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The performance of prognostic nutritional index in predicting the respiratory-related hospitalization risk in bronchiectasis patients: A single-center retrospective cohort analysis

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Abstract

This study aimed to investigate the performance of prognostic nutritional index (PNI) to predict the respiratory-related hospitalization (RRH) risk over the course of a year in bronchiectasis patients. A total of 194 bronchiectasis patients were retrospectively evaluated in terms of chronic bacterial colonization and the bronchiectasis pattern, laboratory findings, FACED score and PNI on the day of presentation to the outpatient clinic in stable period, while patients were further followed up for RRH events over the course of a year. RRH was significantly more common in patients with vs. those without comorbid chronic obstructive pulmonary disease (75.7 vs. 35.8%, $p<0.001$) and previous tuberculosis history (70.0 vs. 44.4%, $p=0.002$). PNI values were significantly lower (46.9 vs. 55.9, $p<0.001$) in patients with vs. those without RRH. PNI was found to be a potential marker of hospitalization risk in bronchiectasis patients at a cut-off value of <50.55 (sensitivity: 90.5%, specificity: 69.7%) The decrease in PNI (OR, 0.782, 95% CI: 0.727-0.840, $p<0.001$) was found to independently predict the hospitalization risk. In conclusion, PNI seems to be a valuable marker in identifying the patients at risk of RRH, which can simply be calculated based on serum albumin level and peripheral lymphocyte count without needing clinical evaluation.

Keywords: Bronchiectasis, hospitalization, prognostic nutritional index, FACED score, diagnostic, performance

Introduction

Bronchiectasis is a potentially debilitating chronic respiratory disease characterized by pathological dilation of the airways and a vicious cycle of recurrent infection and chronic inflammation with progressive bronchial injury [1,2].

The progressive clinical course is accompanied with recurrent exacerbations, hospitalizations, loss of lung function and worsened quality of life in addition to a significant cost burden and the mortality risk [1-3]. Owing to close association of exacerbations with inflammation, decline in lung function, poor quality of life and mortality, the prevention of exacerbations via enabling control of bronchial infection and better mucociliary clearance is the main treatment target, besides the symptom reduction, improved quality of life and prevention of disease

progression [1-3].

The discrimination between high-risk patients as potential candidates for early aggressive treatment and the low-risk patients who are more suitable for simpler treatment regimens is considered critical in the management of bronchiectasis [4-6].

FACED score (for mortality risk), and the Bronchiectasis Severity Index (BSI; for exacerbations and related hospitalization, quality of life and mortality) are multidimensional indexes used to assess disease severity and prognosis in bronchiectasis patients [7,8].

None of these tools include serologic markers (i.e., biomarkers of systemic inflammation or nutritional status) despite the prognostic potential of these markers in patients with bronchiectasis [3,9-11]. Besides, variables included in scoring of FACED and BSI are often recorded at the time of diagnosis,

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not covering the changes over the course of the patient's follow-up [6]. Hence, new and simpler tools reflecting different aspects of bronchiectasis severity are needed, particularly those can predict patients at risk of presenting exacerbations requiring hospitalizations [3,8,12].

Given its strong independent association to bronchiectasis severity, serum albumin level is also likely to be a simple and relevant prognostic biomarker in this setting [13]. The prognostic nutritional index (PNI), using total lymphocyte count and serum albumin, is a novel prognostic score indicating the nutritional and immune status of patients in several disease settings [14,15].

Regarding the chronic respiratory diseases, PNI score was found to be associated with the increased exacerbation risk in elderly with chronic obstructive pulmonary disease (COPD) [16], and to predict 30-day mortality in those with acute exacerbation of COPD [16,17]. The role of nutritional status in improving clinical outcomes in bronchiectasis patients has also been consistently reported [10,16].

