Research Article

Pamukkale Medical Journal
doi:https://dx.doi.org/10.31362/patd.1324430

Relationship between CONUT score and mortality in patients with pulmonary arterial hypertension

Pulmoner arteriyel hipertansiyonlu hastalarda nütrisyonel durum kontrolü (CONUT) skorunun mortalite ile ilişkisi

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Received:09.07.2023 Accepted:19.07.2023

Abstract

Purpose: Data about the association of malnutrition with prognosis in pulmonary arterial hypertension (PAH) is limited. This study aims to evaluate the relationship of Controlling Nutritional Status (CONUT) score with long-term mortality in PAH.

Materials and methods: All consecutive patients newly diagnosed with PAH between 2013 and 2020 were evaluated. CONUT score at diagnosis was calculated through total lymphocyte, albumin and total cholesterol levels. Primary outcome was long-term all-cause mortality. Patients were followed up for 62 (31.3-91.5) months.

Results: 92 patients (mean age=43.9±15.7 years, 65.2% women) were included. 37% of the patients had any degree of malnutrition according to CONUT score (≥2). Patients without malnutrition were significantly more in the low-risk categories of risk stratification tools (44.8% vs 17.6% according to ESC/ERS guideline, *p*=0.03; 70.7% vs 35.3% and 70.7% vs 32.4% according to REVEAL 2.0 and REVEAL Lite 2, *p*<0.01 for both). In multivariate analysis, CONUT score predicted all-cause mortality (HR:1.51, 95% CI:1.01-1.52, *p*=0.03) independently after adjustment with ESC/ERS guideline risk score.

Conclusion: CONUT score is independently associated with worse outcome in PAH patients and may indicate severe disease in this patient group.

Keywords: Pulmonary arterial hypertension, malnutrition, controlling nutritional status score, mortality.

Sungur MA, Sungur A, Can F, Esen Zencirci A, Gungor B, Yildirimturk O. Relationship between CONUT score and mortality in patients with pulmonary arterial hypertension. Pam Med J 2023;16:548-556.

Öz

Amaç: Birçok kronik hastalıkta olumsuz sonuçlarla ilişkili olduğu gösterilen malnütrisyonun, pulmoner arteriyel hipertansiyonda (PAH) prognoz ile ilişkisi net değildir. Bu çalışmada, PAH hastalığında Nütrisyonel Durum Kontrolü (CONUT) skoru ile uzun dönem mortalite arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve yöntem: 2013 ve 2020 tarihleri arasında PAH tanısı alan tüm ardışık hastalar retrospektif olarak incelendi. Tanı anındaki CONUT skoru; toplam lenfosit sayısı, albümin ve total kolesterol düzeyleri ile hesaplandı. Birincil sonlanım uzun dönem tüm nedenlere bağlı mortalite olarak belirlendi. Hastalar 62 (31,3-91,5) ay takip edildi.

Bulgular: Çalışmaya 92 hasta dahil edildi. Ortalama yaşı 43,9±15,7 olan hasta grubunun %65,2'si kadındı. Hastaların %37'sinde CONUT skoruna göre herhangi bir derecede malnütrisyon mevcuttu (CONUT skoru ≥2). Malnütrisyon tespit edilmeyen hastalar, risk değerlendirme skorlarına göre düşük risk kategorisinde anlamlı olarak daha fazla yer almaktaydı (ESC/ERS kılavuzu risk skorlama sistemine göre %44,8'e karşı %17,6, *p*=0,03; REVEAL 2.0 risk sınıflamasına göre %70,7'ye karşı %35,3, *p*<0,01; REVEAL Lite 2 risk sınıflamasına göre %70,7'ye karşı %32,4, *p*<0,01). Çok değişkenli analizde, ESC/ERS kılavuzu risk skoru ile düzeltme yapıldıktan sonra, CONUT skoru (HR:1,51, 95% CI:1,01-1,52, *p*=0,03) uzun dönem tüm nedenlere bağlı mortaliteyi bağımsız olarak öngördürmekteydi.

Sonuç: CONUT skoru, PAH'lı hastalarda kötü prognoz ile ilişkilidir ve bu hasta grubunda hastalığın şiddetini gösterebilir.

