Dicle Tıp Dergisi / Dicle Med J (2025) 52 (2) : 219-226

www.diclemedj.org

Original Article / Özgün Araştırma

Relationship between Fib-4 score and nutritional status in patients with pulmonary hypertension

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Received: 19.02.2025; Revised: 10.04.2025; Accepted: 11.04.2025

Abstract

Objective: Nutritional status has been associated with poor prognosis in many cardiovascular diseases. Recently, the Fib-4 index, which is a marker of liver cirrhosis risk, has also been investigated in cardiovascular diseases, and its association with poor prognosis has been shown. The goal of this study was to examine the connection between pulmonary hypertension patients' Fib-4 scores and nutritional status.

Methods: 216 individuals who received a pulmonary hypertension diagnosis at our hospital between January 1, 2023, and December 31, 2023, were included in the research. The patients were divided into two groups based on their nutritional status: those who were malnourished (51) and those who were not (162).

Results: Laboratory findings indicated that malnourished patients had significantly lower hemoglobin levels (12.3 ± 2.3 vs. 13.5 ± 2, p=0.002), platelet counts (228 ± 88 vs. 267 ± 123, p=0.044), and albumin levels (3.1 ± 0.4 vs. 4.1 ± 0.4, p<0.001) compared to non-malnourished patients. There was a strong correlation between the FIB-4 index and measures of nutritional status and inflammation.

Conclusions: Malnourished individuals with PAH had greater comorbidity burdens and higher liver fibrosis indices. According to our study's findings, individuals with pulmonary hypertension may benefit from nutritional and liver health evaluations as part of their care to enhance their quality of life and clinical results.

Keywords: Pulmonary hypertension, Fib-4 index, Controlling nutritional status, Prognostic nutritional index

DOI: 10.5798/dicletip.1722822

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Pulmoner hipertansiyon hastalarında Fib-4 skoru ile beslenme durumu arasındaki ilişki

Öz

Giriş: Nutrisyonel düzey birçok kardiyovasküler hastalıkta kötü prognozla ilişkilendirilmiştir. Son zamanlarda karaciğer sirozu riskinin bir belirteci olarak kullanılan Fib-4 indeksi de kardiyovasküler hastalıklarda araştırılmış ve kötü prognozla ilişkisi gösterilmiştir. Bu çalışmanın amacı pulmoner hipertansiyon hastalarında Fib-4 skoru ile beslenme durumu arasındaki ilişkiyi araştırmaktı.

Yöntemler: 1 Ocak 2023 ile 31 Aralık 2023 tarihleri arasında hastanemizde pulmoner hipertansiyon tanısı alan 216 kişi araştırmaya dahil edildi. Hastalar beslenme durumlarına göre iki gruba ayrıldı: yetersiz beslenenler (51) ve normal beslenenler (162).

Bulgular: Laboratuvar bulguları yetersiz beslenen hastaların hemoglobin seviyelerinin (12,3 ± 2,3'e karşı 13,5 ± 2, p=0,002), trombosit sayılarının (228 ± 88'e karşı 267 ± 123, p=0,044) ve albümin seviyelerinin (3,1 ± 0,4'e karşı 4,1 ± 0,4, p<0,001) yetersiz beslenmeyen hastalara kıyasla önemli ölçüde daha düşük olduğunu gösterdi. FIB-4 indeksi ile beslenme durumu ve inflamasyon ölçümleri arasında güçlü bir korelasyon vardı.

Sonuç: Pulmoner hipertansiyonlu yetersiz beslenen bireylerde daha fazla komorbidite yükü ve daha yüksek karaciğer fibrozis indeksleri vardı. Çalışmamızın bulgularına göre, pulmoner hipertansiyonu olan bireyler yaşam kalitelerini ve klinik sonuçlarını iyileştirmek için bakımlarının bir parçası olarak beslenme ve karaciğer sağlığı değerlendirmelerinden faydalanabilirler.

Anahtar kelimeler: Pulmoner hipertansiyon, Fib-4 indeksi, Controlling nutritional status, Prognostik nutrisyonel index

INTRODUCTION

A progressive condition that affects the precapillary pulmonary blood vessels, pulmonary arterial hypertension (PAH) is defined by higher pressure in the pulmonary arteries, brought on by pulmonary vasoconstriction and vascular remodeling, which can result in right ventricular (RV) dysfunction and mortality[1].

