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ORIGINAL ARTICLE

Can be the Prognostic Nutritional Index a Prognostic Indicator in Lung Transplantation?

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Abstract

Introduction: To evaluate the role of nutritional status in lung transplant candidates in post-transplant mortality and clinical outcomes.

Methods: 59 patients with end-stage lung diseases were divided into two groups: low prognostic nutritional index (PNI) (Group 1) and high PNI (Group 2). The two groups were compared, and influence factors were analyzed.

Results: PNI scores were grouped into (<43.7) Group 1 and (≥43.7) Group 2. Group 1 (n=29, 50.8%) had significantly higher post-transplant mortality within 1 year compared to Group 2 (n=30, 49.2%) (p=0.027). Post-operative mechanical ventilation day and low PNI score (<43.7) were independent predictors of mortality (OR: 2.46, 95% confidence interval [CI]: 1.71–3.54, p=0.001 and OR: 4.25; 95% CI: 1.59–11.33, p=0.004).

Discussion and Conclusion: Our findings revealed that pre-operative nutritional status is a useful indicator of post-transplant mortality risk. We think that the PNI score can be among the standard evaluation tests as a useful test for lung transplant candidates.

Keywords: Lung transplantation; prognosis; prognostic nutritional index.

Lung transplantation has progressively improved prognosis with advancements in patient management in recent decades and is a promising and effective treatment for patients with end-stage lung diseases. There is generally a dominance of catabolic processes in these critical cases, both in the end-stage phase of the underlying disease and in the perioperative period[1]. Nutritional approaches are critical to the overall management of lung transplant patients. Maintaining adequate nutrient stores is the primary goal of nutritional treatment for patients awaiting transplant[2]. Nutritional status has been associated with post-operative complications and death in transplant patients due to effects on both tissue healing and muscle and respiratory functions[3-5].

To date, various indexes of nutritional status have been developed to predict the prognosis of patients with cancer and those requiring surgery. A study by Onodera et al.[6] calculated prognostic nutritional index (PNI) scores based on serum albumin levels and peripheral blood lym-

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phocyte counts as follows: 10 × serum albumin value (g/dL) + 0.005 × total lymphocyte count in peripheral blood (/mm^3). They suggested that the PNI score could reflect the patient's nutritional status and indicate the prognosis for patients requiring gastrointestinal surgery. The PNI score was subsequently used to predict the prognosis for patients with various solid tumors and chronic liver or kidney failure[7-9].

In the last decade, studies have been increasingly focused on the role of nutritional indexes in the outcomes of transplant patients. It was recently suggested that nutritional scores may be useful in identifying heart and lung transplant patients who would benefit from nutritional support[10]. In addition, several studies have demonstrated that the PNI score is associated with post-transplant complications and mortality[11].

Nutritional status is often neglected in the management of lung transplant patients care. Although lung transplant outcomes have been steadily improving, much remains to be explored to improve the nutritional management of these cases both before and after transplantation. There is a need to establish standard patient treatment supported by mathematical evaluations of nutritional status for better transplant outcomes. However, limited studies to date have explored the role of nutritional indexes on transplantation outcomes. In the present study, we aim to investigate the role of PNI scores in mortality and other clinical outcomes in lung transplant patients.

Materials and Methods

This retrospective single-center cohort study was conducted in the Department of Lung Transplantation of a tertiary hospital. The study was approved by the local ethics committee (Istanbul, Türkiye, May 08, 2020.4/31-336). Ethical approval was obtained in accordance with the Declaration of Helsinki. Data were collected from patients' files in the hospital database. Due to the retrospective nature of the study, informed consent was not required from the patients for the use of medical data for publication purposes with the approval of the local scientific ethics committee. All patients' identifying information was kept confidential.

Study Population

The study included patients who underwent lung transplantation with end-stage lung disease due to various underlying lung diseases between December 2016 and May 2021. While 75 patients were initially enrolled, 16 patients were excluded due to missing data. Thus, finally, 59 patients were enrolled in the study. These patients were divided into two groups: those with low PNI scores (Group 1) and those with high PNI scores (Group 2). Patients were also categorized according to the presence of underlying lung diseases such as obstructive lung disease (OLD), interstitial lung disease (ILD), cystic fibrosis (CF), and non-cystic fibrosis bronchiectasis (non-CF bronchiectasis).

