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Geriatric nutrition risk index as an indicator of acute exacerbation and mortality risk in patients with idiopathic pulmonary fibrosis

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Abstract

Background Idiopathic pulmonary fibrosis (IPF) is more common in older patients, and malnutrition is also frequently detected in IPF patients.

Aims We aimed to use the Geriatric Nutritional Risk Index (GNRI) to evaluate the risk of malnutrition and investigate the relationships between malnutrition risk, the frequency of IPF exacerbations, and the risk of mortality in this patient group.

Methods In this retrospective study, we evaluated consecutive IPF patients who initiated antifibrotic therapy at our hospital between January 1, 2017 and January 1, 2023, and were 65 years or older. Patients classified the GNRI stage as 'at risk' (< 98 points) or 'not at risk' (≥ 98 points) based on their GNR scores. The two groups were compared in terms of acute exacerbation (AE), hospitalization, and mortality.

Results Our study determined that 41% of patients had malnutrition-related risk at the time of diagnosis. The number of IPF exacerbations was significantly higher in the group at high risk of malnutrition compared to the group without malnutrition risk (2.42 ± 3.42 vs. 0.91 ± 1.67, $p = 0.031$). Additionally, during treatment, mortality rates were also significantly higher in the group at high risk of malnutrition (50.0%) compared to the group without malnutrition risk (20.6%) ($p = 0.025$).

Conclusions The present study demonstrated that malnutrition-related risk was significantly associated with increased IPF exacerbations. Importantly, these results suggest that the assessment of malnutrition-related risk by GNRI provides information for predicting AE and mortality risk in patients with IPF.

Keywords Geriatric nutritional risk index, Idiopathic pulmonary fibrosis, Acute exacerbation, Mortality

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Introduction

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive fibrotic interstitial pneumonia characterized by radiological and histological features of usual interstitial pneumonia (UIP), the cause of which is unknown. IPF typically affects older adults and is distinguished by progressive deterioration of dyspnea and lung function, with a poor prognosis [1]. IPF has a prevalence of 0.33 to 2.51 per 10,000 people in Europe and 2.40 to 2.98 per 10,000 people in North America [2]. The incidence of IPF increases with advancing age, with the average age at diagnosis being 65–70 years [3]. Advanced age, smoking, low body mass index (BMI), environmental exposures, occupational exposures (such as livestock handling), significant comorbidities, genetic predisposition, deteriorating lung function, fibrosis extent, and acute exacerbations can all worsen the prognosis of IPF and shorten survival [2–5].

IPF is more commonly seen in the geriatric patient population due to its onset predominantly after the age of 60. Malnutrition is frequent among IPF patients, and it has been associated with increased hospitalizations, mortality, reduced tolerance for antifibrotic medications, and rapid discontinuation of such therapy [6, 7]. The Geriatric Nutritional Risk Index (GNRI) is a validated nutritional index that uses serum albumin, body weight, and ideal body weight to assess nutritional status. GNRI was developed to evaluate the nutritional status and assess morbidity and mortality associated with malnutrition in older hospitalized patients. Subsequent researches have indicated that low GNRI is related to elevated mortality in patients with infectious diseases and malignancies [7, 8].

While serum albumin levels and BMI are essential markers for evaluating nutritional status, researches have indicated that GNRI offers a more thorough assessment of nutritional condition [9]. Consequently, assessing the risk of insufficient nutrition by GNRI might be beneficial in estimating mortality among IPF patients, exploring the relationships between malnutrition risk and IPF exacerbation frequency, hospitalization, and tolerability of antifibrotic therapy (AFT) in this patient population [7].

Based upon previous studies, we hypothesized that the assessment of malnutrition-related risk by GNRI might provide more information for predicting acute exacerbation (AE) and mortality risk in patients with IPF [7–9].

Methods

Study population

This retrospective cross-sectional study at a single center analyzed data from patients aged 65 and older diagnosed with IPF who initiated AFT at our hospital between January 1, 2017, and January 1, 2023. Of 108 consecutive patients, 75 were aged 65 years or older. Due to inadequate available data, we excluded seventeen patients from the study, leaving us with a final analysis of fifty-eight patients.