Malnutrition has recently been associated with poor outcomes in many cardiovascular diseases[2,3]. The association of malnutrition with poor outcomes in patients with pulmonary hypertension has also been demonstrated in several studies[4,5]. Patients with PH are also at risk of malnutrition for various reasons[5,6]. Prognostic nutritional index (PNI) and controlling nutritional status (CONUT) have been used to measure malnutrition in a variety of cardiovascular disorders. The predictive value of these scores has been demonstrated in PH in some studies and several cardiovascular diseases[7,8].

Applying the FIB-4 index in the cardiovascular area has recently gained attention because liver impairment is a known consequence of chronic heart failure. The FIB-4 index has been linked to coronary atherosclerosis and has been shown to predict cardiovascular events and death in individuals with non-alcoholic fatty liver disease[9,10]. The Fib-4 index has been additionally used in recent studies as a poor prognostic indicator for those with pulmonary hypertension associated with left heart disease[11].

The main goal of this study was to investigate the relationship between pulmonary hypertension patients' nutritional state and Fib-4 score, which is a predictor of worse outcomes in cardiovascular disorders.

METHODS

Study Population

Participants in the research were those having a diagnosis of pulmonary hypertension at our hospital between January 1, 2023, and December 31, 2023. According to the relevant criteria of diagnosis, during resting right cardiac catheterization, individuals with mean pulmonary arteries pressure ≥25 mmHg, pulmonary arterial wedge pressure of below 15 mmHg, and pulmonary vascular resistance >3 Wood units were found to have PAH[12].

Trained medical staff used Dicle University's digital health record system to gather clinical data from the patients who were ultimately included in this study. Demographical clinical factors like gender, body mass index, age, initial treatment status, laboratory tests (complete blood count, liver functions, renal functions, and electrolytes), and detailed echocardiography findings of all participants included in the study were recorded. In our study, certain exclusion criteria were applied to minimize factors that could affect the FIB-4 index and nutritional status.

Participants with chronic liver disorders (cirrhosis, hepatitis B/C, alcoholic liver disease), acute hepatitis, history of malignancy, advanced renal failure, active infections (HIV, tuberculosis, sepsis), autoimmune diseases, NYHA III-IV heart failure, malabsorption syndromes, severe malnutrition or morbid obesity, use of medications affecting liver function, immunosuppressive therapy, excessive alcohol or substance abuse, those with incomplete laboratory data, those with severe COPD or interstitial lung diseases were excluded. After exclusion criteria, analyses were performed with data from 216 patients.

CONUT and PNI scores of the patients were calculated. CONUT scores of 0 and 1 were considered normal, and those with ≥2 were considered malnourished. A PNI score of ≥40 was considered the cut-off value for malnourishment. Patients were split into two groups according to the PNI and CONUT scores. According to both scoring systems, patients with malnutrition were included in the malnourished group (51 patients), and the other patients were included in the non-malnourished group (162 patients). The study was carried out in accordance with the guiding principles of the Declaration of Helsinki. Gazi Yaşargil Education and Research Hospital's ethical committee of the Health Sciences University gave its approval to the project (347-07/02/2025). We do not have patient-informed consent because our study is retrospective.

To avoid bias, malnutrition was defined for patients who were malnourished according to both scores, the identity of the groups was concealed during data analysis, patients with missing data were excluded from the study, and different records (patient files, laboratory results) were compared to avoid relying on a single source.

CONUT, PNI, and Fib-4 index calculation

The patients' total lymphocyte count (TLC), serum albumin, and total cholesterol values were used to calculate the CONUT score. Four groups were created for each characteristic, and scores were given based on the patient's test results (Figure 1). The CONUT score was subsequently established by adding the scores from the three factors. Patients with scores between 0 and 1 were considered normal. Mild and moderate-severe malnutrition were indicated by scores of 2 to 4 and ≥5, respectively[13].

Parameters	*Degree of Malnutrition*			
	Normal	**Mild**	**Moderate**	**Severe**
Serum albumin (g/dL)	≥3.5	3-3.49	2.5-2.99	<2.5
Score	0	2	4	6
Total lymphocyte count (x10^9/L)	≥1.6	1.2-1.59	0.8-1.19	<0.8
Score	0	1	2	3
Total cholesterol (mg/dL)	≥180	140-179	100-139	<100
Score	0	1	2	3

Figure 1: Calculation of the CONUT score

PNI was computed from the formula of 10 × albumin (g/dl) + 0.005 × TLC (per mm3)[14].