The rise in hospitalization rates in bronchiectasis patients in recent years, despite the available effective therapeutics, emphasizes the need for a simple and timely recognition of patients at risk of having more frequent or severe exacerbations in the future [12,18]. PNI is based on the results of peripheral blood tests, which allows easy and objective assessment of the immune-nutritional status of patients in clinical practice [10,16,17]. Therefore, PNI may serve as a simple tool to assess patients with bronchiectasis who are at risk of severe exacerbation/hospitalizations [10,16,17]. However, no study to date has evaluated the predictive value of PNI in bronchiectasis patients in terms of the respiratory-related hospitalizations.

This retrospective study aimed to investigate the performance of PNI to predict the respiratory-related hospitalization risk over the course of a year in patients with bronchiectasis.

Material and Methods

Study Population

A total of 194 patients with bronchiectasis who were treated at a tertiary care chest disease clinic between January 2020 and January 2022 were included in this retrospective cohort analysis. All patients were under routine outpatient follow-up protocol with stable disease without exacerbation or complications such as infections at the time of baseline data collection. Overall, 1456 patients were followed-up with the diagnosis of bronchiectasis at our hospital between January 2020 and January 2022, while the final study population was composed of 194 patients, after exclusion of 1262 patients due to incomplete medical records (n=853), presentation with exacerbation (n=303), lack of access to imaging data (n=78) and presence of comorbidities associated with reduced life expectancy, connective tissue diseases (cancer, dialysis-requiring chronic kidney failure, liver cirrhosis, n=28) (Figure 1).

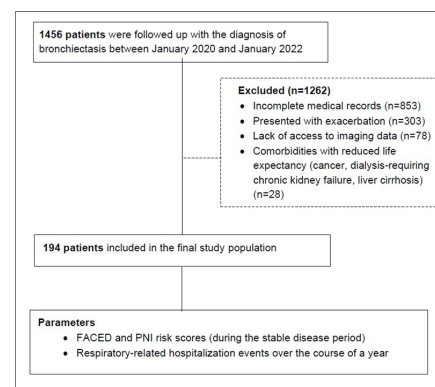


Figure 1. Study flowchart

This study was conducted in accordance with the ethical principles stated in the “Declaration of Helsinki” and approved by University of Health Sciences, İstanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital Ethical Committee (Date of Approval: 01.06.2023, Protocol No: 116.2017.R-300). The informed consent was waived by the ethics committee due to retrospective design of the study.

Assessments

Data on patient demographics, smoking status, comorbid diseases, chronic bacterial colonization (by *P. aeruginosa* and other organisms) and the bronchiectasis pattern were retrieved from hospital records. Baseline laboratory findings, as well as FACED and PNI risk scores were recorded on the day of initial presentation to the outpatient clinic during the stable disease period, while patients were further followed up for respiratory-related hospitalization events over the course of a year.

FACED score was determined based on FEV1% predicted ($\geq 50\%$: 0 points, $< 50\%$: 2 points), age (< 70 years: 0 points, ≥ 70 years: 2 points), chronic colonization by *P. aeruginosa* (no: 0 points, yes: 1 point), radiological extent of the disease (1-2 lobes affected: 0 points, > 2 lobes affected: 1 point), and dyspnea (modified Medical Research Council scale [mMRC] score 0-2: 0 points, 3-4: 1 point) [11].

The isolation of potentially pathogenic bacteria in sputum culture more than once with at least 3 months interval in the same year in a one-year period was considered as the colonization with bacteria.

PNI was calculated via the formula: $10 \times \text{serum albumin (g/dL)} + 0.005 \times \text{peripheral lymphocyte count/mm}^3$ [14,15].

Demographic and clinical characteristics, laboratory findings and FACED and PNI risk scores were evaluated with respect to presence of respiratory-related hospitalization over the course of a year.

Statistical Analysis

Statistical analysis was performed via IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY). Pearson

Chi-square test was used for the comparison of categorical data, while Mann-Whitney U test and Kruskal Wallis tests were used to analyze two and three independent non-normally distributed variables, respectively. ROC curve was plotted to determine the diagnostic performance of PNI and FACED score in identification of hospitalization risk with calculation of area under curve (AUC) values and optimal cut-off value via receiver operating characteristic (ROC) analysis according to the maximal Youden index. Logistic regression analysis was performed to identify independent predictors of hospitalization risk with use of Hosmer-Lemeshow test to determine the goodness of fit of the logistic regression model. Data were expressed as mean±standard deviation (SD), median, minimum-maximum, 25-75%, 95% confidence interval (CI), and percent (%) where appropriate. p<0.05 was considered statistically significant.