Data Collection

Data were collected from the hospital database and patients' files. Data on patients' demographics and characteristics, including age, gender, and body mass index (BMI), were obtained. Results of laboratory examinations recorded at the time of diagnosis included a complete blood cell count, albumin (g/L), hemoglobin (g/dL), PNI score, iron (µg/dL), ferritin (ng/mL), total cholesterol (mg/dL), low-density lipoprotein (LDL) (mg/dL), high-density lipoprotein (HDL) (mg/dL), triglyceride (mg/dL), 1,25-dihydroxyvitamin D (ng/dL), calcium (mg/dL), forced expiratory volume in 1 s (FEV1, %), forced vital capacity (FVC, %), and distance (m) in the 6-min walk test (6MWD). As clinical parameters, waiting time (days), duration of intensive care unit (ICU) stay (days), hospitalization days, and days on mechanical ventilation were also recorded. Mortality data for all patients were recorded from the government's electronic mortality declaration system (http://obs.gov.tr).

Statistical Analysis

The data obtained in this study were analyzed statistically using IBM SPSS Statistics 23.0 software. Descriptive statistics were used to illustrate the demographic and clinical characteristics of the patients. Medians and interquartile ranges were provided for non-parametric variables, while values of mean±standard deviation were used for parametric variables. In addition, Kruskal-Wallis analysis was used because the underlying diseases of OLD, ILD, CF, and non-CF bronchiectasis represented more than two independent groups. Categorical variables were compared with chi-square tests. A receiver operating characteristic (ROC) curve analysis was performed to evaluate the discriminative power of the PNI score with respect to mortality and to determine the cut-off value. The area under the ROC curve (AUC) and 95% confidence interval (CI) were calculated.

Results

This study included a total of 59 patients who were divided into two groups, with 29 in Group 1 (50.8%) and 30 in Group 2 (49.2%). Seventy-six percent of all participants were male (n=45), and the median age was 48 years (IQR: 28–56 years).

The most common underlying diseases of these lung transplant candidates were OLD, ILD, CF, and non-CF bronchiectasis (n=9, 15.3%; n=26, 44.1%; n=8, 13.6%; and n=16, 27.1%, respectively).

In the comparison of underlying lung disease groups, age (p=0.001) was significantly younger, BMI was lower (p=0.012), and time spent waiting for a transplant was longer (p=0.007) in the CF group. FEV1 was significantly higher in patients with ILD compared to other disease groups (p<0.001). Other demographic, clinical, and laboratory results were similar between the groups. The demographic characteristics of the patients are summarized in Table 1.

In order to distinguish cases with a high risk of mortality from other lung transplant patients, the most appropriate cut-off value for the PNI score was 43.7. At this cut-off value, the PNI had a sensitivity of 76% and a specificity of 63.5%, while the AUC was 0.622 (95% CI: 0.538–0.705, p=0.011). PNI scores were grouped based on this cut-off limit (<43.7, Group 1; ≥43.7, Group 2). Group 1 (n=29, 50.8%) had significantly higher post-transplant mortality within 1 year compared to Group 2 (n=30, 49.2%) (p=0.027). In other comparisons of these groups, days on mechanical ventilation, length of hospital stay, 6MWD, and total cholesterol, LDL, HDL, triglyceride, and calcium levels differed. Other considered variables were similar between the groups (Table 2).

In logistic regression analysis, univariate predictors were days spent on mechanical ventilation, days in the ICU, and a PNI score of <43.7. Multivariate analysis identified days spent on mechanical ventilation and a PNI score of <43.7 as independent predictors of mortality (OR: 2.46, 95% CI: 1.71–3.54, p=0.001 and OR: 4.25, 95% CI: 1.59–11.33, p=0.004) (Table 3).