The diagnosis of IPF was established in accordance with the criteria stated by the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Association guidelines. Acute exacerbation was identified in accordance with the American Thoracic Society Guidelines [4, 10].

Data collection

We retrospectively obtained clinical data from the patients' medical records. We obtained gender-age-physiology (GAP) indexes, antifibrotic treatment durations, side effects, hospitalization histories, number of adverse events, and mortality from the patients' medical records, along with BMI at the time of diagnosis, laboratory findings, and pulmonary functional test (PFT) results.

Evaluation of the GNRI

Using data from the start of AFT, we calculated the GNRI score as follows: GNRI = [(1.489) serum albumin, g/L] + [(41.7 actual weight/ideal body weight)]. The GNRI was originally divided into four levels: <82, ≥ 82 to < 92, ≥92 to < 98, and ≥ 98 [8]. Our study categorized the GNRI stage into 'at risk' (< 98 points) and 'not at risk' (≥ 98 points) according to the GNRI score due to the low number of patients as, previously performed in the other studies [7, 11].

Statistical analyses

Continuous variables were represented as mean ± standard deviation, while categorical data were represented as numbers and percentages. We used the Kolmogorov-Smirnov goodness of fit test to conduct normality analyses for the continuous variables in the intergroup analysis. We employed the Student's T test for intergroup analysis of normally distributed data, and the Mann-Whitney U test for data deviating from normal distribution. We conducted comparisons of categorical data using either the chi-square test or Fisher's exact test. We initially assessed independent risk predictors for IPF patients using univariate logistic regression analysis (Enter method), which was based on potential factors identified in prior analyses. In the multivariate model, factors that were significant at the ($p < 0.25$) threshold in univariate analyses were evaluated using multiple logistic regression analysis (backward LR). We provided the Hosmer and Lemeshow Test, Omnibus Tests of Model Coefficient, and Nagelkerke R Square values to assess the model fit and significance. We determined overall survival probabilities using the Kaplan-Meier method and assessed disparities using the log-rank test. We utilized Cox proportional hazards regression models to identify

factors correlated with mortality. In the multivariate model, factors that were significant at the ($p < 0.10$) level in univariate analyses were assessed using multivariate Cox regression analysis (backward: LR). Analyses were performed using IBM SPSS version 27.0 (IBM Corporation, Armonk, NY, USA), with a statistical significance threshold set at $p < 0.10$. It was acknowledged as 0.05.

Table 1 Clinical characteristics of IPF patients

	GNRI ≥ 98 (No malnutrition-related risk) (*n* = 34)	**GNRI < 98 (malnutrition-related risk) (*n* = 24)**	***p***
Age, year (mean ± Sd)	71,67 ± 5,34	72,00 ± 5,09	0.818*
BMI (kg/m^2) (mean ± Sd)	28,04 ± 3,82	28,94 ± 3,73	0.374*
Age (*n*, %)			
65–70	15 (%44,1)	9 (%37,5)	0.614****
> 70	19 (%55,9)	15 (%62,5)	
Gender (*n*, %)			
Male	27 (%79,4)	23 (%95,8)	0.123***
Female	7 (%20,6)	1 (%4,2)	
Smoking status (*n*, %)			
Current smoker	2 (%5,9)	1 (%4,2)	0.763****
Ex-smoker	24 (%70,6)	19 (%79,2)	
Never smoker	8 (%23,5)	4 (%16,7)	
Comorbidities (*n*, %)			
Ischemic heart disease	14 (%41,2)	13 (%54,2)	0.329****
Hypertension	17 (%50,0)	9 (%37,5)	0.329****
Pulmonary hypertension	0 (%0,0)	2 (%8,3)	0.167***
Diabetes mellitus	8 (%23,5)	7 (%29,2)	0.629****
GERD	5 (%14,7)	1 (%4,2)	0.385***
Emphysema	2 (%5,9)	3 (%12,5)	0.640***
Initial FVC (%) predicted (mean ± Sd)	85,27 ± 18,44	76,73 ± 18,22	0.093*
1 st year FVC (%) predicted (mean ± Sd)	81,81 ± 18,84	79,00 ± 20,80	0.691*
	$p = 0.047$**	$p = 0.484$**	
Initial DLCO (%) predicted (mean ± Sd)	42,14 ± 16,22	41,04 ± 12,15	0.782*
1 st year DLCO (%) predicted (mean ± Sd)	47,52 ± 16,86	38,16 ± 14,95	0.127*
	$p = 0.360$*****	$p = 0.316$*****	
GAP stage (*n*, %)			
GAP stage I	8 (%23,5)	3 (%13,0)	0.550***
GAP stage II	21 (%61,8)	15 (%65,2)	
GAP stage III	5 (%14,7)	5 (%21,7)	
HRCT patern (*n*, %)			
UIP Pattern	26 (%76,5)	20 (%83,3)	0.712***
Probable UIP Pattern	7 (%20,6)	3 (%12,5)	
Indeterminate for UIP	1 (%2,9)	1 (%4,2)	