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Anahtar kelimeler: Pulmoner arteriyel hipertansiyon, malnütrisyon, nütrisyonel durum kontrolü skoru, mortalite.

Sungur MA, Sungur A, Can F, Esen Zencirci A, Güngör B, Yıldırımtürk Ö. Pulmoner arteriyel hipertansiyonlu hastalarda nütrisyonel durum kontrolü (CONUT) skorunun mortalite ile ilişkisi. Pam Tıp Derg 2023;16:548-556.

Introduction

Progressive remodelling of the pulmonary vasculature and increased pulmonary vascular resistance that eventually leads to right heart dysfunction and death characterize pulmonary arterial hypertension (PAH) [1]. Despite advances in medical therapy, PAH still carries a high morbidity and mortality burden.

Malnutrition is associated with poor prognosis in many chronic diseases. PAH patients are prone to malnutrition due to various disease-related factors [2, 3]. Despite this, role of nutritional status in PAH is unclear since there are few studies on this subject [4-6]. The Controlling Nutritional Status (CONUT) score was developed to assess nutritional status of hospitalized patients by Ignacio de Ulíbarri et al. [7]. It is calculated through serum albumin concentration (as an indicator of protein reserve and inflammation), total cholesterol (TC) level (as a parameter of caloric depletion and inflammation) and total lymphocyte count (TLC, as a parameter reflecting immune system). Since then malnutrition defined by CONUT score was evaluated in various diseases and shown to be associated with prognosis. To our knowledge, there are no studies about CONUT score in patients with PAH in the literature. Therefore, we aimed to evaluate the relationship of CONUT score with prognosis in PAH patients.

Materials and methods

Study design and participants

We retrospectively evaluated all consecutive incident patients with PAH in our hospital between 01.2013 and 01.2020. PAH was diagnosed in patients with mean pulmonary artery pressure ≥25 mm Hg, pulmonary arterial wedge pressure ≤15 mm Hg and pulmonary vascular resistance >3 Wood unit measured during right heart catheterization at rest based on the valid guidelines at the time of diagnosis [1]. Patients <18 years of age; pulmonary hypertension patients other than group 1; patients with estimated glomerular filtration rate <60 ml/min/1.73 m^2, hepatic diseases, hematological or other malignancies; patients that were on antilipidemic drug therapy and patients without essential laboratory data for the assessment of CONUT score at diagnosis were excluded from the study. Permission was obtained from the local ethics committee and the study conformed to the principles in the Declaration of Helsinki.

Demographical, clinical, biochemical, echocardiographic and invasive hemodynamic data at the time of diagnosis were collected from medical records of the patients.

CONUT score

CONUT score was evaluated from TLC, serum albumin and TC levels of the patients. Each parameter was categorized into four groups and scores were assigned according to the levels of the patients' test results (Figure 1). Then CONUT score was calculated as the sum of scores taken from three parameters. Scores of 0 and 1 reflected normal patients. Scores of 2 to 4 and ≥5 indicated mild and moderate-severe malnutrition, respectively [7]. Patients were grouped into two according to presence of any degree of malnutrition (CONUT score <2=Normal patients, CONUT score ≥2=Patients with Malnutrition).

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 Controlling Nutritional Status (CONUT) score

PAH risk assessment

Disease severity at the time of diagnosis was defined using several PAH risk assessment tools: Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL) Lite 2, REVEAL 2.0 and 2015 European Society of Cardiology/European Respiratory Society (ESC/ERS) guideline.

REVEAL Lite 2 score was evaluated using World Health Organization-functional class (WHO-FC), N-terminal pro-brain natriuretic peptide (NT-proBNP), six-minute walking distance (6MWD), estimated glomerular filtration rate, systolic blood pressure and heart rate. REVEAL 2.0 score was assessed using REVEAL Lite 2 variables, etiology, demographics, pericardial effusion, right atrial pressure and pulmonary vascular resistance [8, 9].

ESC/ERS PAH guideline risk score was calculated using available variables; WHO-FC, NT-proBNP, 6MWD, right atrial area, pericardial effusion, right atrial pressure and cardiac index [1].

Then according to calculated risk scores, patients were categorized into low-, intermediate- or high-risk categories.

