had the higher rates at tertile 1 and had 4.6 times higher mortality rates (95% CI: 2.6-10.9) than tertile 1, which had the lower rates and was used as the reference.

Discussion

This is a pilot study presenting nutritional status in patients with PE by the help of internationally accepted nutritional

Table 1. Baseline Characteristics.^{a,b}

	Prognostic Nutritional Index			P
	T1 (n = 84)	T2 (n = 84)	T3 (n = 83)	
Age, years	68 ± 12	65 ± 13	64 ± 17	.091
Male gender	39 (46.4)	35 (41.7)	44 (53.0)	.337
In-hospital stay, days	9 ± 6	10 ± 5	10 ± 6	.063
Comorbidities				
Hypertension	39 (46.4)	35 (41.7)	32 (38.6)	.583
Diabetes mellitus	27 (32.1)	18 (21.4)	27 (32.5)	.197
Hyperlipidemia	14 (16.7)	16 (19.0)	11 (13.3)	.596
Current smoking status	23 (27.4)	24 (28.6)	28 (33.7)	.635
Previous MI	9 (10.7)	3 (3.6)	7 (8.4)	.202
Previous PCI	4 (4.8)	4 (4.8)	3 (3.6)	.916
Previous CABG	6 (7.1)	4 (4.8)	2 (2.4)	.358
Chronic kidney disease	11 (13.1)	5 (6.0)	7 (8.4)	.265
Heart failure	5 (6.0)	4 (4.8)	4 (4.8)	.926
Chronic lung disease	10 (11.9)	10 (11.9)	7 (8.4)	.706
Cerebrovascular disease	7 (8.3)	4 (4.8)	2 (2.4)	.220
Cancer	8 (9.5)	10 (11.9)	11 (13.3)	.747
DVT history	22 (26.2)	25 (29.8)	24 (28.9)	.866
Prior PE	6 (7.1)	4 (4.8)	5 (6.0)	.809
Use of OCS	5 (6.0)	2 (2.4)	3 (3.6)	.486
Use of warfarin	4 (4.8)	5 (6.0)	1 (1.2)	.277
Use of steroid	1 (1.2)	0 (0.0)	4 (4.8)	.068
At admission				
Systolic blood pressure, mm Hg	129 ± 20	126 ± 25	126 ± 27	.375
Altered mental status	7 (8.4)	3 (3.6)	2 (2.4)	.163
Heart rate, beats per minute	99 ± 19	100 ± 22	110 ± 24	.088
Respiratory rate, beats per minute	20 ± 3	19 ± 3	20 ± 6	.298
Temperature	36.5 ± 0.3	36.5 ± 0.2	36.5 ± 0.3	.115
O ₂ saturation, %	91 ± 7	92 ± 5	94 ± 4	.117
PESI score	115 ± 43	97 ± 40	76 ± 38	<.001
Intensive care unit stay, days	5 ± 6	4 ± 2	4 ± 3	.943
Admission blood gas analysis				
pH	7.4 ± 0.1	7.4 ± 0.1	7.4 ± 0.1	.950
Lactate	3.7 ± 2.7	3.3 ± 2.7	2.7 ± 1.8	.593
HCO ₃	21 ± 5	21 ± 4	21 ± 4	.981
Admission symptoms				
Syncope	23 (27.7)	20 (24.1)	20 (24.4)	.838
Chest pain	7 (8.5)	14 (17.1)	18 (22.0)	.059
Fatigue	4 (4.9)	8 (9.8)	9 (11.0)	.335
Dyspnea	64 (78.0)	74 (90.2)	71 (86.6)	.081
Lower limb pain	28 (24.4)	30 (44.8)	42 (60.0)	.116
Lower limb edema	27 (43.5)	27 (41.5)	37 (52.9)	.369
USG findings of DVT	25 (54.3)	25 (47.2)	42 (68.9)	.057
Electrocardiography				
Sinus tachycardia	57 (91.9)	62 (92.5)	58 (87.9)	.604
Right bundle branch block	23 (41.1)	24 (38.1)	24 (40.0)	.945
T-wave inversion (leads V1-3)	24 (42.1)	28 (44.4)	24 (40.0)	.883
Atrial dysrhythmia	5 (8.8)	10 (15.4)	5 (8.3)	.367
S ₁ Q ₃ T ₃	36 (64.3)	38 (58.5)	36 (60.0)	.798

(continued)

Table 1. (continued)