* Student's T Test

** Mann Whitney U Test

*** Fisher's Exact Test

**** Chi-square Test

***** Paired Samples T Test

Abbreviations: *IPF* idiopathic pulmonary fibrosis, *GNRI* Geriatric Nutritional Risk Index, *BMI* body mass index, *GERD* gastroesophageal reflux disease, *DLCO* diffuse capacity of the lung for carbon monoxide, *FVC* forced vital capacity, *GAP* gender–age–physiology, *HRCT* high-resolution computed tomography, *UIP* usual interstitial pneumonia

Results

Baseline characteristics and outcomes

Patients were classified into two groups based on GNRI categories, determined by the presence or absence of malnutrition-related risk (GNRI ≥ 98 points or GNRI < 98 points).

There were 34 patients with a GNRI > 98 and 24 with a GNRI < 98. When evaluating groups with and without malnutrition risk, the ages were 72.00 ± 5.09 and 71.67 ± 5.34, respectively. The male sex ratio is 95.8% and 79.4%, with mean BMIs of 28.94 ± 3.73 and 28.04 ± 3.82, respectively. There were no significant differences between the groups in terms of age, sex, BMI, smoking status, or presence of chronic comorbidities ($p > 0.05$). The group at risk of malnutrition had lower FVC (%) and DLCO (%) values before and after AFT, but there were no statistically significant differences ($p = 0.093$, $p = 0.691$, $p = 0.782$, $p = 0.127$, respectively).

In the group without malnutrition, FVC (%) values declined significantly after 12 months of treatment compared to before ($p = 0.047$). When disease severity and radiological findings were compared between the two groups, the GAP index and HRCT patterns were similar ($p = 0.550$ and $p = 0.712$, respectively) (Table 1).

When the treatments received by the groups were evaluated, there was no statistically significant difference between the two groups in terms of receiving USOT treatment, duration of AFT, types of antifibrotic drugs, and their side effects. However, it was found that the number of IPF exacerbations and the percentage of exacerbations were significantly higher in the group at high risk of malnutrition (2.42 ± 3.42 and 66.7%, respectively) compared to the group without malnutrition risk (0.91 ± 1.67 and 38.2%, respectively) ($p = 0.031$ and $p = 0.033$, respectively). Additionally, during treatment, mortality rates were also significantly higher in the group at high risk of malnutrition (50.0%) compared to the group without malnutrition risk (20.6%) ($p = 0.025$) (Table 2).

It was determined that the median values of FVC (%) and DLCO (%) were lower in patients who discontinued AFT compared to those who continued, but the differences were not statistically significant ($p = 0.738$ and $p = 0.288$, respectively). The discontinuation of AFT developed no significant differences based on age, gender, BMI, or malnutrition-related risk ($p > 0.05$) (Table 3).

In univariate analyses performed according to GNRI < 98, it was determined that having a malnutrition-related risk increased the presence of IPF exacerbation

Table 2 Comparison of IPF patients with and without malnutrition risk in terms of treatment, exacerbation, adverse events and mortality

