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The prognostic nutritional index is associated with mortality of patients in intensive care unit

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Ethics Committee Approval
This study was approved by University of Health Sciences, Ankara Diskapi Yildirim Beyazit Training and Research Hospital Ethics Committees (Approval No: 13.12.2021-126/27). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: It has been reported that the prognostic nutritional index (PNI) is), an immunonutritional index, associated with poor prognosis, especially in cardiovascular and malignant diseases. However, the clinical significance of PNI in intensive care (ICU) patients remains unclear. In this study, we aimed to measure the predictive value of the PNI in predicting mortality in patients hospitalized in the ICU.

Methods: A total of 80 patients hospitalized in the internal medicine ICU of our hospital between January 2021 and September 2021 were included in this observational cohort study. The patients' demographic characteristics, comorbidities, laboratory parameters, need for and duration of mechanical ventilation, length of stay in ICU, and mortality rates were retrospectively analyzed. The patients were divided into two groups according to their survival; the first group comprised of survivors while the second group comprised of those who died in the ICU. The two groups were compared in terms of all variables.

Results: The mean age of all subjects included in the study was 63 (18.2) years and 50% (n=40) were female and 50% (n=40) were male. When patients are grouped as survivors and non-survivors, the mean age and sex distribution were similar (P=0.23, P=0.27, respectively). The median follow-up period of the patients was 5 (IQR 3-11) days and the mortality rate was 38.7% (n=31). Those in the non-survivor group had higher APACHE II and SOFA scores (P=0.02, P<0.001, respectively), and a lower PNI level (P=0.01). In the multivariate regression analysis, PNI value [OR: 1.210 (95%CI: 1.048-1.396) P=0.009] was the negative independent risk factor and SOFA score [OR: 1.697 (95%CI: 1.201-2.398) P=0.03] was a positive independent risk factor.

Conclusion: Despite our small cohort, we believe our findings corroborate our hypothesis that as a simple and inexpensive test, PNI is a useful biomarker to assess mortality risk in ICU patients.

Keywords: Prognostic nutritional index, Intensive care, Mortality

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Introduction

The intensive care unit (ICU) is a special treatment unit equipped with high technology for rapid intervention, where patients with life-threatening organ failure and who need to be kept under constant observation are followed up and treated [1]. With the increase in the aging population, the increase in the demand for intensive care beds and the high cost of intensive care treatments require careful selection of patients who will benefit from hospitalization in the ICU [2]. Calculation of expected mortality rates of intensive care patients is important in terms of rapid identification of critical patients requiring urgent diagnosis and treatment, standardization of intensive care units, and evaluation and provision of service quality. Scales used in the ICU to determine mortality and disease severity include scoring systems such as Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA). These mortality prediction models predict disease severity and risk of morbidity and mortality associated with a direct worse outcome [3].

The prognostic nutritional index (PNI) is a combined score that reflects both the immunological and inflammatory status and the nutritional status of the individual, based on serum albumin and lymphocyte values [4]. Total blood lymphocyte count is recognized as a biomarker of nutritional status of patients as well as a prognostic factor in various clinical situations. It has been previously shown that low lymphocyte count predicts increased mortality in many chronic diseases [5,6]. Another parameter indicating a poor prognosis, especially in the ICU, is low albumin levels [7]. Hypoalbuminemia in critically ill patients can have various causes, such as poor nutritional status, impaired liver function, increased loss through the kidneys, and particularly the response to systemic inflammation (negative acute phase reactant) [8]. PNI using these two parameters was also proven to have prognostic value in various clinical conditions, including malignancy, infection, and cardiovascular disease [9-12].

Incorporating simple and useful biomarkers into prognostic strategies can significantly improve outcomes for patients followed in the ICU. In this study, we aimed to measure the predictive value of PNI in predicting mortality in patients hospitalized in the internal medicine ICU.

Materials and methods

This study was designed as a retrospective, cross-sectional study. The Ethics Committee of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital approved this study regarding the principles of the Declaration of Helsinki. Written-informed consents of all patients were obtained before inclusion (App. No: 13.12.21-126/27).