	Prognostic Nutritional Index			P
	T1 (n = 84)	T2 (n = 84)	T3 (n = 83)	
Localization of thrombosis in PCTA				
Common pulmonary artery	12 (14.2)	14 (16.6)	14 (16.8)	
Right pulmonary artery	11 (13.0)	12 (14.2)	11 (13.2)	
Left pulmonary artery	6 (7.1)	4 (4.7)	4 (4.8)	
Left and right pulmonary artery	8 (9.5)	7 (8.3)	8 (9.6)	
Segmental pulmonary artery	2 (2.3)	2 (2.3)	1 (1.2)	
Subsegmental pulmonary artery	48 (57.1)	42 (50.0)	45 (54.2)	

Abbreviations: CABG, coronary artery bypass graft; DVT, deep vein thrombosis; HCO₃, bicarbonate; MI, myocardial infarction; OCS, oral contraception; PCI, percutaneous coronary intervention; PCTA, pulmonary CT angiography; PE, pulmonary embolism; PESI, Pulmonary Embolism Severity Index; SD, standard deviation; USG, ultrasonography.

^aContinuous variables are presented as mean ± SD.

^bNominal variables are presented as frequency (%).

index, PNI. Nutritional status determines the patients' general medical conditions comprising immune competence, protein turnover, and physical condition. Our retrospective observational study revealed a significant correlation between admission PNI and long-term survival. Malnutrition, which is easily adjusted using PNI, manifests a state of decreased food intake and protein turnover despite the regular necessities of the human metabolism. As a matter of fact, it leads decreased response to acute disease, exacerbations of chronic diseases, and decreased long-term survivals. Considering cardiovascular diseases, PNI was first adopted in ST-segment elevation myocardial infarction recently.¹⁶ Thus, for the first time, we introduce association with PNI and PE with a median follow-up of 53.8 ± 5.4 months. The predictor value of PNI in PE is up-and-coming. In- and out-hospital PE mortality was strongly correlated with patients' PNI.

Pulmonary embolism is a major cause of mortality, morbidity, and hospitalization in Europe. Numerous prediction indices originated from clinical status have been shown in patients with PE. For instance, PESI is one of the most extensively validated score.¹⁷ Pulmonary Embolism Severity Index score includes age, gender, cancer, chronic heart failure, chronic pulmonary disease, pulse rate, systolic blood pressure, respiratory rate, body temperature, altered mental status, and arterial oxyhemoglobin status.⁵ Its strength underlies in the reliable identification of patients for 30-day mortality.⁵ Despite its serious strength, access to admission data and calculation may sometimes be problematic. Therefore, we introduced a simple calculation, PNI, whose validity was proved with long-term follow-up. Admission albumin and lymphocyte count were

Table 2. Laboratory and Echocardiography Findings.^{a,b}

	Prognostic Nutritional Index			P
	T1 (n = 84)	T2 (n = 84)	T3 (n = 83)	
Laboratory variables				
Glomerular filtration rate (CKD-EPI)	62 ± 24	64 ± 28	69 ± 26	.072
Albumin, mg/dL	2.3 ± 0.4	2.9 ± 0.4	3.4 ± 0.5	<.001
Troponin I, ng/mL	1.2 ± 2.2	0.6 ± 0.9	0.8 ± 1.6	.171
Creatinine, mg/dL	1.2 ± 0.8	1.1 ± 0.5	1.0 ± 0.3	.089
D-Dimer, ng/mL	5002 ± 5856	4679 ± 5519	5110 ± 4474	.513
Creatine kinase-MB, U/L	32 ± 25	29 ± 18	24 ± 20	.098
Brain-type natriuretic peptide, pg/mL	785 ± 959	409 ± 287	482 ± 449	.680
White blood cell count, cells/ μ L	11.8 ± 3.8	11.6 ± 4.4	12.2 ± 3.8	.354
Lymphocyte, cells/ μ L	1.2 ± 0.5	1.8 ± 0.7	2.4 ± 1.0	<.001
Neutrophil, cells/ μ L	10.0 ± 5.6	8.8 ± 4.1	14.9 ± 5.2	.108
Hemoglobin, g/dL	12.6 ± 2.1	12.9 ± 1.8	12.8 ± 2.2	.431
Blood urea nitrogen mg/dL	30 ± 19	23 ± 11	19 ± 8	.001
Echocardiography parameters				
LVEF, %	55 ± 8	57 ± 5	59 ± 4	.103
RV TAPSE	18 ± 3	19 ± 4	20 ± 4	.053
RV S' velocity, cm/s	10 ± 2	10 ± 2	10 ± 2	.207
PASP, mm Hg	54 ± 14	56 ± 15	54 ± 13	.354
LV diameter, mm	4.7 ± 0.4	5.1 ± 0.4	5.0 ± 0.4	.129
RV diameter, mm	5.0 ± 0.8	4.6 ± 0.8	4.4 ± 0.7	.062
LA diameter, mm	3.9 ± 0.4	3.7 ± 0.5	3.9 ± 0.7	.153
RV dilatation	67 (97.1)	66 (95.1)	66 (95.3)	.852
Presence of thrombus	8 (14.5)	7 (10.9)	3 (4.7)	.185