	GNRI ≥ 98 (No malnutrition-related risk) (*n* = 34)	**GNRI < 98 (malnutrition-related risk) (*n* = 24)**	***p***
Duration of antifibrotic treatment, months [median (min-max)]	17 (1–60)	18 (1–71)	0.918*
Duration of İPF, months [median (min-max)]	25 (12–60)	25 (1–76)	0.527*
İPF AE number (mean ± Sd)	0,91 ± 1,67	2,42 ± 3,42	**0.031****
İPF AE, yes (*n*, %)	13 (%38,2)	**16 (%66,7)**	**0.033*****
Number of Respiratory hospitalization (mean ± Sd)	0,74 ± 1,44	1,13 ± 1,70	0.351**
AFT (*n*, %)			
Pirfenidone	11 (%32,4)	14 (%58,3)	0.059***
Nintedanib	22 (%64,7)	8 (%33,3)	
Pirfenidone + Nintedanib (switch)	1 (%2,9)	2 (%8,3)	
AFT adverse events (*n*, %)			
Nausea	11 (%32,4)	6 (%25,0)	0.545****
Hepatic enzyme elevation	7 (%20,6)	4 (%18,2)	1.000***
Weight loss	13 (%38,2)	12 (%50,0)	0.373****
Rash	3 (%8,8)	5 (%20,8)	0.255***
Photosensitivity	3 (%8,8)	2 (%8,3)	1.000***
Loss of appetite	12 (%35,3)	9 (%37,5)	0.863****
Diarrhea	13 (%38,2)	7 (%29,2)	0.474****
Discontinuation of AFT (*n*, %)	6 (%17,6)	4 (%16,7)	1.000***
Dose reduction (*n*, %)	10 (%29,4)	3 (%12,5)	0.202***
Temporary interruption (*n*, %)	9 (%26,5)	6 (%25,0)	1.000***
Switch (*n*, %)	1 (%2,9)	2 (%8,3)	0.564***
LTOT, yes (*n*, %)	10 (%29,4)	12 (%50,0)	0.111****
Death (*n*, %)	7 (%20,6)	**12 (%50,0)**	**0.025*****

* Mann Whitney U Test

** Student's T Test

*** Fisher's Exact Test

**** Chi-square Test

Abbreviations: *IPF* idiopathic pulmonary fibrosis, *GNRI* Geriatric Nutritional Risk Index, *BMI* body mass index, *AE* acute exacerbation, *AFT* antifibrotic therapy, *LTOT* long-term oxygen therapy

by 3.9 times (OR = 3.231, 95% CI = 1.081–9.656, $p = 0.036$) (Table 4).

The presence of IPF exacerbation and male gender remained significant factors in the multivariate multiple logistic regression analysis ($p = 0.020$ and $p = 0.064$, respectively) where gender, IPF exacerbation, and LTOT variables were included in the model.

Table 3 Comparison of age, gender, GNRI, BMI, FVC (%) and DLCO (%) levels according to antifibrotic treatment discontinuation status

	AFT discontinue (*n* = 10)	**AFT continue (*n* = 48)**	***p***
FVC (%)[median (min-max)]	78,5 (57–105)	81,5 (49–114)	0.738*
DLCO (%)[median (min-max)]	31,5 (15–55)	44 (15–76)	0.288*
BMI (mean ± Sd)	28,56 ± 4,04	28,38 ± 3,78	0.896**
Age (n, %)			
65–70	5 (%20,8)	19 (%79,2)	0.726***
> 70	5 (%14,7)	29 (%85,4)	
Gender (n, %)			
Male	8 (%16,0)	42 (%84,0)	
Female	2 (%25,0)	6 (%75,0)	
GNRI < 98			
Yes	6 (%17,6)	28 (%82,4)	1.000***
No	4 (%16,7)	20 (%83,3)	

* Mann Whitney U Test

** Student's T Test

*** Fisher's Exact Test

Abbreviations: *DLCO* diffuse capacity of the lung for carbon monoxide, *FVC* forced vital capacity, *BMI* body mass index, *GNRI* Geriatric Nutritional Risk Index, *AFT* antifibrotic therapy

Table 4 Analysis of variables associated with the risk of malnutrition with univariate logistic regression

	OR (%95 GA)	***p***
Age, >70	1.316 (0.452–3.829)	0.615*
Gender, male	5.963 (0.682–52.113)	0.106*
IPF acute exacerbation, yes	3.231 (1.081–9.656)	**0.036***
Hospitalization	1.178 (0.833–1.665)	0.353*
GAP stage 2	1.905 (0.432–8.394)	0.394*
GAP stage 3	2.667 (0.434–16.390)	0.290*
LTOT, yes	2.400 (0.808–7.126)	0.115*