Power analysis based on sample size and the mean difference between hospitalized and not-hospitalized groups for the PNI and FACED score revealed the power of study to be >90%.

Results

Demographic and Clinical Characteristics

The mean age of the patients was 55.7±15.5 years, and males comprised 55.2% of the study population. Bronchial asthma was noted in 32.0% of patients, while 25.8% of patients had previous tuberculosis (TB) history and 21.6% were active smokers (Table 1). Cystic bronchiectasis (58.8%) was the most common bronchiectasis pattern and chronic P. aeruginosa colonization was evident in 7.7% of patients. Overall, 51.0% of patients were hospitalized over the course of a year, and 34% were hospitalized for once (Table 1).

Table 1. Demographic and clinical characteristics and hospitalization status (n=194)

Age (year)	Mean±SD	55.7±15.5
	Median (min-max)	56.5 (22-91)
Gender, n (%)		
Female		87 (44.8)
Male		107 (55.2)
Smoking status, n (%)		
None-smoker		82 (42.3)
Active smoker		42 (21.6)
Ex-smoker		70 (36.1)
Comorbid diseases, n (%)		
Bronchial asthma		62 (32.0)
Previous tuberculosis history		50 (25.8)
Hypertension		33 (17.0)
Cardiovascular disease		28 (14.4)
Diabetes		6 (3.1)
Depression		11 (5.7)
Bacterial colonization, n (%)		
by Pseudomonas aeruginosa		15 (7.7)
by other organisms		17 (8.8)
Bronchiectasis pattern, n (%)		
Cystic bronchiectasis		114 (58.8)
Cylindrical bronchiectasis		68 (35.1)
Varicose bronchiectasis		12 (6.2)
Respiratory-related hospitalization over the course of a year, n (%)		
Yes		99 (51.0)
No		95 (49.0)
Number of hospitalization(s) over the course of a year, n (%)		
1		66 (34.0)
2		22 (11.3)
≥3		11 (5.7)

Hospitalization Status with Respect to Demographic and Clinical Characteristics

Patients with hospitalization compared to those without hospitalization were older (median 60.0 vs. 53.0 years, $p<0.001$), while there was no significant gender influence on the hospitalization status. Hospitalization was more common in patients with *P. aeruginosa* colonization vs. those without

P. aeruginosa colonization (86.7% vs. 48.0%, $p=0.004$), and in those with cystic bronchiectasis pattern (60.5%) compared to those with cylindrical (36.8%) or varicose (41.7%) patterns ($p=0.006$). Hospitalization was significantly more frequent in patients with comorbid COPD (75.7 vs. 35.8%, $p<0.001$), comorbid hypertension (72.7 vs. 46.6%, $p=0.006$) and previous tuberculosis history (70.0 vs. 44.4%, $p=0.002$) compared to patients without these conditions (Table 2).

Table 2. Hospitalization status with respect to patient demographics and clinical characteristics

