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Applied nutritional investigation

A 1-year follow-up study in patients with idiopathic pulmonary fibrosis regarding adverse outcomes to unintended weight loss

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A B S T R A C T

Objectives: Malnutrition in pulmonary fibrosis may influence clinical outcomes negatively. This project aimed to investigate if weight, unintended weight loss (UWL) at baseline and weight development, and signs of sarcopenia measured by the strength, assistance with the walking, rising from a chair, climbing stairs, and falls questionnaire (SARC-F) are associated with hospital admissions and mortality for idiopathic pulmonary fibrosis outpatients in ≤ 1 y as well as referral to pulmonary rehabilitation.
Methods: At baseline, prevalence of weight and UWL were sought in a cross-sectional questionnaire study, consecutively, including 100 patients in an outpatient clinic. Medical records were sought for time from diagnosis and comorbidities. One year after inclusion weight, UWL and SARC-F were collected by phone interviews, and medical records were revisited for clinical outcomes.
Results: Of the 100 patients, two patients died and seven were lost to follow-up. The prevalence of UWL increased within the year (10−13%), and the amount of UWL increased (9.1−11.8 kg). Patients with a UWL at baseline had a significantly higher risk of mortality (odds ratio = 29.8; $P = 0.037$). UWL at baseline was associated with risk of hospital admissions (odds ratio = 14.7; $P = 0.009$). Based on the results from SARC-F, 20.9% have signs of sarcopenia. UWL at follow-up was associated with the risk of sarcopenia by SARC-F. Patients with risk of sarcopenia and those with body mass index ≥ 30 kg/m^2 were to a higher degree offered pulmonary rehabilitation; however, participation was low.
Conclusions: UWL at baseline was significantly associated with risk of hospital admissions and mortality in ≤ 1 y in idiopathic pulmonary fibrosis outpatients. Patients with signs of sarcopenia and body mass index ≥ 30 kg/m^2 were most often referred to pulmonary rehabilitation.

Introduction

Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease, which is characterized by dyspnea, fatigue, anxiety, and depression as well as reduced functional capacity and health-related quality of life [1,2]. Unintended weight loss (UWL) is common in patients with pulmonary fibrosis and may be a result of decreased caloric intake in combination with increased inflammation. This may lead to disease-related malnutrition, which is defined as a condition due to lack of intake or absorption of nutrition, leading to altered body composition, decreased physical and mental function, altered hospitalizations, and mortality [3−7]. Even though the burdens associated with disease-related malnutrition and UWL are only sparsely investigated in patients with IPF, UWL has been found independently associated with the survival of IPF patients [8−10]. Most studies regarding malnutrition in IPF are cross-sectional and describe a large variation in body mass index (BMI) and UWL [8,10,11]. Although nutritional status in chronic obstructive pulmonary disease in various settings is widely illuminated, including the outcomes and effects of nutritional interventions [12−15], the outcomes of malnutrition as well as the presence of nutrition impact symptoms (NISs), which are modifiable symptoms that have an effect on the ability to eat, for instance

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dyspnea, dry mouth, constipation, and pain [16,17], are not. Furthermore, risks regarding the growing incidence of obesity in IPF are also only sparsely described [9,11,18]. In the study on which this follow-up study is based, a high variation in BMI was found, and, even though the prevalence of UWL in these outpatients was only 18%, the patients lost a mean of 6.2 kg in the past $\leq$3 mo [11]. In the narrative review by Faverio et al. [18], it is suggested that there is a paucity of longitudinal studies that evaluate nutritional issues, also including the prognostic impact of comorbidities on IPF patients. Furthermore, pulmonary rehabilitation has been advocated [19,20]; however, the standard for actually using pulmonary rehabilitation in these patients varies. In the present follow-up study, we aimed to investigate the association between weight, UWL at baseline, weight development and signs of sarcopenia with hospital admissions, and mortality in $\leq$1 y in a cohort of IPF outpatients. Furthermore, we aimed to investigate the participation in pulmonary rehabilitation and the prevalence and associations with signs of sarcopenia measured by the self-reported the strength, assistance with walking, rising from a chair, climbing stairs, and falls questionnaire (SARC-F) [21,22].