The Fib-4 index: [Age (years) Å~ AST (U/L)] / [Platelet count (Å~10^9/L) Å~ √ALT(U/L)][15].

Statistically Analysis

Normality was tested using the Shapiro-Wilk test (for $n < 50$) and the Kolmogorov-Smirnov test (for $n \geq 50$). Non-normal distributions were determined if $p < 0.05$. Normally distributed continuous variables are presented as mean ± Standard Deviation (SD) and compared with Student's t-test. Non-normal variables are presented as median (Interquartile Range, IQR) and compared with the Mann-Whitney U test. Categorical variables are presented as numbers (%) and analyzed with Chi-square (χ^2) or Fisher's exact test (if the expected cell count is <5). Pearson's correlation coefficient (r) was used to establish the correlations of the Fib-4 index. P-values with less than 0.05 were deemed statistically significant.

RESULTS

The total population consisted of 216 participants, of whom 51 (23.6%) were classified as malnourished and 162 (75%) as non-malnourished. The population's average age was 52.5 ± 17.6 years, and the percentage of females was 63.3% (n=95). There was no significant difference in terms of age (p=0.257) and gender (p=0.543) across the groups. Table 1 displays the research population's initial demographic characteristics, split down by nutritional status.

Table I: Baseline characteristics of the total population

Parameters	**Malnourished patients (n=51)**	**Non-malnourished population (n=162)**	**Total Population (n=216)**	**p-value**
Age	54.8 ±17.1	51.3 ±17.9	52.5±17.6	0.257
Female gender, n (%)	34 (66.7)	61 (61.6)	95 (63.3)	0.543
Pulmonary arterial hypertension, n (%)	38 (70.4)	47 (29)	85 (39.4)	**<0.001**
Hypertension, n (%)	27 (52.9)	30 (30.3)	57 (38)	**0.007**
Diabetes mellitus, n (%)	22 (43.1)	20 (20.2)	42 (28)	**0.003**
Coronary artery disease, n (%)	18 (36)	32 (32.3)	50 (33.6)	0.654
Echocardiography findings				
Ejection fraction (%)	56.3±7.9	57.5±6.5	57.1±7	0.287
Left ventricular diameter (cm)	4.2±0.9	4.7±0.5	4.6±0.7	**0.046**
Left atrial diameter (cm)	3.9±0.8	3.9±0.7	3.9±0.8	0.728
Right atrial diameter (cm)	4.6±1	4.4±1	4.5±1	0.190
Right ventricular diameter (cm)	4.2±0.9	4±0.9	4.1±0.9	0.133
TAPSE	2.1±1.4	1.9±0.7	2±1.1	0.480
PAP_{mean} (mmHg)	61.9±30	49.6±22	53.8±29	**0.013**
Laboratory findings				
White blood cell (10^3/μL)	8.1±3.4	8.3±2.1	8.3±2.6	0.614
Hemoglobin (g/dL)	12.3±2.3	13.5±2	13.1±2.2	**0.002**
Platelet count (10^3/μL)	228±88	267±123	254±114	**0.044**
Neutrophil count (10^3/μL)	5.5±2.6	5.1±1.9	5.2±2.1	0.327
Lymphocyte count (10^3/μL)	1.44±0.58	2.3±0.68	2±0.76	**<0.001**
Creatinine (mg/dL)	1.1±0.44	0.77±0.37	0.88±0.41	**0.020**
Total protein (g/dL)	6.4±1.6	7.2±1	6.9±1.3	**0.006**
Albumin (g/dL)	3.1±0.4	4.1±0.4	3.7±0.6	**<0.001**
ALT (U/L)-IQR	13 (10)	16.2 (9.8)	15 (10)	0.517
AST (U/L)-IQR	22 (14)	21 (9.4)	21 (13)	**0.034**
Total cholesterol (mg/dL)	155±43	170±43	165±43	**0.042**
Los-density lipoprotein (mg/dL)	88±31	98.8±33	95±33	0.063
CRP (mg/L)-IQR	1.1 (3.1)	0.33 (0.77)	0.44 (1.1)	**<0.001**
CONUT score-IQR	4 (2)	1 (2)	2 (2.3)	**<0.001**
PNI score	38.6±4.7	52±4.8	47.4±8	**<0.001**
FIB-4 index-IQR	1.48 (1.51)	1.02 (0.91)	1.2 (1.12)	**0.009**