Medical records of patients admitted to the internal medicine ICU between January 2021 and September 2021 were retrospectively reviewed. Patients who stayed in the ICU for less than 24 hours, those younger than 18 years old, pregnant, positive for COVID-19 PCR test and/or patients with suspected COVID-19 infection by clinical and imaging methods, patients requiring postoperative follow-up and coronary intensive care patients, patients with an indication for intensive care due to newly developed cerebrovascular disease were excluded from the study. Patients whose albumin levels were measured before the initiation of treatment in the ICU were included in the study. After the patients meeting the exclusion criteria were excluded from a total of 114 patients who were followed up in the internal medicine ICU between the specified dates, all the remaining patients (80 patients) were included in the study, and other factors that could affect survival (comorbidity, etc.) were not excluded from the study in order to avoid bias.

The patients' demographic characteristics, accompanying comorbidities, laboratory parameters on admission to ICU, need for and duration of mechanical ventilation, length of stay in the ICU, and mortality rates were retrospectively analyzed. The patients were divided into two groups according to their survival, the first group comprised survivors (survivor), while the second group comprised patients who died in the ICU (non-survivor).

SOFA and APACHE II scores were used to analyze disease severity and mortality. The data required to make the relevant calculations were collected from the hospital database on the first 24 hours in the ICU and the results were classified according to the literature. In APACHE-II scoring, twelve clinical and biochemical parameters are calculated by assigning a score between 0-4. In the calculation; age, patient's pre-existing diseases, worst value of the body temperatures, mean arterial pressure, heart rate, respiratory rate, oxygenation, arterial pH, serum sodium, potassium, creatinine, white blood cell count, hematocrit, Glasgow coma scale measured in the first 24 hours of intensive care admission are evaluated; a score below 10 indicate mild disease, while a score above 15 indicate moderate-to-severe disease. In SOFA scoring, a total of six organ systems, which include respiration where arterial partial pressure of oxygen (PaO2)/oxygen concentration (FiO2) is calculated, cardiovascular system where blood pressure and adrenergic drug infusion are evaluated, liver where bilirubin level is scored, coagulation where platelets are evaluated, kidney where creatinine and urine output are evaluated, and Glasgow coma scale, are scored between 1 and 4, and the worst value is recorded daily. The total score ranges from 6 to 24; a higher score indicates worsening morbidity [13]. The PNI was calculated using the formula: PNI = 10 x serum albumin (g/dL) + 0.005 x total lymphocyte count (per mm3). The two groups were compared in terms of all variables.

Statistical analysis

Kolmogorov-Smirnov and Shapiro-Wilk tests were used to test the normality of the data. The results were expressed as *n* for the number of observations, mean (SD), and median (interquartile range) values. The Chi-square test was used for comparisons of categorical variables. Ordinal variables and continuous variables that do not have normal distribution were compared by the Mann–Whitney *U* test. The Student's *t*-test was used to evaluate differences between the two groups in normally distributed continuous variables. Multivariate regression analysis was used for detecting laboratory parameters and demographic characteristics associated with patients' mortality. Data were analyzed using the Statistical Package for the Social Sciences, version 20.0 (SSPS Inc., Chicago IL, USA). A *P*-value of <0.05 was considered statistically significant.

Results

Of the 80 patients included in the study, 50% (n=40) were female and 50% (n=40) were male. The median follow-up period of the patients was 5 (IQR 3-11) days and the mortality rate was 38.7% (n=31). When patients are grouped as survivors and non-survivors, the mean age and sex distribution were similar (P=0.23, P=0.27, respectively). The demographic, clinical and laboratory parameters of the groups are shown in Table 1. When compared in terms of co-morbidities, the non-survivor group had a significantly higher rate of diabetes mellitus (DM) (P<0.001) and malignancy (P=0.04) (Table 1). The intubation rate was higher (P<0.001) and the duration of mechanical ventilation was shorter in the non-survivor group (P=0.01) (Table 1). Those who did not survive had higher APACHE II and SOFA scores (P=0.02, P<0.001, respectively), and a lower PNI level (P=0.01) (Table 1). In the multivariate regression analysis, PNI value [OR: 1.210 (95%CI: 1.048-1.396) P=0.009] was a negative independent risk factor, SOFA score [OR: 1.697 (95%CI: 1.201-2.398) P=0.03] was a positive independent risk factor (Table 2).