		Respiratory-related hospitalization over the course of a year, n (%)		p value ¹
		No (n=95)	Yes (n=99)	
Patient demographics				
Gender, n (%)				
Female		48 (55.2)	39 (44.8)	0.119
Male		47 (43.9)	60 (56.1)	
Age (year), median (25-75%)		53.0 (42.0-61.0)	60.0 (49.0-72.0)	<0.001 ²
Bacterial colonization, n (%)				
By <i>Pseudomonas aeruginosa</i>	No	93 (52.0)	86 (48.0)	0.004
	Yes	2 (13.3)	13 (86.7)	
By other organisms	No	93 (52.5)	84 (47.5)	0.001
	Yes	2 (11.8)	15 (88.2)	
Bronchiectasis pattern, n (%)				
Cystic bronchiectasis		45 (39.5)	69 (60.5)	0.006
Cylindrical bronchiectasis		43 (63.2)	25 (36.8)	
Varicose bronchiectasis		7 (58.3)	5 (41.7)	
Comorbidities, n (%)				
COPD	No	77 (64.2)	43 (35.8)	<0.001
	Yes	18 (24.3)	56 (75.7)	
Bronchial asthma	No	56 (12.4)	76 (57.6)	0.008
	Yes	39 (62.9)	23 (37.1)	
Hypertension	No	86 (53.4)	75 (46.6)	0.006
	Yes	9 (27.3)	24 (72.7)	
Previous TB history	No	80 (55.6)	64 (44.4)	0.002
	Yes	15 (30.0)	35 (70.0)	
COPD: chronic obstructive pulmonary disease, TB: tuberculosis; ¹ Pearson Chi-square test, ² Mann-Whitney U test				

Hospitalization Status with Respect to Laboratory Findings

Respiratory-related hospitalization was associated with significantly higher values for WBC ($p<0.001$), neutrophil count ($p<0.001$), neutrophil % ($p<0.001$) and CRP ($p<0.001$), and with significantly lower values for lymphocyte count ($p=0.006$), hemoglobin ($p=0.001$), total protein ($p<0.001$) and albumin ($p<0.001$). BMI ($p=0.001$), FEV1 ($p<0.001$) and FEV1 % ($p<0.001$) values were also significantly lower in patients with respiratory-related hospitalization vs. those without respiratory-related hospitalization (Table 3)

Hospitalization Status with Respect to Risk Scores

Median PNI values were significantly lower (46.9 vs. 55.9, $p<0.001$), and FACED scores were significantly higher (3.0 vs. 0.0, $p<0.001$) in patients with without respiratory-related hospitalization vs. those without respiratory-related hospitalization ($p<0.001$) (Table 3).
A further decrease was noted in the median PNI values with the increasing number of hospitalizations, which was 48.2 in patients hospitalized for once, 42.5 in those hospitalized for twice and 40.2 in those hospitalized for three times ($p<0.001$).

Table 3. Hospitalization status with respect to patient laboratory finding and risk scores

	Respiratory-related hospitalization over the course of a year, n(%)		p value
	No (n=95)	Yes (n=99)	
Laboratory findings, median (25-75%)			
WBC (10 ³ /μL)	7.5 (6.2-8.4)	8.1 (6.9-9.3)	0.001
Neutrophil count (10 ³ /μL)	4.2 (3.20-5.1)	4.8 (4.0-6.5)	<0.001
Neutrophil (%)	58.0 (51.0-64.6)	65.0 (55.4-73.0)	<0.001
Lymphocyte count (10 ³ /μL)	2.2 (1.7-2.7)	1.8 (1.3-2.5)	0.006
Lymphocyte (%)	29.0 (25.0-36.1)	22.9 (16.0-30.0)	<0.001
Hemoglobin (g/dL)	13.6 (12.8-15.0)	13.0 (11.5-14.3)	0.001
Platelet (10 ³ /μL)	256.0 (225.0-299.0)	258.0 (215.0-327.0)	0.559
MPV (fL)	9.5 (8.9-10.5)	9.3 (8.7-10.1)	0.263
Total protein (g/L)	70.5 (68.0-75.0)	68.0 (64.0-71.0)	<0.001
Albumin (g/dL)	4.5 (4.3-4.7)	3.80 (3.4-4.1)	<0.001
CRP (mg/L)	3.0 (1.4-3.2)	4.2 (3.0-6.0)	<0.001
FEV ₁ (L)	2.2 (1.7-2.4)	1.1 (8.8-1.7)	<0.001
FEV ₁ (%)	78.0 (68.0-86.0)	50.0 (33.00-65.0)	<0.001
BMI	26.5 (24.1-29.1)	23.4 (21.8-27.0)	0.001
Risk scores, median (min-max)			
PNI	55.9 (44.6-91.5)	46.9 (27.0-68.5)	<0.001
FACED score	0.0 (0.0-4.0)	3.0 (0.0-7.0)	<0.001
WBC: white blood cell, MPV: mean platelet volume, CRP: C-reactive protein, FEV ₁ : forced expiratory volume in 1 second, BMI: body mass index; PNI: prognostic nutritional index; Mann-Whitney U test			