Materials and methods

The study design is a follow-up cohort study based on a baseline study and 1-y follow-up data. The data are based on the survey and medical record data from the prevalence study in 100 IPF outpatients of Jensen et. al [11]. At baseline, the patients were recruited in the waiting room before their clinical consultation. The investigator approached the patients and invited them to participate in the study after giving oral and written information about the study. If the patients were willing to participate in the study, they signed the statement of consent, and thereafter the questionnaire was completed along with the measurements of height and weight. Then the patients either completed the questionnaire by themselves or the investigator sat next to them and helped fill it out, based on the patients' information. Follow-up data were collected 1 y after first enrollment, when the patients gave written informed consent for follow-up. Patients' medical records and phone-interviews were used to collect follow-up data. Patient-reported data regarding current weight (double-checked in medical records), SARC-F, and participation in pulmonary rehabilitation were collected from phone-interviews.

A pragmatic convenience sample of 100 patients was used and no power calculation was performed.

Data at baseline

Data used from baseline were the following:

- descriptive information: sex, age (years), BMI (kilograms per square meter), civil status, comorbidity
- NISs
- UWL in the past $\leq$3 mo (kilograms)
- hospitalization information: hospital admissions in the past $\leq$3 mo

Further information regarding the baseline study can be retrieved in the baseline study (Jensen et. al [11]).

Data at 1-y follow-up

Medical record data

Data from the patients' medical records were collected from the electronic patient medical record (clinical suite) before telephone interviews, to be able to clarify data from patient records with patients on the phone, for instance, in case weight was noted very differently in the patient record from what the patient informed. Patient records were assessed for

- all-cause hospital admissions during the past year
- mortality
- the last noted weight and date for this monitoring
- referral to pulmonary rehabilitation
- last noted weight

Medical record data were collected by M. H. and S. L. M. In this follow-up study, we used a 5% cutoff for UWL, according to international guidelines [9,23,24]. This is opposed to the background article, which used a 2-kg UWL.

Therefore, the number of registered patients with UWL varies between the initial publication and this study.

Patient-reported data

Telephone interviews were performed by two research assistants using the same order of questions with all patients. The interview guide was developed with structured interviews and consisted of the following:

- Current weight in kilograms. Patients were asked to weigh themselves if they had not done so the same morning or the day before. If not, an appointment was made for the patient to call back after weighing or to call the patient on the next day after weighing.
- Weight changes in $\leq$1 y (difference between baseline weight and current weight)
- If the patients had experienced a weight change, then the patients were asked if the loss or gain of weight was intentional or unintentional. If a patient-reported weight was different from the weight found in the patient record, this was clarified with the patient.
- SARC-F was fulfilled to assess the degree of sarcopenia risk measured by screening with SARC-F [21,22,25].

The structured telephone interviews each lasted between 20 and 30 min. All data from the interviews were directly entered in the program Research Electronic Data Capture.

Statistics

For data management, Research Electronic Data Capture was used, and for data analysis we used Stata for Windows. Descriptive statistics are presented as number of filled-in-replies (n) and percent (%) or median and 25th and 75th percentiles or mean $\pm$ SD. Mean and SD were used for normally distributed data, whereas median and 25th and 75th percentiles were used for not normally distributed data. The Shapiro-Wilk test was used as test of normality regarding scaled data.

Furthermore, a χ^2 test and simple logistic regression analysis were performed to investigate the association between the dependent and independent variables. A multiple logistic regression analysis was performed to investigate the association between the dependent and independent variables adjusted for sex, age, comorbidity, civil status, and NIS. The dependent variables were UWL at baseline, UWL at follow-up, obesity at baseline, obesity at follow-up, risk of sarcopenia (SARC-F), and offered pulmonary rehabilitation, which were dichotomized variables, "yes" and "no". The independent variables were mortality, hospital admission at follow-up, risk of sarcopenia (SARC-F), offered pulmonary rehabilitation, obesity, overweight, BMI <25 kg/m^2, BMI <18.5 kg/m^2, and finally UWL at follow-up. Hazard ratios were calculated using Cox proportional hazard model regressions. A P < 0.05 significance level and 95% confidence interval were used.