Outcome and follow-up

The primary outcome was all-cause mortality. Patients were followed up since the diagnosis of PAH. After diagnosis, all patients received guideline-directed optimal PAH-specific drug therapy. None of the patients received lung or lung-heart transplant during follow-up. Dates of death were obtained from medical records.

Statistical analysis

Distribution of the data was determined by Shapiro-Wilk test. Continuous data were presented as mean±standard deviation or median (interquartile range) and categorical data were presented as numbers (percentages). Student's *t*-test or Mann-Whitney *U* test was used to compare continuous data, as appropriate. Categorical data was compared using x^2 or Fisher's exact test, as appropriate. Correlates of CONUT score was defined by Pearson's correlation coefficient (r). Predictors of long-term all-cause mortality was identified with multivariate Cox regression analysis. The results were presented as hazard ratios (HR) and 95% confidence intervals (CI). Survival probabilities of the groups with and without malnutrition were graphically presented with Kaplan-Meier survival curves and compared with log-rank test. Two-tailed *p*-values <0.05 were considered statistically significant. All analyses were performed using R 4.02 software (R Foundation for Statistical Computing, Vienna, Austria) with ''ggplot'' and ''rms'' packages.

Results

A total of 92 patients were included in the study. 65.2% of the patients were women and the mean age of the participants was 43.9±15.7 years. 34 patients had idiopathic PAH (37%), 14 patients had connective tissue disease-associated PAH (15.2%) and 44 patients had congenital heart disease-associated PAH (47.8%). Characteristics of the study group are represented in Table 1 and 2.

Table 1. Baseline clinical characteristics of the study population according to CONUT score

Variables		All (n=92)	Normal (CONUT score <2) (n=58)	Malnutrition (CONUT score ≥2) (n=34)	*p* value
Age (years)		43.9±15.7	42.8±16	45.9±15.1	0.36
Female		60 (65.2)	36 (62.1)	24 (70.6)	0.41
Etiology					
Idiopathic PAH		34 (37)	25 (43.1)	9 (26.5)	0.28
CTD-APAH		14 (15.2)	8 (13.8)	6 (17.6)	
CHD-APAH		44 (47.8)	25 (43.1)	19 (55.9)	
Comorbidities					
Hypertension		21 (22.8)	13 (22.4)	8 (23.5)	0.90
Diabetes Mellitus		12 (13)	7 (12.1)	5 (14.7)	0.72
Atrial Fibrillation		18 (19.6)	8 (13.8)	10 (29.4)	0.07
Body Mass Index (kg/m^2)		24.6±5.8	24.8±5.4	24.7±6.5	0.99
Systolic Blood Pressure (mmHg)		131±29	133±25	136±33	0.66
Diastolic Blood Pressure (mmHg)		75±11.5	78±12	75±13	0.18
Heart rate (beats/min)		86±14	86±13	86±17	0.94
WHO functional class	II	52 (56.5)	39 (67.2)	13 (38.2)	**0.007**
	III-IV	40 (43.5)	19 (32.8)	21 (61.8)	
6MWD (meters)		366±128	402±105	299±142	**<0.001**
ESC/ERS guideline risk assessment tool	low	32 (34.8)	26 (44.8)	6 (17.6)	**0.03**
	intermediate	56 (60.9)	30 (51.7)	26 (76.5)	
	high	4 (4.3)	2 (3.4)	2 (5.9)	
REVEAL 2.0 risk assessment tool	low	53 (57.6)	41 (70.7)	12 (35.3)	**0.003**
	intermediate	16 (17.4)	6 (10.3)	10 (29.4)	
	high	23 (25)	11 (19)	12 (35.3)	
REVEAL Lite 2 risk assessment tool	low	52 (56.5)	41 (70.7)	11 (32.4)	**0.002**
	intermediate	15 (16.3)	6 (10.3)	9 (26.5)	
	high	25 (27.2)	11 (19)	14 (41.2)	
PAH-specific treatment					
Combination treatment		61 (66.3)	37 (63.8)	24 (70.6)	0.50
Long-term mortality		24 (26.1)	13 (22.4)	11 (32.4)	0.29