ROC Analysis for Diagnostic Performance of PNI and FACED Score

ROC analysis revealed the PNI to be a potential marker of hospitalization risk in bronchiectasis patients at a cut-off value of <50.55 (AUC: 0.855, 95% CI: 0.800-0.909, p<0.001) with a sensitivity of 90.5% and specificity of 69.7% (Figure 2).

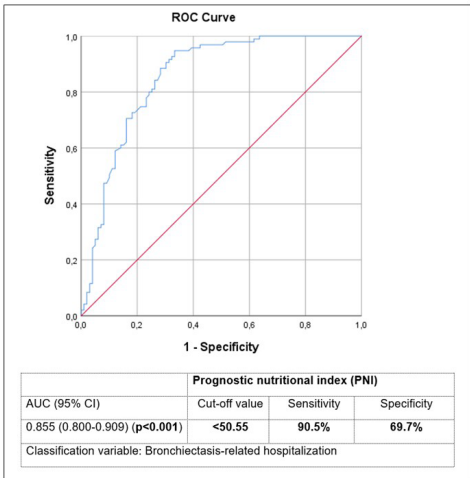


Figure 2. ROC curve analysis of the role of PNI in prediction of respiratory-related hospitalization. AUC: Area under curve

ROC analysis revealed the FACED score to be a potential marker of hospitalization risk in bronchiectasis patients at a cut-off value of >1.5 (AUC: 0.817, 95% CI: 0.757-0.878, p<0.001) with a sensitivity of 66.7% and specificity of 81.1% (Figure 3).

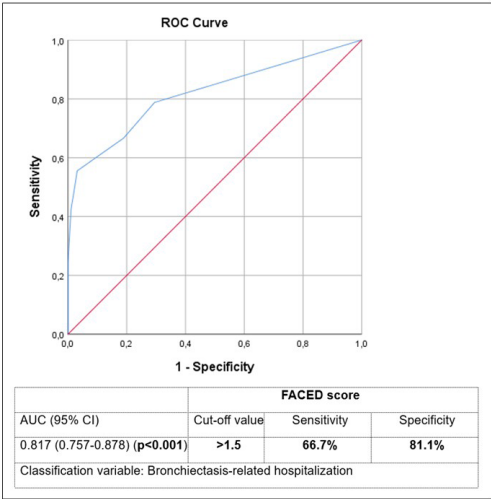


Figure 3. ROC curve analysis of the role of FACED score in prediction of respiratory-related hospitalization. AUC: Area under curve

The diagnostic performance of different PNI and FACED cut-off values in predicting hospitalization is provided in Table 4. The lower cut-off values of PNI were associated with higher specificity (increased from 33.68% at a cut-off value of <58 to 100.0% at a cut-off value of <44) in predicting hospitalization risk. The higher cut-off values of FACED score were associated with higher specificity (increased from 81.05% at a cut-off value of >1 to 100.0% at a cut-off value of >4) in predicting hospitalization risk (Table 4).

Table 4. Diagnostic performance of difference PNI and FACED cut-off values in predicting patients at risk of hospitalization