* Unvariate (Binary) Regression Analysis

Abbreviations: *IPF* idiopathic pulmonary fibrosis, *GAP* gender–age–physiology, *LTOT* long-term oxygen therapy

In our study, IPF patients with GNRI < 98 had a 1-year survival rate of 83.3% and a 3-year survival rate of 53.1%, whereas IPF patients without malnutrition (GNRI ≥ 98) had a 1-year survival rate of 100% and a 3-year survival rate of 78.8% ($p = 0.060$). When considering the factors impacting the risk of mortality, univariate analyses revealed that GAP stage, LTOT, low FVC (%), and low DLCO (%) variables were significant predictors of mortality in IPF patients. The multivariate model demonstrated that the GAP stage and LTOT variables remained significant (Table 5).

Table 5 Prediction of mortality in patients with IPF by univariate and multivariate Cox analyses

	Univariate		Multivariate	
Predictor	**HR (%95 GA)**	***p***	**HR (%95 GA)**	***p***
Age, year	1.060 (0.976–1.151)	0.164*		
Gender, male	1.030 (0.294–3.602)	0.964*		
BMI (kg/m^2)	0.955 (0.845–1.079)	0.460*		
FVC (%)	0.950 (0.917–0.984)	**0.005***		
DLCO (%)	0.948 (0.917–0.984)	**0.004***		
GAP stage	5.770 (2.359–14.110)	**< 0.001***	3.369 (1.243–9.132)	**0.017****
LTOT, yes	5.981 (1.966–18.195)	**0.002***	3.131 (0.890–11.020)	0.075**
Malnutrition-related risk (GNRI < 98)	2.350 (0.916–6.033)	0.076*		
Hospitalization	1.184 (0.983–1.426)	0.075*		
IPF AE number	1.067 (0.952–1.196)	0.268*		
Discontinuation of AFT, yes	1.214 (0.397–3.714)	0.733*		
Temporary interruption, yes	0.500 (0.143–1.750)	0.278*		
Switch, yes	0.495 (0.062–3.924)	0.505*		

* Univariate Cox Regresyon Analizi

** Multivariate Cox Regresyon Analizi (Backward: LR)

Age, gender, FVC (%), DLCO (%), GAP stage, LTOT, Malnutrition-related risk (GNRI < 98), hospitalization number variables included to multivariate model.

Abbreviations: *IPF* idiopathic pulmonary fibrosis, *GNRI* Geriatric Nutritional Risk Index, *BMI* body mass index, *DLCO* diffuse capacity of the lung for carbon monoxide, *FVC* forced vital capacity, *GAP* gender–age–physiology, *LTOT* long-term oxygen therapy, *AE* acute exacerbation

Discussion

The present study demonstrated that malnutrition-related risk was significantly associated with increased IPF exacerbations. Importantly, these results suggest that the assessment of malnutrition-related risk by GNRI provides information for predicting AE and mortality risk in patients with IPF.

Malnutrition is a common disorder among older people. Different indices have been developed to evaluate malnutrition status in various diseases. Mini Nutritional Assessment, Malnutrition Universal Screening Tool (MUST), and Nutritional Risk Index are some of them. In 2005, Bouillanne et al. developed the GNRI, a simple, objective, and practical index used to evaluate the malnutrition status of geriatric patients [8]. Later, this index was used as a prognostic tool for patients in long-term care, acute ischemic stroke, heart failure, peritoneal dialysis, malignancy, and respiratory failure [9, 12–14]. Mochizuka et al. also used this index to evaluate AFT tolerability and rates of mortality in IPF patients [7].

Malnutrition is common among IPF patients. Our study determined that 41% of patients had malnutrition-related risk (GNRI < 98) at the time of diagnosis. Mochizuka et al. found a rate of 37.5% [7]. These findings confirm the frequent occurrence of malnutrition-related risk in older IPF patients.

Several studies have explored the association between malnutrition and increased mortality in patients with IPF [12, 13]. Although the pathophysiological mechanisms underlying this association are not fully elucidated, malnutrition likely contributes to sarcopenia and cachexia, both of which are prevalent in IPF. Recent evidence also highlights the clinical relevance of sarcopenia in ILDs. In IPF, skeletal muscle loss correlates with lower body mass index (BMI) and poorer clinical outcomes, suggesting that BMI may serve as a surrogate marker of muscle wasting [15]. A secondary analysis of the INPULSIS trial supported this, showing that lower BMI (< 25 kg/m^2) and weight loss > 5% over 52 weeks were associated with accelerated FVC decline and reduced survival [16].