Categorical data are presented as numbers (percentages) and continuous data are presented as mean ± standart deviation and median (interquartile range), as appropriate, CHD-APAH= Congenital heart disease-associated pulmonary arterial hypertension
CONUT= Controlling nutritional status, CTD-APAH= Connective tissue disease-associated pulmonary arterial hypertension
ESC/ERS= European Society of Cardiology/European Respiratory Society, PAH= pulmonary arterial hypertension
REVEAL= Registry to Evaluate Early and Long-Term PAH Disease Management, 6MWD= 6-minute walking distance
WHO= World Heart Organization. Bold *p* values indicate statistical significance

Table 2. Baseline laboratory, echocardiographic and hemodynamic parameters of the study group according to CONUT score

Variables	All (n=92)	Normal (CONUT score <2) (n=58)	Malnutrition (CONUT score ≥2) (n=34)	*p* value
Laboratory parameters				
Neutrophil (x10^9/L)	4.8±1.6	4.6±1.6	5±1.5	0.29
Lymphocyte (x10^9/L)	2.1±0.8	2.4±0.7	1.6±0.8	***<0.001***
Monocyte (x10^9/L)	0.5±0.2	0.6±0.2	0.5±0.2	0.43
Hemoglobin (g/dL)	14.1±2.4	14.3±2.4	13.4±2.2	0.10
Glucose (mg/dL)	97.3±26.3	92.1±16.3	105.9±36	***0.01***
Creatinine (mg/dL)	0.8±0.2	0.8±0.2	0.8±0.2	0.73
Estimated GFR (ml/min/1.73m^2)	99.8±21.9	101.2±19.6	97.9±25.2	0.48
Total cholesterol (mg/dL)	169±34	184±29	145±29	***<0.001***
Aspartate transaminase (IU/L)	25.1±11.6	24±8.4	26.9±14.9	0.24
Alanine transaminase (IU/L)	22.3±13.6	22.1±12.6	23.1±14.5	0.70
Albumin (g/dL)	4.2±0.5	4.3±0.3	3.9±0.6	***<0.001***
NT-proBNP (pg/mL)	179 (80-480)	119 (48-342)	313 (99-1106)	***0.02***
C-reactive protein (mg/dL)	0.6 (0.2-1.6)	0.4 (0.1-1.1)	1.2 (0.3-2.8)	***0.01***
Echocardiographic parameters				
Right atrial area (cm^2)	21.1±7.2	20.7±8.1	22±5.9	0.43
RV basal diameter (mm)	43.9±9.4	41.7±12.4	45.1±6.4	0.15
TAPSE (mm)	18.4±4.8	18.7±4.3	17.8±4.9	0.34
RV S' velocity (cm/s)	10.7±2.6	11±2.5	9.6±2.6	***0.01***
sPAP (mm Hg)	80±26.7	80.3±27	79.2±26.8	0.84
Inferior vena cava (mm)	19.4±5.3	19.1±5.8	20.4±5.1	0.26
Pericardial effusion	14 (15.2)	5 (8.6)	9 (26.5)	***0.02***
Hemodynamic parameters				
RAP (mm Hg)	10 (7-17)	10 (7-15)	12 (6.8-17.3)	0.64
mPAP (mm Hg)	52±17.5	47±17.3	54.7±17.2	0.23
PAWP (mm Hg)	10 (8-12)	10 (7.5-14)	10 (8.8-12)	0.74
PVR (Wood units)	11 (4.8-19)	8 (5-15.2)	13 (4.3-20)	0.15
Cardiac index (L/min/m^2)	2.2 (1.6-2.7)	2.5 (1.7-3.2)	2.1 (1.6-2.6)	0.11

Categorical data are presented as numbers (percentages) and continuous data are presented as mean ± standart deviation and median (interquartile range), as appropriate, CONUT= Controlling nutritional status, GFR= Glomerular filtration rate
mPAP= mean pulmonary artery pressure, NT-proBNP= N-terminal pro-brain natriuretic peptide, PAWP= pulmonary arterial wedge pressure PVR= pulmonary vascular resistance, RAP= right atrial pressure, RV= Right ventricular
RV S' velocity= Tissue Doppler-derived tricuspid lateral annular systolic velocity
sPAP= systolic pulmonary artery pressure, TAPSE= Tricuspid annular plane systolic excursion
TR= Tricuspid regurgitation, Bold *p* values indicate statistical significance