Cut-off values	Sensitivity (95% CI) (%)	Specificity (95% CI) (%)	Youden index	PPV (95% CI) (%)	NPV (95% CI) (%)	PLR (95% CI)	NLR (95% CI)
PNI							
<44	33.33 (24.18-43.52)	100.00 (96.19-100.00)	0.33	100.00 (89.42-100.00)	59.01 (50.99-66.68)	-	0.67 (0.58-0.77)
<50	67.68 (57.53-76.73)	92.63 (85.41-96.99)	0.60	90.54 (81.48-96.11)	73.33 (64.49-80.99)	9.18 (4.44-18.98)	0.35 (0.26-0.47)
<53	77.78 (68.31-85.52)	74.74 (64.78-83.09)	0.53	76.24 (66.74-84.14)	76.34 (66.40-84.54)	3.08 (2.14-4.42)	0.30 (0.20-0.44)
<58	91.92 (84.70-96.45)	33.68 (24.31-44.11)	0.26	59.09 (50.89-66.94)	80.00 (64.35-90.95)	1.39 (1.19-1.62)	0.24 (0.12-0.49)
FACED							
>1	66.67 (56.48-75.82)	81.05 (71.72-88.37)	0.48	78.57 (68.26-86.78)	70.00 (60.52-78.37)	3.52 (2.27-5.46)	0.41 (0.31-0.55)
>2	55.56 (45.22-65.55)	96.84 (91.05-99.34)	0.52	94.83 (85.62-98.92)	67.65 (59.10-75.41)	17.59 (5.70-54.32)	0.46 (0.37-0.57)
>3	42.42 (32.55-52.77)	98.95 (94.27-99.97)	0.41	97.67 (87.71-99.94)	62.25 (54.01-70.00)	40.30 (5.66-287.02)	0.58 (0.49-0.69)
>4	24.24 (16.19-33.89)	100.00 (96.19-100.00)	0.24	100.00 (85.75-100.00)	55.88 (48.08-63.48)	-	0.76 (0.68-0.85)

PNI: prognostic nutritional index, CI: confidence interval

Logistic Regression Analysis

In logistic regression analysis, the decrease in PNI (OR, 0.782, 95% CI: 0.727-0.840, $p<0.001$) and the increase in FACED score (OR, 2.423, 95% CI: 1.863-3.152, $p<0.001$) were found to be independent determinants of increased respiratory-related hospitalization risk over the course of a year. Overall, 1 unit decrease in PNI, and 1 unit increase in FACED score were associated with the increase in the respiratory-related

hospitalization risk by 1.28 times and 2.42 times, respectively (Table 5, Figure 4).

The logistic regression models including PNI or FACED along with comorbidities (COPD, previous TB, hypertension) revealed no significant association between comorbidities and hospitalization risk in the PNI-based model, while COPD (OR, 3.220, 95% CI: 1.259-8.235, $p=0.015$) predicted increased risk of hospitalization in the FACED-based model (Table 5, Figure 4).

Table 5. Logistic regression analysis for factors predicting respiratory-related hospitalization risk

	B	S.E.	Wald	Sig.	Exp(B)	95% CI for EXP(B)	
						Lower bound	Upper bound
PNI	-0.246	.037	44.412	<0.001	0.782	0.727	0.840
Constant	12.827	1.946	43.465	<0.001	372213.802		
FACED score	0.885	0.134	43.576	<0.001	2.423	1.863	3.152
Constant	-1.206	0.229	27.779	<0.001	0.299		
PNI plus comorbidities/age							
Smoking				0.619	1.298	0.464	3.633
COPD				0.203	1.880	0.711	4.974
Previous TB				0.525	1.352	0.533	3.429
Hypertension				0.270	1.907	0.606	6.006
Age				0.771	0.995	0.965	1.027
PNI				<0.001	0.799	0.739	0.863
Constant				<0.001	246310.951		
FACED plus comorbidities/age							
Smoking				0.321	1.702	0.595	4.867
COPD				0.015	3.220	1.259	8.235
Previous TB				0.164	1.913	0.767	4.773
Hypertension				0.053	3.162	0.987	10.124
Age				0.046	0.967	0.936	0.999
FACED				<0.001	2.605	1.895	3.582
Constant				.177	3.938		

PNI: prognostic nutritional index, COPD: chronic obstructive pulmonary disease, TB: tuberculosis CI: confidence interval