Abbreviations: LA, left atrium; LV, left ventricle; LVEF, left ventricular ejection fraction; PASP, pulmonary artery systolic pressure; RV, right ventricle; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.

^aContinuous variables are presented as mean \pm SD.

^bMann-Whitney *U* test was used for continuous variables.

Table 3. In-Hospital and Long-Term Outcomes.^{a,b,c}

	Prognostic Nutritional Index			P
	T1 (n = 84)	T2 (n = 84)	T3 (n = 83)	
In-hospital course				
All-cause mortality	19 (22.6)	6 (7.1)	2 (2.4)	<.001
Major bleeding	13 (15.5)	10 (11.9)	13 (15.7)	.736
Intracranial hemorrhage	1 (1.2)	0 (0.0)	1 (1.2)	.602
Use of fresh frozen plasma	1 (1.2)	1 (1.2)	1 (1.2)	1.000
Red cell transfusion	10 (11.9)	4 (4.8)	7 (8.5)	.248
Hemodialysis	5 (6.0)	2 (2.4)	2 (2.4)	.360
Minor bleeding	35 (41.7)	35 (41.7)	28 (33.7)	.480
Asystole	18 (21.4)	7 (8.3)	3 (3.6)	<.001
Hypotension, <90 mm Hg	22 (26.2)	9 (10.7)	5 (6.0)	<.001
Cardiogenic shock	13 (15.5)	8 (9.5)	2 (2.4)	.014
Out-hospital course				
All-cause mortality	17 (26.2)	10 (12.8)	4 (4.9)	<.001
Recurrent pulmonary embolism	3 (4.6)	2 (2.6)	2 (2.5)	.714
Major bleeding	2 (3.1)	2 (3.1)	3 (3.7)	.918
Minor bleeding	4 (6.2)	1 (1.3)	6 (7.4)	.174
History of INR >5	9 (13.8)	11 (14.1)	16 (19.8)	.528
Use of fresh frozen plasma	2 (3.1)	4 (5.3)	7 (8.8)	.339

Abbreviation: INR, international normalized ratio.

^aNominal variables presented as frequency (%).

^bContinuous variables are presented as median and 25 to 75 percentiles; nominal variables are presented as frequency (%).

^cMann-Whitney *U* test used for continuous variables and Pearson χ^2 test used for nominal variables.

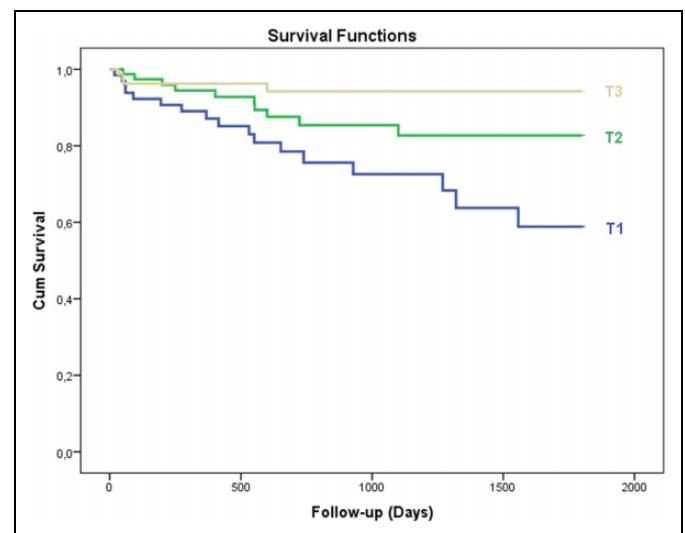


Figure 2. The Kaplan-Meier cumulative survival curve is shown. The 5-year Kaplan Meier survival for T1, T2, and T3 was 77.4%, 92.9%, and 97.6% respectively.

enough to determine PNI, whose long-term predictive role is valuable. The mortality in acute PE is strongly correlated with PNI score similar to myocardial infarction.^{16,18} The decreased response of albumin and lymphocytes to acute disease indicates

Table 4. In-Hospital Event Rates and Logistic Regression Models for Mortality by Prognostic Nutritional Index and Cox Proportional Analysis and Long-Term Mortality by Prognostic Nutritional Index.