Table 1. Demographic and clinical characteristics of the study

	OLD 9 (15.3%)	ILD 26 (44.1%)	CF 8 (13.6%)	Non-CF bronchiectasis 16 (27.1%)	p
Age, years, median (IQR)	55 (53–57)	52 (46–58)	24 (23–36)	30 (26–56)	0.001
Gender, male, n (%)	8 (17.8)	25 (55.6)	3 (6.7)	9 (20)	0.001
BMI, kg/m^2, median (IQR)	25 (24–26)	26.3 (22.2–28.6)	19.1 (16.5–24.6)	20 (16.8–24.3)	0.012
Waiting time, days, median (IQR)	96 (69–116)	82 (42–171)	214 (163–436)	130 (36–177)	0.007
Mortality, n (%)	5 (19.2)	9 (34.6)	3 (11.5)	9 (34.6)	0.430
6MWD, m, mean±SD	233±95	231±126	234±115	273±121	0.714
FEV1%, median (IQR)	22 (18–28)	43.5 (30–50)	21 (20–40)	24.9 (19–27)	<0.001
FVC%, median (IQR)	38 (33–52)	38.5 (28–43)	31.5 (32–34)	29.6 (22–35.5)	0.060
Leukocyte count, median (IQR)	6500 (5700–7800)	9600 (7600–10900)	9500 (9600–10300)	9300 (6900–10700)	0.051
Lymphocyte count, median (IQR)	2100 (1300–2800)	2060 (1300–3200)	1600 (1450–1780)	2230 (1275–2820)	0.689
Hemoglobin, g/dL, mean±SD	12.3±1.8	14.8±1.4	12.0±3.0	13.0±2.2	0.001
PNI score, mean±SD	43.5±4.6	45.5±13.5	43.2±4.3	46.2±6.6	0.357
Albumin, g/L, median (IQR)	4.1 (3.7–4.2)	4.0 (3.7–4.3)	3.5 (3.3–3.8)	3.7 (3.5–4.0)	0.032
Iron, µg/dL, median (IQR)	29 (21–48)	47 (29–85)	21 (17–32)	40 (31–66)	0.021
Total cholesterol, mg/dL, median (IQR)	205 (199–228)	187 (159–225)	117 (100–185)	165 (134–197)	0.009
LDL, mg/dL, median (IQR)	98 (64–107)	95 (159–225)	78 (36–103)	53 (39–129)	0.388
HDL, mg/dL, median (IQR)	47 (37–138)	187 (45–120)	42 (35–52)	65 (44–91)	0.249
Triglyceride, mg/dL, median (IQR)	150 (128–157)	124 (82–158)	110 (73–140)	98 (65–113)	0.127
1,25-Dihydroxyvitamin D, ng/dL, median (IQR)	13.4 (7.0–15.6)	10.9 (9.1–14.1)	13.2 (10.7–17.9)	12.7 (9.1–14.6)	0.655
Calcium, mg/dL, median (IQR)	9.2 (8.9–9.7)	9.5 (9.1–9.8)	9.1 (8.7–9.3)	8.9 (8.6–9.6)	0.098

SD: Standard deviation; IQR: Interquartile ratio; 6MWD: Six-minute walk distance; OLD: Obstructive lung disease; ILD: Interstitial lung disease; CF: Cystic fibrosis; FEV1: Forced expiratory volume in 1 s; FVC: Forced vital capacity; BMI: Body mass index; PNI: Prognostic nutritional index; LDL: Low-density lipoprotein; HDL: High-density lipoprotein.

Table 2. Demographic, clinical, and laboratory parameters according to study groups

	Group 1 (PNI <43.7) n=29 (50.8%)	Group 2 (PNI ≥43.7) n=30 (49.2%)	p
Age, years, median (IQR)	44 (28–55)	52 (34–57)	0.074
Gender, male, n (%)	23 (51.1)	22 (48.9)	0.942
BMI, kg/m^2, median (IQR)	25.4 (19.7–26.8)	23.3 (19.8–26.3)	0.118
BMI < 18, n (%)	5 (16.7)	6 (20.7)	0.692
OLD, n (%)	4 (44.4)	5 (55.6)	0.731
ILD, n (%)	16 (53.3)	10 (34.5)	0.192
CF, n (%)	2 (6.7)	6 (20.7)	0.145
Non-CF bronchiectasis, n (%)	8 (26.7)	8(27.6)	0.937
Mortality, n (%)	17 (58.6)	9 (30)	0.027
Mechanical ventilation, days, median (IQR)	1 (1–5)	3 (2–9)	0.013
ICU stay, days, median (IQR)	6 (3–17)	5 (3–11)	0.156
Hospitalization, days, median (IQR)	30 (16–44)	19 (14–26)	0.001
FEV1%, median (IQR)	31.5 (22–48)	26 (20–39)	0.470
FVC%, median (IQR)	35 (25–43)	33 (28–39)	0.069
6MWD, m, median (IQR)	233 (160–318)	266 (198–335)	0.016
6MWD < 200 m, n (%)	8 (27.6)	12 (40)	0.314
Total cholesterol, mg/dL, median (IQR)	191 (159–219)	178 (129–195)	0.033
LDL, mg/dL, median (IQR)	99 (48–141)	64 (38–107)	0.020
HDL, mg/dL, median (IQR)	47 (37–66)	53 (38–100)	0.037
Triglyceride, mg/dL, median (IQR)	118 (82–158)	104 (68–143)	0.013
Calcium, mg/dL, median (IQR)	9.5 (8.9–9.7)	9.1 (8.7–9.4)	0.013
1,25-Dihydroxyvitamin D, ng/dL, median (IQR)	11.9 (9.6–15)	11.4 (9.1–14.6)	0.083

SD: Standard deviation; IQR: Interquartile ratio; 6MWD: Six-minute walk distance; OLD: Obstructive lung disease; ILD: Interstitial lung disease; CF: Cystic fibrosis; FEV1: Forced expiratory volume in 1 s; FVC: Forced vital capacity; BMI: Body mass index; PNI: Prognostic nutritional index; LDL: Low-density lipoprotein; HDL: High-density lipoprotein.