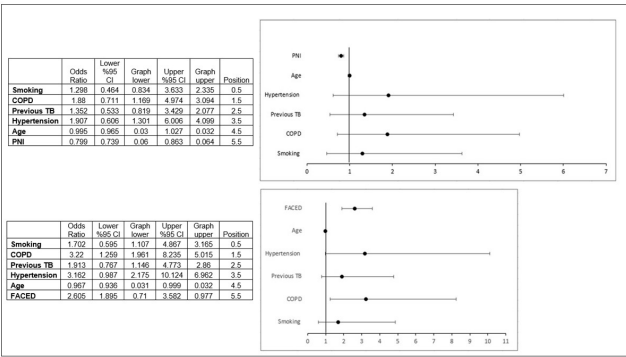


Figure 4. Forest plot showing the Odds ratios, confidence intervals, and p-value for interaction of PNI and FACED with respiratory-related hospitalization risk

Discussion

Our findings in a retrospective cohort of bronchiectasis patients indicated that both PNI (a cut-off value of <50.55) and FACED (a cut-off value of >1.5) are potential markers in discriminating the patients at risk of respiratory-related hospitalization over the course of year. Also, the lower PNI values and the higher FACED scores were independently associated with 1.28 times and 2.42 times higher risk of hospitalization, respectively.

FACED score is a complex tool that evaluates the mortality risk based on concomitant assessment of five parameters [7]. However, in diseases with multidimensional and heterogenous characteristics such as bronchiectasis, the impact of disease cannot be primarily measured in terms of mortality [5].

In a meta-analysis of 17 unique cohorts (6525 bronchiectasis patients) from 10 studies, FACED (a cut-off value ≥5) was found to predict all-cause mortality and to help in predicting hospitalization risk [19].

In our cohort, a FACED cut off value >1.5 (sensitivity 66.7%, specificity 81.1%) was found to identify those patients at risk of respiratory-related hospitalizations. However, a PNI cut-off value <50.55 (sensitivity 90.5%, specificity 69.7%) predicted the hospitalization risk through a simpler algorithm which is based solely on the peripheral blood test. This seems an important advantage of PNI over the FACED which uses a multidimensional (FEV1% predicted, age, colonization by *P. aeruginosa* and mMRC dyspnea scale) scoring system [7]. Hence, PNI seems to be a valuable marker in identifying the bronchiectasis patients at risk of respiratory-related hospitalization, which can simply be calculated by albumin level and peripheral lymphocyte count without needing clinical evaluation [20].

Similarly, low serum albumin levels and the decrease in peripheral lymphocyte count was associated with adverse clinical outcomes in patients with respiratory diseases, as markers reflecting the deterioration in nutritional and immune status [17,21,22]. Low serum albumin levels were also demonstrated to correlate with FACED and BSI scores as well as with increased respiratory related hospitalization in bronchiectasis patients [9,23]. Hence, inclusion of serum albumin level as a parameter in the

bronchiectasis severity scores may serve a simple and relevant prognostic biomarker of disease prognosis [9,13,23].

Accordingly, from a practical perspective, besides its simplicity and easier calculation, the inclusion of albumin in the overall PNI score seems to enable the assessment of a different but important aspect of bronchiectasis severity by reflecting both systemic inflammation and nutritional status [9,13,24]. The combined assessment of PNI and FACED scores may be a useful prognostic tool in predicting respiratory-related hospitalization risk and mortality in bronchiectasis patients and should be further investigated in larger multi-center observational studies.

PNI has also been suggested to be a useful prognostic tool in the setting of COPD, as the presence of a low PNI combined with a high COPD-assessment test (CAT) value increased the risk of an exacerbation in elderly subjects with COPD [16]. In addition, decreased PNI levels at baseline were related to worse hospitalization outcomes in patients with acute exacerbation of COPD [25], while PNI was also found to be an independent predictor for 30-day mortality in these patients [17].

The cut-off values (<50.55) of PNI found for bronchiectasis-related hospitalization in our study seem to be higher than those used for COPD-related exacerbations in elderly (a cut-off 48.8) [16] and COPD-related ICU stay (cut-off 38.5) [20]. Nonetheless, the lower cut-off values of PNI in our study were associated with higher specificity (100.0% at a cut-off value of <44) in predicting hospitalization risk, while the median PNI values (46.9, min-max 27.0 - 68.5) in our hospitalized group may also emphasize the likelihood of high-risk bronchiectasis patients to benefit from nutritional interventions over the course of the disease [10].