The prevalence of patients with any degree of malnutrition (CONUT score ≥2) was 37% (n=34). Moderate-to-severe malnutrition (CONUT score ≥5) was encountered in 5.4% (n=5). Demographical variables, PAH etiologies and comorbidities did not differ in patients with and without malnutrition. Body mass indexes of the groups were also similar. Presentation with WHO-FC III-IV was observed more in patients with malnutrition (61.8% vs 32.8%, p<0.01). Significantly shorter 6MWD was found in malnutrition (+) group (299±142 vs 402±105 meters, p<0.001). Patients without malnutrition were significantly more in the low-risk categories of the risk stratification tools at the time of diagnosis (44.8% vs 17.6%, p=0.03 according to ESC/ERS guideline; 70.7% vs 35.3%, p<0.01 according to REVEAL 2.0 and 70.7% vs 32.4%, p<0.01 according to REVEAL Lite 2).

Regarding laboratory parameters, patients with malnutrition had significantly lower levels of the parameters used to calculate CONUT score (TLC, TC and albumin levels). Besides that, they had significantly higher levels of fasting blood glucose, NT-proBNP and C-reactive protein levels.

In echocardiographic examination, pericardial effusion was encountered more in malnutrition (+) group and they had significantly lower tricuspid lateral annular peak systolic velocity than patients without malnutrition. Other echocardiographic parameters and invasive hemodynamic parameters at diagnosis were similar among groups.

CONUT score was negatively correlated with 6MWD (r=-0.398, p<0.001), tricuspid lateral annular peak systolic velocity (r=-0.237, p=0.024) and positively correlated with ESC/ERS (r=0.247, p=0.018), REVEAL 2.0 (r=0.312, p=0.002) and REVEAL Lite 2 risk scores (r=0.369, p<0.001), NT-proBNP (r=0.279, p=0.007) and C-reactive protein (r=0.494, p<0.001).

Mortality occured in 24 (26.1%) patients in the follow-up period of 62 (31.3-91.5) months. Survival rate were 67.6% and 77.6% in malnourished and normal patients, respectively. Kaplan-Meier curves demonstrated a trend towards lower survival among patients with malnutrition without reaching statistical significance (Figure 2). Multivariate analysis (Table 3) revealed that CONUT score, as a continuous variable, is an independent predictor of all-cause mortality (HR:1.51, 95% CI:1.01-1.52, p=0.03) after adjustment with ESC/ERS risk score (HR:6.9, 95% CI:2.4-19.9, p<0.001).