Significant differences were observed in the prevalence of comorbidities between the two groups. Malnourished patients had a higher prevalence of pulmonary arterial hypertension (70.4% vs. 29%, p<0.001), hypertension (52.9% vs. 30.3%, p=0.007), and diabetes mellitus (43.1% vs. 20.2%, p=0.003) compared to non-malnourished patients. No significant difference was observed in the prevalence of coronary artery disease (36% vs. 32.3%, p=0.654).

Echocardiographic findings showed that malnourished patients had a significantly smaller left ventricular diameter (4.2 ± 0.9 vs. 4.7 ± 0.5, p=0.046) and higher mean pulmonary artery pressure (PAPmean) (61.9 ± 30 vs. 49.6 ± 22, p=0.013) compared to non-malnourished patients. The two groups did not vary significantly in terms of TAPSE, left atrial, right atrial, right ventricular diameter, or ejection fraction.

Laboratory findings indicated that malnourished patients had significantly lower hemoglobin levels (12.3 ± 2.3 vs. 13.5 ± 2, p=0.002), platelet counts (228 ± 88 vs. 267 ± 123, p=0.044), lymphocyte counts (1.44 ± 0.58 vs. 2.3 ± 0.68, p<0.001), total protein levels (6.4 ± 1.6 vs. 7.2 ± 1, p=0.006), and albumin levels (3.1 ± 0.4 vs. 4.1 ± 0.4, p<0.001) compared to non-malnourished patients. Additionally, malnourished patients had higher creatinine levels (1.1 ± 0.44 vs. 0.77 ± 0.37, p=0.020), CRP levels (1.1 [3.1] vs. 0.33 [0.77], p<0.001), and FIB-4 index (1.48 [1.51] vs. 1.02 [0.91], p=0.009). White blood cell and neutrophil count, ALT, AST, and total cholesterol levels were not different between the two groups.

Correlation of FIB-4 Index with other parameters

Table 2 shows how the FIB-4 index correlates with other characteristics. The CONUT score (r=0.287, p<0.001), age (r=0.324, p<0.001), and CRP levels (r=0.564, p<0.001) all significantly positively correlated with the FIB-4 index. On the other hand, the FIB-4 index had a negative correlation with the platelet count (r=-0.218, p=0.007), hemoglobin levels (r=-0.205, p=0.012), albumin levels (r=-0.260, p=0.001), and PNI score (r=-0.274, p<0.001). No significant correlations were observed between the FIB-4 index and PAPmean, ejection fraction, TAPSE, or right atrial diameter.

Table II: Correlation of FIB-4 index with other parameters

Age	0.324	**<0.001**
PAP_{mean}	0.059	0.472
Ejection fraction	-0.044	0.590
CONUT	0.287	**<0.001**
PNI	-0.274	**<0.001**
TAPSE	-0.012	0.938
RAD	0.188	**0.048**
Albumin	-0.260	**0.001**
Hemoglobin	-0.205	**0.012**
Platelet	-0.218	**0.007**
CRP	0.564	**<0.001**

These results imply that a higher FIB-4 score, a sign of liver fibrosis, a larger load of comorbidities, and worse echocardiographic and laboratory parameters are all linked to malnutrition. The connection between liver function, nutrition, and systemic inflammation in this group is highlighted by the substantial correlation found between the FIB-4 index and indicators of inflammation and nutritional status.

DISCUSSION

Our results demonstrate that malnourished patients exhibit a higher burden of systemic inflammation, worse echocardiographic parameters, and poorer nutritional and liver fibrosis indices compared to non-malnourished patients. These findings align with previous research and provide further insights into the interplay between malnutrition, liver health, and cardiovascular outcomes.