Oxidative stress, chronic inflammation, physical inactivity, and overall poor health status have been proposed as potential contributors to weight loss in patients with IPF. Several studies have demonstrated that weight loss is associated with adverse clinical outcomes and poorer prognosis in this population. For instance, Lee et al. reported that weight loss significantly increases mortality risk in patients with IPF [17]. Similarly, Pugashetti et al. found that a 1% annual decline in BMI corresponds to a 5% increase in mortality risk in patients with ILD [18]. In addition, malnutrition has been shown to be common among IPF patients and is associated with both increased hospitalization rates and higher mortality [6]. Yoon et al. identified low BMI as an independent predictor of poor prognosis in IPF, attributing this to hormonal influences on fibrosis, such as adiponectin, which was negatively correlated with BMI and shown to promote collagen synthesis and fibroblast differentiation [5].

The clinical course of IPF is highly variable, making it challenging to predict disease progression. As a result, distinct patient subgroups with differing clinical behaviors and phenotypes have been described [19]. In our study, although mortality rates were higher in the group at high risk of malnutrition, multivariate analysis revealed that only GAP stage and LTOT use were independent predictors of mortality. In contrast to our findings, Mochizuki et al. identified GNRI < 98 as a poor prognostic factor in IPF patients, independent of age, sex, FVC (%), or GAP index. In that study, patients at risk of malnutrition had significantly shorter survival times [7]. Similarly, other studies have reported associations between low BMI or low fat-free mass index and worse outcomes in IPF [15, 20–22]. The lack of statistical significance of GNRI as a mortality predictor in our study

may be attributed to the relatively small sample size. Moreover, it is possible that malnutrition does not act as an isolated risk factor but rather as one component of a broader interplay of clinical determinants influencing prognosis. In our cohort, multivariate analysis showed that only the GAP stage remained a significant predictor for mortality. This finding reinforces the established role of the GAP index as a reliable tool for mortality prediction in IPF, as also demonstrated in previous studies [23].

In our study, we determined that the number and percentage of IPF exacerbations were higher in the group at high risk of malnutrition. Univariate analysis and multiple logistic regression analysis revealed that having a malnutrition-related risk increased the probability of IPF exacerbation by 3.9 times. In a previous study as well, patients at risk of malnutrition were observed to experience more AEs than those who were not at risk [7]. It is widely recognized that acute exacerbations increase in-hospital mortality in IPF patients [12]. Furthermore, GNRI scores are associated with a severity score, which takes into consideration complications such as bedsores or infections related to nutritional status [8]. In our study, the frequency of acute exacerbations, which is directly related to hospitalization, was found to be associated with GNRI status. Previous studies have also demonstrated that malnutrition is associated with increased infection-related mortality [24].This may be explained by the fact that the GNRI is based on serum albumin levels and weight loss, both of which are independent risk factors for mortality in the elderly [25, 26].

Two drugs, nintedanib and pirfenidone, are used safely and effectively in the treatment of IPF. These two antifibrotic drugs have been shown to slow FVC decline by about 50% over a year and lower mortality [4]. However, due to some adverse effects, these medications may be permanently or temporarily discontinued, or the dosage may be lowered. Antifibrotic drug discontinuation rates have been reported to vary between 15 and 45% in various studies [27–29]. Cottin et al. demonstrated that older age and female gender were associated with an increased risk of early discontinuation of pirfenidone treatment [29]. Çilli et al. determined that while adverse events and dose reductions were more common in patients over 70 years of age, discontinuation of AFT was equal in both geriatric and non-geriatric patients [30]. In the study conducted by Yamakawa et al., older age, lower baseline body weight, and weight loss during the first year after initiating nintedanib treatment were significantly associated with a higher rate of treatment discontinuation [12]. Similarly, another study demonstrated that in Japanese patients with IPF treated with nintedanib, advanced age, male sex, smaller body surface area, severe IPF, and lower baseline FVC (%) were associated with an increased risk of early treatment discontinuation [31].