Table 3. Logistic regression analysis for mortality

	Univariate logistic regression			Multivariate logistic regression		
	Odds ratio	Confidence interval (95%)	p	Odds ratio	Confidence interval (95%)	p
MV, days	1.57	1.12–2.20	0.008	2.46	1.71–3.54	0.001
ICU, days	1.12	1.03–1.21	0.005	1.03	0.95–1.11	0.443
PNI <43.7	3.30	1.12–9.68	0.029	4.25	1.59–11.33	0.004

MV: Mechanical ventilation; ICU: Intensive care unit; PNI: Prognostic nutritional index.

Discussion

The primary findings of this study show that a low PNI score is an independent predictor of poor prognosis in lung transplantation recipients. The duration of time spent on mechanical ventilation also predicted post-transplant mortality in these patients.

Many indicators have been proposed to determine nutritional status. One of them is the PNI, which has been suggested for use in malnourished solid-cancer patients and those requiring gastrointestinal surgery, as well as for patients with various diseases such as myocardial infarction, hematological malignancies, liver cirrhosis, and chronic renal failure, with PNI scores having been associated with prognosis and mortality in these patient groups[6,12-15]. Although limited studies have evaluated the relationship between nutritional status and mortality in transplant recipients, Barge-Caballero et al.[10] reported that patients who were malnourished before a heart transplant had a higher risk of postoperative complications and mortality. Thus, they suggested the identification of patients at pre-operative nutritional risk in order to determine who could benefit more from nutritional intervention.

Kim et al.[11] showed that lung transplant patients with high PNI scores (≥41.15; 78.3%) had significantly higher overall survival rates compared to patients with low PNI scores (<41.15; 28.6%). Another study by Kanou et al.[16] found that a low PNI score (<48) was a predictor of mortality and associated with chronic lung allograft dysfunction in transplant patients. They emphasized that PNI scores may be useful for identifying high-risk patients and patients who should receive nutritional supplementation before transplantation. On the other hand, Lu et al.[17] found that PNI scores did not affect post-operative mortality.

Thus, based on the results of previous studies, the impact of the PNI score on mortality outcomes in lung transplant patients is still controversial. In our study, patients with low PNI scores had approximately twice the mortality rate of those with high PNI scores (58.6% vs. 30%). A low PNI score was furthermore an independent predictor with a risk of a 4.25-fold increase in mortality.

Lymphocytes have been shown to contribute to cell-mediated immunity[18,19]. Chamogeorgakis et al.[1] reported that lymphocyte counts are important prognostic factors in lung transplantation patients. Another parameter, albumin, is most commonly used to determine nutritional status, and its relationship with post-operative complications in lung transplantation has been demonstrated.

One of the important limitations of this study was that our lung transplantation department is one of only two such main centers in Türkiye. The small number of transplants resulted in a limited number of patients, limiting further analyses in turn.

This study has demonstrated that PNI scores are potentially useful in identifying patients who critically need nutritional supplementation programs. Exciting potential for the PNI as a nutritional marker to guide clinicians in the prediction of mortality, patient management, and prognosis in cases of lung transplantation is further suggested by these results.

Nutrition is an increasingly important issue in lung transplant pathophysiology. The pathogenesis of malnutrition involves neurohormonal or immunoinflammatory mechanisms due to the catabolic state imposed by diseases[20]. To our knowledge, few studies have evaluated the relationship between pre-lung transplant nutritional status and post-transplant survival, and this relationship has not yet been fully clarified. Our study, however, is consistent with the research performed by Kim et al.,[11] who showed that the post-operative mortality rate was significantly higher in patients with low pre-transplant PNI scores. Furthermore, Kanou et al.[16] found that a low PNI score was both a predictor of mortality and associated with chronic lung allograft dysfunction in 46 patients. Considering the existence of this relationship, patient management with evaluations in terms of nutritional status before transplantation should be appropriately arranged. Thus, consideration of the PNI may contribute to improved post-transplant survival. On the other hand, Lu et al.[17] found that PNI scores did not affect post-operative mortality. Therefore, larger patient populations and further prospective studies are needed to prove the hypothesis that PNI scores affect mortality.

Conclusion

In conclusion, these findings suggest that pre-operative nutritional status is a useful marker for determining a patient's risk of post-transplant mortality. In addition to the pre-operative PNI score, comparative studies with anthropometric measurements are also needed in the future.

In light of these findings, we think that this score may be included among the standard evaluation tests for lung transplant candidates.

Ethics Committee Approval: The study was approved by the local ethics committee (Istanbul, Türkiye, May 08, 2020.4/31-336). Ethical approval was obtained in accordance with the Declaration of Helsinki.

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Conflict of Interest: None declared.

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