Table 1: Demographic, clinical, and laboratory parameters of patients followed in the ICU, grouped as survivors and non-survivors

Variables	Total	Survivors	Non-survivors	*P*-value
n, (%)	80 (100)	49 (61.3)	31 (38.7)	
Age	63 (18.2)	61.5 (19.3)	66.5 (16.3)	0.23
Sex				
Male, n (%)	40 (50)	24 (49)	16 (51.6)	0.27
Female, n (%)	40 (50)	25 (51)	15 (48.4)	
Co-morbidity				
DM, n (%)	30 (37.5)	16 (32.7)	14 (45.2)	<0.001
HT, n (%)	37 (46.3)	19 (38.8)	18 (58.1)	0.09
CCF, n (%)	10 (12.5)	6 (12.2)	4 (12.9)	0.93
CKD, n (%)	5 (6.3)	3 (6.1)	2 (6.5)	0.95
CAD, n (%)	17 (21.3)	10 (20.4)	7 (22.6)	0.81
COPD, n (%)	13 (16.3)	7 (14.3)	6 (19.4)	0.54
Malignancy, n (%)	21 (26.3)	9 (18.4)	12 (38.7)	0.04
WBC, (10^3/µL) median (IQR%25-75)	8.91 (6-15.9)	9.02 (6.29-13.86)	8.64 (5.74-18.89)	0.51
Lymphocyte, (10^3/µL) median (SD)	0.9 (0.7)	1.03 (0.6)	0.92 (0.7)	0.45
Hemoglobin, g/dL median (SD)	10.4 (2.5)	10.4 (2.5)	10.2 (2.6)	0.74
Platelet, (10^3/µL) median (SD)	203 (1.5)	210 (1.2)	192 (1.9)	0.6
Creatinine, mg/dL median (IQR%25-75)	0.99 (0.61-2.2)	0.91 (0.55-1.73)	1.35 (0.73-2.67)	0.3
Albumin, g/dL median (IQR%25-75)	3.57 (2.71-4.48)	2.95 (2.36-3.26)	2.5 (2-3.03)	0.009
AST, U/L median (IQR%25-75)	33 (18-66)	28 (15.5-46.5)	51 (26.4-162)	0.06
ALT, U/L median (IQR%25-75)	25 (11-50)	17 (10-37)	45 (17-100)	0.02
CRP, mg/L median (IQR%25-75)	58.6 (23-145)	44 (15-126)	101 (52-194)	0.47
PO2 mmHg median (IQR%25-75)	88 (75-137)	93.4 (76.3-141)	86 (64-113)	0.29
PaCO2 mmHg median (SD)	32.8 (11)	32.1 (9.5)	34 (13.1)	0.44
Length of stay in the ICU, days median (IQR%25-75)	5 (3-11)	6 (3-11)	5 (2-12)	0.85
Intubation (%)	34 (42.5)	12 (24.5)	22 (71)	<0.001
Mechanical ventilation time, days median (IQR%25-75)	4 (2.75-9)	9 (5.2-15.5)	3 (2-4)	0.01
APACHE II score median (SD)	20.6 (8.4)	18.4 (7.3)	24.4 (8.8)	0.02
SOFA at admission median (SD)	5.4 (3.5)	4.08 (2.8)	7.7 (3.4)	<0.001
PNI median (IQR%25-75)	43.9 (31.4-56)	32.8 (28.1-39.8)	30.5 (24.6-35.5)	0.01

DM: Diabetes mellitus, HT: Hypertension, CCF: Congestive cardiac failure, CKD: Chronic kidney disease, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, WBC: White blood cell, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, PaO2: Partial pressure of oxygen, PaCO2: Partial pressure of carbon dioxide, APACHE-II: Acute Physiology and Chronic Health Evaluation II, SOFA: Sequential Organ Failure Assessment, PNI: Prognostic nutritional index