CRP and other markers of systemic inflammation are also considered valuable in the context of the interaction between nutritional status and clinical outcomes (i.e., exacerbations) in respiratory disorders including the bronchiectasis [10,26]. In our cohort, respiratory-related hospitalization was associated with significantly higher CRP values but lower hemoglobin, total protein and albumin levels. Likewise, CRP was consistently reported as a valuable marker of inflammation and prognosis in bronchiectasis, alongside its marked correlation with FACED and BSI scoring systems [3,9,11]. Besides, among different chronic respiratory diseases, bronchiectasis has been reported to be the one with the highest CRP level and the lowest BMI, albumin, and prealbumin levels [26]. The association of both serum CRP and serum albumin with the severity of bronchiectasis seems to be consistent with its close relation to chronic inflammation and malnutrition [3,9,11,24].

BMI values were significantly lower in hospitalized patients compared to non-hospitalized patients in our cohort. Similarly, a decrease in BMI was reported to be an independent predictor of increased hospitalization risk in bronchiectasis patients [27]. However, BMI was also reported not to be associated with frequency of hospitalizations or exacerbations in bronchiectasis patients, despite the association of low BMI with a poorer lung

function [10]. These findings emphasize a need for further studies addressing the utilization of better indicators of nutritional status and body composition (i.e., bioelectrical impedance) in bronchiectasis patients [10].

Importantly, more than half of our patients were hospitalized over the course of year, and nearly one-third of these patients were hospitalized for more than once. The further decrease was noted in the PNI values with the increasing number of hospitalizations, emphasizing the likelihood of previous hospitalization to be associated with the risk of future hospitalization, and to significantly contribute to PNI scoring.

In our cohort, comorbid COPD, hypertension and previous tuberculosis history were all associated with increased risk of hospitalization. Hence, concomitant assessment of inflammatory markers and comorbidities may enable a better prognostic tool in bronchiectasis patients, as systemic inflammation is a common risk factor for both bronchiectasis and comorbid conditions [9,28]. In particular, the comorbid COPD and bronchiectasis (overlap syndrome) is considered to reflect a specific clinical phenotype associated with frequent exacerbations, high-volume sputum production, , chronic colonization by *P. aeruginosa* and increased mortality [29,30]. Pulmonary hypertension, cardiovascular disease, cognitive impairment and malignancies (lung, esophageal and hematological) are also considered amongst the comorbidities that can potentially influence the clinical outcomes in bronchiectasis patients [28].

The retrospective design and relatively small number of participants is the main limitation of this study. Also, lack of data on predictive performance of other tools such as BSI or E-FACED, or other relevant outcomes such as mortality are other limitations.

Conclusion

In conclusion, our findings indicate a favorable diagnostic performance of PNI (a cut-off value of <50.55) in discriminating the bronchiectasis patients at risk of respiratory-related hospitalization over the course of year. Also, the lower PNI values were independently associated with the 1.28 times higher risk of hospitalization. Hence, PNI seems to be a valuable marker in identifying the bronchiectasis patients at risk of respiratory-related hospitalization, which can simply be calculated by peripheral lymphocyte count and albumin level and without needing clinical evaluation. Accordingly, use of PNI in clinical practice may enhance bronchiectasis management by assisting timely recognition of at-risk patients and implementation of personalized intensive or preventive treatments in these patients. Nonetheless, the clinical relevance of using PNI in terms of improved clinical outcomes in bronchiectasis patients should be further investigated in larger prospective observational studies.

Conflict of Interests

The authors declare that there is no conflict of interest in the study.

Financial Disclosure

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Ethical Approval

This study was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and approved by University of Health Sciences, İstanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital Ethical Committee (Date of Approval: 01.06.2023, Protocol No: 116.2017.R-300).

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