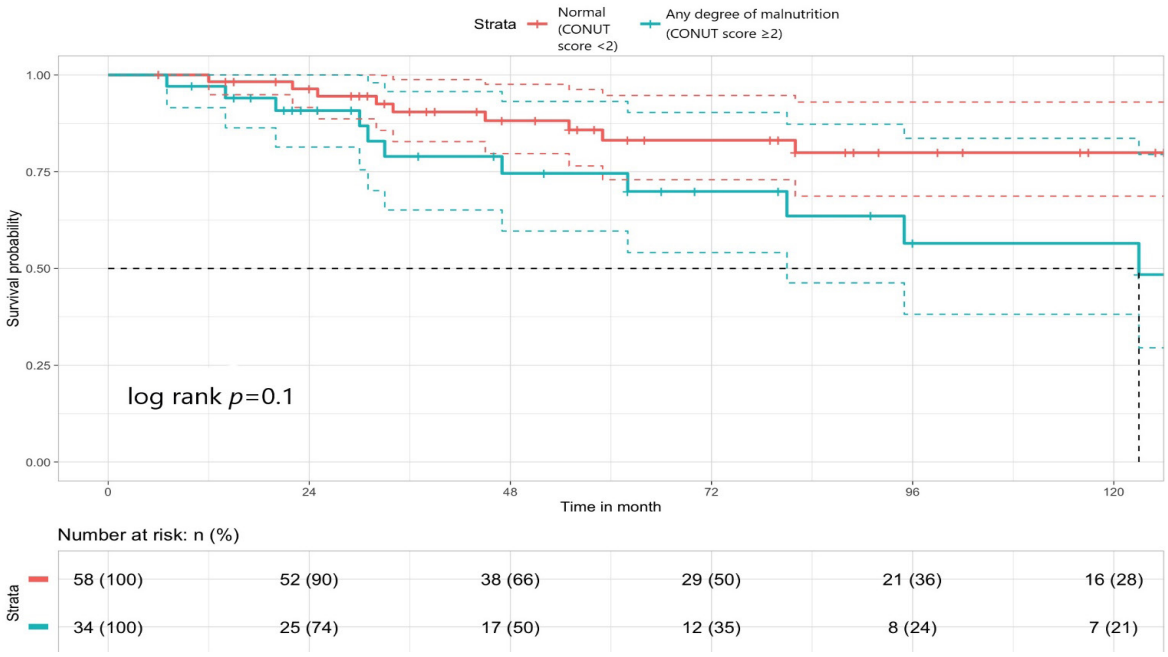

Figure 2. Kaplan-Meier curves for all-cause mortality by the Controlling Nutritional Status (CONUT) score

Table 3. Multivariable Cox regression analysis to predict all-cause mortality

Variables	Hazard Ratio	95% CI	*p* value
ESC/ERS risk score	6.95	2.4-19.9	<0.001
*CONUT, continuous (increase from 0 to 2)	1.51	1.01-1.52	0.03
*Age (increase from 32 to 56)	1.79	0.90-3.53	0.09
*eGFR (increase from 91 to 114)	1.08	0.66-1.78	0.76

*Adjusted with European Society of Cardiology/European Respiratory Society (ESC/ERS) risk score; CI= Confidence interval
CONUT= Controlling nutritional status; eGFR= estimated glomerular filtration rate; Bold *p* values indicate statistical significance

Discussion

Our main findings were: (1) Any degree of malnutrition assessed with CONUT score was observed in 37% of PAH patients, (2) CONUT score predicts long-term all-cause mortality in PAH, (3) CONUT score was related with parameters and risk scores indicating more severe disease.

Malnutrition is common in chronic diseases including heart failure and indicates increased morbidity and mortality [10]. Patients with PAH are at risk of malnutrition due to various reasons. Right heart failure with low cardiac output and venous congestion causing intestinal edema, alterations in gut microbiome, chronic inflammatory status and altered immune function, dysfunctional mitochondrial energy metabolism due to chronic hypoxia, higher prevalence of insulin resistance, changes in gut-derived satiety hormones and side effects of the drugs used in the treatment of the disease can be counted as some of these factors [2, 3]. There are studies reporting vitamin and micronutrient deficiences in patients with PAH more than general population like vitamin D and iron [11, 12]. Guidelines recommend supplemental iron treatment in PAH patients with iron deficiency but other than that, there are no recommendations in the guidelines except general measures like restriction of fluid and salt intake to relieve symptoms of heart failure [1].

Serum albumin concentration, TC level and TLC are commonly used in the assessment of malnutrition. Serum albumin level is frequently used as an indicator of nutritional status but in PAH besides malnutrition decreased serum albumin levels may result from liver dysfunction, systemic inflammatory state or vascular leakage [13, 14]. Snipelisky et al. [6] reported that prevalence of hypoalbuminemia was 25.2% and lower albumin levels were associated with increased mortality in PAH. Low cholesterol levels were defined in chronic illnesses and thought to result from malnutrition and chronic inflammation [15, 16]. Also lower TC level was shown to associate with higher death or lung transplantation risk in PAH together with higher NT-proBNP and lower von Willebrand factor [17]. Nutritional status affects immune cells in terms of number, metabolism and function. In states of malnutrition, lymphocytes, especially T cells, decrease in number due to reduced survival and proliferation [18, 19]. Therefore, TLC, is often incorporated in nutritional scores as a simple measure of the effect of nutrition on immune system. CONUT score, based on serum albumin concentration, TC level and TLC, reflects patients' nutritional, inflammatory and immune status.

Literature about the general nutritional status of PAH patients is limited. We found that 37% of the patients with PAH had any degree of malnutrition based on CONUT score. Luo et al. [4] recently reported 39.7% malnutrition, assessed with prognostic nutritional index (PNI) calculated through serum albumin level and TLC, in patients with idiopathic PAH similar to our findings. As a common finding, clinicians should be aware of malnutrition in patients with PAH and utilize screening tools like CONUT score that are simple to calculate and shown to be related to disease severity and prognosis in our study to identify patients at risk.