Table 2: Multivariate logistic regression analysis to determine the independent risk factors for mortality according to PNI and SOFA

	Odds Ratio	95% Confidence Interval	*P*-value
PNI	1.210	1.048- 1.396	0.009
SOFA	1.697	1.201- 2.398	0.03

PNI: Prognostic nutritional index, SOFA: Sequential Organ Failure Assessment

Discussion

This study showed that PNI was significantly lower in non-survivor ICU patients and was associated with mortality. The PNI had a performance similar to SOFA score in assessing mortality in patients in ICU.

Patients followed in the ICU is a heterogeneous group with various complications and different clinical conditions, and it is known that the mortality rate of these patients is high. SOFA, one of the mortality estimation models used in the ICU, was first developed to determine the severity of organ dysfunction in septic patients, but later it was determined that it could also be an indicator of disease severity in critically ill patients in ICU, and it started to be used as a mortality indicator in recent years [14-16]. In our study, expectedly, the SOFA score was higher in the non-survivor group. Moreover, in patients followed in the ICU, the SOFA score was effective in indicating increased mortality.

Scorings such as SOFA are commonly used but are comprehensive, difficult to calculate, and time consuming for patients followed in the ICU because they utilize multiple physiological variables from different organ systems. Clinicians need a clinically applicable, inexpensive, and easy to interpret biomarker which will be helpful for early determination of serious disease and poor outcome. PNI is a combined marker that reflects both the immunological and inflammatory status and the nutritional status of the individual [4]. Hypoalbuminemia indicates the patient's malnutrition, which is the main reason for the relationship between albumin and patient prognosis [17]. However, since albumin has a long half-life, it does not have sensitivity to detect acute changes in nutritional status. Therefore, it is not recommended as an indicator of nutritional assessment alone. There is also evidence to suggest that albumin also reflects disease severity [18]. Albumin, a negative acute phase reactant, is more susceptible to acute inflammation as it is inhibited by proinflammatory cytokines in case of systemic inflammation [19]. The importance of lymphocytes, another determining factor of the PNI index, in the human immune system has been proven in many studies [20,21]. Progression of inflammation is the decisive factor in consequence of critically ill patients. In addition, there is an inverse relationship between the progression of inflammation and the lymphocyte count [22].

PNI, on the other hand, was initially defined to determine the surgical risk and perioperative immunonutrition status in patients undergoing initial gastrointestinal surgery [23]. It was later reported to be useful in evaluating malnutrition and prognosis in cardiovascular diseases [24]. Keskin et al. [25] reported that it is an independent predictor of mortality in patients undergoing coronary artery bypass surgery; Hayashi et al. [26] found that higher PNI scores were associated with shorter mechanical ventilation time, shorter follow-up time in ICU, and lower infection ratio in patients undergoing cardiovascular surgery. Again, there are also studies in the literature showing that there is a relationship between low PNI and poor prognosis in different cancer types [4]. In our study, we found PNI as an independent predictor of mortality in patients followed in the ICU. Due to the combined effect of two immunonutritional markers (albumin and lymphocyte) reflecting

the severity of the disease, we believe that low PNI may be a marker of poor survival in ICU patients.

Our main limitations are the lack of data on long-term clinical events due to the retrospective nature of the study and the small sample size. Another limitation is that patients' nutritional status was not analyzed prior to admission to ICU.

Conclusion

In our study, we identified PNI as an independent predictor of mortality in patients followed in the ICU. In intensive care, instead of comprehensive mortality estimation scores, which are complex to calculate and subjective to evaluate, the use of easy to calculate objective markers such as PNI, which can eliminate inter-clinician variability, can be considered. However, these data should be corroborated by prospective multicenter studies. We think that the evaluation of markers such as PNI together with mortality prediction scores will help clinicians to quickly assess the severity of disease and improve patient prognosis.

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