In our study, discontinuation of AFT did not show a statistically significant association with age, sex, BMI, or the presence of malnutrition-related risk. While Mochizuka et al. found a strong association between GNRI < 98 and higher AFT discontinuation rates, our study did not replicate this finding [7]. There may be several explanations for this discrepancy. First, the patient populations differed: our study included Caucasian patients, while theirs focused on East Asians. Ethnic differences in BMI, body composition, drug metabolism, and tolerability may influence treatment adherence. It is well known that BMI in Asian populations tends to be lower compared to populations such as those of Kazakh ethnicity. These ethnic differences in BMI may influence drug tolerability. In the cohort studied by Mochizuka et al., the mean BMI was 23.2, whereas in our patient group, the mean BMI was 28.94 ± 3.73 for those with GNRI > 98 and 28.04 ± 3.82 for those with GNRI < 98. Second, the analytic approaches between the two studies differ. While Mochizuka et al. focused primarily on treatment discontinuation as a key outcome, our study also examined broader treatment management strategies, including AFT switching and temporary interruptions.

Although previous studies have reported higher discontinuation rates among older patients, the underlying reasons remain unclear [32–34]. Frailty and reduced tolerance to adverse effects may play a role. In a study by Uchida et al., a high discontinuation rate (46.4%) was observed, especially among older patients with low BMI and low FVC. Conversely, another study found no difference in adverse effect profiles or treatment discontinuation between patients aged above and below 80 [35]. When evaluating the literature, there are contradictory results about the effect of older age on discontinuation. These inconsistencies may reflect heterogeneity in study populations, particularly in terms of ethnicity, comorbidities, and BMI. Perhaps this suggests that, rather than focusing entirely on age, indices that evaluate age, gender, disease severity, and malnutrition status may be more effective in predicting antifibrotic discontinuation.

In our cohort, adverse effects of AFT did not differ significantly between groups. However, weight loss, anorexia, and diarrhea were more common in patients without nutritional risk, although the differences were not statistically significant. This may suggest that individual factors beyond nutritional status contribute to adverse effect profiles.

Despite the relatively small sample size, our study contributes to the literature by including a distinct ethnic population and examining additional clinical variables such as AFT-related side effects, dose reduction, and treatment interruption.

This study has several limitations. First, it was a single-center, retrospective study. Due to its retrospective

design, we were unable to include all variables that may influence mortality, and unmeasured confounding factors may have influenced the results. Second, the study included only 58 patients, with further subgroup classifications based on GNRI scores. The limited sample size reduces statistical power and may affect the reliability of the multivariate analyses. It also prevented us from evaluating GNRI in more detailed categories (e.g., < 82, ≥82 to < 92, ≥92 to < 98, and ≥ 98). Moreover, our findings may not be generalizable to the entire IPF population, as our cohort consisted exclusively of individuals of Caucasian ethnicity. Finally, GNRI values during follow-up could not be calculated due to missing data, which precluded the assessment of the impact of longitudinal changes in GNRI on prognosis. Future prospective observational studies could provide additional insights into this aspect.

In conclusion, our study demonstrated that geriatric IPF patients at risk of malnutrition, as assessed by the GNRI, experienced more frequent acute exacerbations. GNRI is a practical and objective tool based on routinely available parameters such as serum albumin and body weight, offering a cost-effective method to assess nutritional status. These findings highlight the importance of nutritional evaluation in IPF management. Regular monitoring of GNRI, serum albumin, and weight changes may help identify high-risk patients and guide individualized care strategies in older adults with IPF.

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Author contributions
PPD, İH, PDÇ, SK: contributed to the design and concept of the study. PPD, SK: carried out the data collection. PPD and PDÇ : performed the statistical analyses and data interpretation. PPD, İH and PDÇ: drafted the manuscript. PPD, İH, and PDÇ : checked the final manuscript and revised it critically. All authors read and approved the final manuscript.

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Data availability
The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Ethical Committee of Cukurova University School of Medicine (41–137) and was conducted in accordance with the approved guidelines. The study was planned and conducted in accordance with the principles of the Declaration of Helsinki. The Ethical Committee of Cukurova University School of Medicine waived the need for patient approval and/or informed consent due to the study's retrospective nature.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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