	Prognostic Nutritional Index		
	T1	T2	T3
In-hospital mortality			
Number of deaths	19	6	2
Mortality, %	22.6	7.1	2.4
Mortality, OR (95% CI)			
Model 1: unadjusted	11.8 (2.6-52.6)	3.1 (0.6-15.9)	1 (Reference)
Model 2: adjusted for age and sex	11.9 (2.4-38.2)	2.9 (0.8-12.5)	1 (Reference)
Model 3: adjusted for all covariates ^a	8.1 (2.1-27.1)	2.5 (0.9-10.4)	1 (Reference)
Long-term mortality			
Number of deaths	17	10	4
Mortality, %	26.2	12.8	4.9
Mortality, HR (95% CI)			
Model 1: unadjusted	5.5 (1.8-16.4)	2.4 (0.7-7.9)	1 (Reference)
Model 2: adjusted for age and sex	5.2 (2.1-13.3)	2.1 (0.9-6.8)	1 (Reference)
Model 3: adjusted for all covariates ^a	4.6 (2.6-10.9)	1.8 (1.0-5.5)	1 (Reference)

Abbreviations: CI, confidence interval; HR, hazard ratio; OR, odds ratio.

^aDemographics (age and sex); first measurement of systolic blood pressure and heart rate; first measurement during hospitalization of the following laboratory values (admission glomerular filtration rate calculated by CKD-EPI, blood urea nitrogen, white blood cell count, hematocrit, and platelet count); creatine kinase-MB, troponin I, D-dimer, and brain-type natriuretic peptide; comorbidities (diabetes, chronic kidney disease, hypertension, stroke, heart failure, cancer, chronic lung disease, and atrial dysrhythmia), and medications (use of oral contraceptives, warfarin, and steroid).

low immune-nutritional status. Therefore, the PNI score should be considered as a clinical element and indicator of disease severity in acute PE. Its role can be defined as an identifier for high-risk patients who may benefit long duration of anticoagulation therapy or close follow-up. Whereas considering chronic diseases, the prognostic power of PNI has not been tested. Thus, it is difficult to correlate chronic PE with PNI at the present moment.

Albumin is the most abundant plasma protein produced by hepatocytes. During inflammation, there are decreases in plasma albumin concentration and albumin synthesis.¹⁹ When isolated hepatocytes are incubated in the presence of pro-inflammatory cytokines, negative acute phase proteins such as albumin are reduced.²⁰ Moreover, lymphocyte count is influenced in inflammatory events due to increased apoptosis and is a frequent finding secondary to increased levels of corticosteroids in acute stress conditions such as acute coronary syndrome and PE.²¹ Therefore, complete blood cell subgroups (neutrophils, lymphocytes, and platelets) are used as inflammation markers with ease.²² As we explained in detail, a novel predictive parameter, PNI, was introduced to patients with PE, which includes both albumin and lymphocyte counts. Prognostic nutritional index brings these 2 important measurements together and presents a noteworthy prognostic value.

According to the ROC curve analysis of the current study, an optimal cutoff value of 38 was obtained. The only cardiovascular study in the literature, which was performed in patients with ST-segment elevation myocardial infarction, also found the same cutoff value of 38.¹⁶ From this view, this increases the predictive value of PNI not only in PE but also in overall cardiovascular patients.

Study Limitations

The current study has several limitations. First, this was a single-center, retrospective, observational study. Second, PNI levels after discharge were not recorded; thus, the effect of post discharge PNI level on clinical outcomes could not be determined. Third, although PNI level might be influenced by hormonal changes, we could not measure hormones such as serum catecholamine and cortisol. Fourth, because albumin is not a standard laboratory test during PE follow-up, we are lacking in follow-up PNI score. Finally, because of methodological limitations of retrospective analysis, it is not possible to define the exact causal relationship between PNI level and mortality. These limitations require further examinations to validate our present findings; a prospective study in a larger number of patients is needed.

Conclusion

Our pilot study indicated that PNI, calculated based on serum albumin level and lymphocyte count, is an independent prognostic factor for survival of patients with PE. This result confirmed that nutritional and immunological situations are important when considering the long-term outcome in patients with PE. Patients with low PNI were demonstrated to have poor prognosis. Further investigations on independent multicenter cohorts should be performed in order to validate our findings.

Declaration of Conflicting Interests

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