We demonstrated that CONUT score was an independent predictor of long-term all-cause mortality in PAH patients after adjustment with ESC/ERS guideline risk score. This is consistent with the findings from Kubota et al. [5] (studied geriatric nutritional risk index in PAH and chronic thromboembolic pulmonary

hypertension) and Luo et al. [4] (assessed PNI in patients with idiopathic PAH) although different nutritional screening tools were employed in different study groups. Low geriatric nutritional risk index, evaluated at diagnosis using serum albumin level and body mass index, was related to mortality and hospitalization in group 1 and 4 pulmonary hypertension [5]. Luo et al. [4] reported a 4% decrease in mortality risk with a one-point increase in PNI in idiopathic PAH. When they categorized patients as normal and malnourished (PNI cut-off 44.8), malnutrition was associated with mortality with borderline statistical significance after adjustment (HR:1.88, 95% CI:1.00-3.52, *p*=0.05). In the present study, when we grouped patients as normal and malnourished based on their CONUT scores and performed survival analysis although the difference between survival curves increased over time, statistical significance was not observed which might be due to small sample size.

To our knowledge, association of nutritional status with disease severity assessed by commonly used and validated PAH prognostic risk scores was not studied before. Patients with any degree of malnutrition according to CONUT score (≥2) had higher WHO-FC, NT-proBNP, lower 6MWD and more frequent pericardial effusion at presentation. And patients with normal CONUT scores at diagnosis presented more with low-risk according to commonly used risk scores in everday practice evaluated in this study. In a small study with 8 stable PAH patients, Kawamoto et al. [20] reported correlation between markers of nutritional status (body mass index, blood urea nitrogen and serum prealbumin) and markers of congestion (estimated pulmonary arterial pressure, inferior vena cava diameter). Contrary to their findings, we observed no significant difference in right ventricular diamaters, inferior vena cava diameter, systolic pulmonary arterial pressure and invasively measured mean pulmonary arterial pressure among groups. In another study, hypoalbuminemia was not found to be associated with parameters like WHO-FC and 6MWD in PAH patients. Only pericardial effusion was more frequent in patients with hypoalbuminemia similar to our results [6]. Important parameters like 6MWD and NT-proBNP were not evaluated in the study of Luo et al. [4] but they observed similar New York Heart Association functional class across PNI quartiles. Unlike our findings, Kubota et al. [5] reported that the severity of pulmonary hypertension was not associated with geriatric nutritional risk index in terms of WHO-FC and NT-proBNP. Invasive hemodynamic parameters were not found to be related with PNI, geriatric nutritional risk index or hypoalbuminemia in these studies, supporting our findings. Although more comprehensive studies are needed on the subject, in the light of the present literature, CONUT score may outperform PNI and geriatric nutritional index in predicting disease severity in patients with PAH.

There are some limitations to our study. Inherit disadvantages secondary to study design exist and casuality can not be determined. Sample size was small which also prevented us from further statistical analysis in this complex disease with different etiologies. CONUT score was not compared with more comprehensive nutritional assessment methods. Changes in nutritional status during follow-up and its relation with mortality were not evaluated.

To conclude, this study showed that malnutrition was common among PAH patients based on CONUT score and CONUT score, an easy to calculate screening tool of nutritional status through routinely taken laboratory parameters, predicts long-term mortality and associated with higher risk in this patient group. Randomized controlled trials are needed to determine how nutrition affects PAH patients' prognosis and whether nutritional intervention can improve the outcome.

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

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Ethics committee approval: Permission was obtained from Haydarpaşa Numune Research and Training Hospital, Clinical Research Ethics Committee (approval date: 27.06.2022, and number: 2022/KK/144)

Authors' contributions to the article

M.A.S., A.S. and O.Y. constructed the main idea and hypothesis of the study. M.A.S., A.S., F.C., A.E.Z., B.G. and O.Y. developed the theory and arranged the material and method section. M.A.S., F.C., A.E.Z. and B.G. have done the evaluation of the data in the Results section. Discussion section of the article was written by M.A.S. and A.S.

M.A.S., A.S., F.C., A.E.Z., B.G. and O.Y. have reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.