Malnutrition and pulmonary hypertension

The role of malnutrition in the development and outcome of PAH is becoming more well acknowledged. In line with Kawamoto et al.'s results that malnutrition affects outcomes for PAH patients and exacerbates congestion, our investigation revealed that the prevalence of PAH was considerably greater in malnourished individuals (70.4% vs. 29%, p<0.001).[4] Similarly, Kwant et al. emphasized the role of dietary intervention in managing malnutrition in PAH, suggesting that nutritional support could mitigate disease severity.[5] The elevated mean PAP observed in malnourished patients (61.9 ± 30 vs. 49.6 ± 22, p=0.013) further underscores the hemodynamic burden associated with malnutrition, as highlighted by Simonneau et al. in their updated clinical classification of pulmonary hypertension[1].

The CONUT and PNI scores, which are well-validated tools for assessing nutritional status, were significantly worse in malnourished patients. These findings are consistent with research conducted by Pulley et al.[3] and Kamran et al.[2] who demonstrated that malnutrition is linked with systemic inflammation and poor life quality in chronic disease populations. The elevated CRP levels (1.1 [3.1] vs. 0.33 [0.77], p<0.001) and lower albumin levels (3.1 ± 0.4 vs. 4.1 ± 0.4, p<0.001) in malnourished patients further support the link between malnutrition and inflammation, as previously reported[7,8].

Malnourished individuals had substantially higher levels of the FIB-4 index, a measure of liver fibrosis (1.48 [1.51] vs. 1.02 [0.91], p=0.009), which may indicate that liver dysfunction plays a part in the pathophysiology of malnutrition-related outcomes. This finding aligns with the work of Jin et al.[9] and Vieira Barbosa et al.10 who demonstrated that liver fibrosis indices are independently associated with poor outcomes. The link between the FIB-4 index and markers of congestion, such as PAPmean, further supports the concept of cardio hepatic interactions, as described by Møller et al.[16] and Samsky et al.[17] Additionally, Yoshihisa et al.[18] and Gelow et al.[19] have shown that liver fibrosis scores predict mortality in heart failure patients, reinforcing the clinical relevance of our findings.

Relationship between malnutrition and hepatic fibrosis

Malnutrition leads to periportal steatosis due to mitochondrial/peroxisomal dysfunction in the liver. Decreased protein intake impairs the tricarboxylic acid (TCA) cycle, oxidative phosphorylation, and β-oxidation, thereby reducing ATP production. This triggers hepatic lipid accumulation with amino acid/iron metabolism, microbiota imbalance, and increased lipogenesis; steatohepatitis and fibrosis develop in the long term[20].

According to a study by Li et al., malnourished patients may have higher Fib-4 scores because of reduced liver function, demonstrating that the Fib-4 index is a valid indicator of liver fibrosis[21].

The strong association between malnutrition, systemic inflammation, and liver fibrosis underscores the need for comprehensive nutritional assessment and intervention in high-risk populations, particularly those with PAH and other chronic conditions. Along with liver fibrosis measures like the FIB-4 index, validated instruments like the CONUT and PNI scores can be used to identify individuals who are at risk for negative outcomes and direct focused therapies. Pasini et al.[22] emphasized the importance of addressing muscle wasting and cachexia in chronic heart failure, and our findings suggest that similar approaches may benefit patients with PAH and malnutrition.

Limitations

The study's retrospective design and the small number of malnourished individuals in the sample are two of its many drawbacks.

Furthermore, we are unable to prove a causative link between liver fibrosis, malnutrition, and clinical outcomes due to the cross-sectional character of the research. Our study was limited to a single location; thus, it is impossible to generalize the findings. We could not access data on various factors that may affect nutritional status, such as physical activity level, socioeconomic status, and dietary habits. These deficiencies may have affected the results. Larger cohorts are needed for future studies to validate these findings and look into the potential benefits of dietary and anti-inflammatory treatments in this population.

CONCLUSION

In conclusion, individuals with PAH who are malnourished had larger comorbidity burdens and higher liver fibrosis indices. In this cohort, the FIB-4 index, in particular, is becoming a useful indicator for evaluating liver function and forecasting unfavorable consequences. These results emphasize how crucial it is to incorporate liver health and nutritional evaluations into the management of pulmonary hypertension patients to enhance clinical results and quality of life.

Ethics Committee Approval: The study was carried out in accordance with the guiding principles of the Declaration of Helsinki. Gazi Yaşargil Education and Research Hospital's ethical committee of the Health Sciences University gave its approval to the project (347-07/02/2025).

Conflict of Interest: The authors declared no conflicts of interest.

Financial Disclosure: The authors declared that this study has receivet no financial support.

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