Ethical considerations

Patients gave written informed consent before inclusion in the study and were informed that they could withdraw their consent at any time. The project was approved by the Danish/North Jutland Data Protection Agency (application ID: 2020-119). The ethics committee was approached for project review but replied that, according to the Danish legislation, ethical approval was not required for this study [11].

Results

Demographic data

At baseline [11], 100 patients were recruited for the study. Unfortunately, two patients withdrew their consent, when they were contacted for follow-up. Therefore, 98 patients were included at baseline and 91 patients at follow-up, because two patients died and five patients never picked up the phone and therefore were lost to follow-up.

The median BMI at baseline was 27.8 kg/m^2, and at follow-up the median BMI was 27.4 kg/m^2. Among the remaining patients, 10.2% had a UWL at baseline, whereas 13.2% were found with UWL at follow-up. Mean UWL increased from 9.1 $\pm$ 3.8 kg to 11.8 $\pm$ 5.5 kg. At baseline, 26.5% of the patients had been admitted to hospital in the past $\leq$3 mo from inclusion. Of these, 30.8% of the patients were admitted due to their primary diagnosis and 69.2% for other reasons. At follow-up, 39.6% of the patients had been

Table 1
Demographic data for baseline and 1-y follow-up

Variable	Baseline, *n* = 98 *n* (%) or median (25th−75th percentile) or mean ± SD	Follow-up, *n* = 91 *n* (%) or median (25th−75th percentile) or mean ± SD
Sex (men)	65 (66.3)	60 (65.9)
Age, y	70.5 (60−77)	71 (60−78)
BMI*, kg/m²	27.8 (24.4−30.4)	27.4 (24.6−30.8)
Underweight (<18.5)	3 (3.1)	4 (4.4)
Normal weight (18.5−24.9)	26 (26.5)	23 (25.3)
Overweight (25−29.9)	41 (41.8)	36 (39.6)
Obesity (≥30)	28 (28.6)	28 (30.8)
Unintended weight loss (5% of body weight)	10 (10.2)	12 (13.2)
Unintended weight loss, kg	9.1 ± 3.8	11.8 ± 5.5
Hospital admission in ≤3 mo (yes)	26 (26.5)	
Hospital admission within the past year (yes)		36 (39.6)
Hospital admissions within the past year, *n*	—	2 (1−4)

BMI, body mass index.
*BMI was defined according to World Health Organization definitions of BMI groups.

hospitalized within the year with a median of two hospitalizations. These results are presented in Table 1.

Among the primarily included patients, two of the patients died during the follow-up period. Of the 91 patients available for follow-up, 12.1% were offered pulmonary rehabilitation, and of these 36.4% participated in the rehabilitation. About one-fifth of the patients had a SARC-F score of ≥ 4 and were thus at risk of sarcopenia according to the SARC-F at the time of follow-up (Table 2).

Associations and confounders

Female sex, age ≥71 y, comorbidities, NISs, and UWL at baseline were independently associated with UWL at follow-up. Patients with UWL at baseline had higher OR for mortality (odds ratio [OR] = 29.81 [1.22−728.00]) and admission to hospital during the follow-up period (OR = 14.68 [1.94−110.68]). Patients with BMI ≥30 kg/m² had more comorbidities ($P \leq 0.001$) and had a tendency of being admitted to hospital more often (OR = 3.8 [0.58−24.88]) compared with those with BMI <30 kg/m². No significant associations were found between UWL at follow-up regarding sarcopenia and hospital admissions ($P > 0.05$). Age was found to modify the association between UWL at follow-up and sarcopenia ($P = 0.03$). Patients with UWL at baseline had a tendency of lower OR for UWL at follow-up (OR = 0.43 [0.03 − 5.50]), but the association was not significant ($P > 0.05$) (Table 3).

The background variable, comorbidity, was found to modify the association between severe obesity (BMI ≥30 kg/m²) at follow-up and risk of hospitalization ($P = 0.01$).

Patients with obesity at baseline and at follow-up had a tendency for lower OR for hospital admission (OR = 0.58 [0.20−1.69] and OR = 0.53 [0.18−1.57]); however, these associations were not significant ($P > 0.05$) (Table 4).

Patients with risk of sarcopenia by SARC-F ≥ 4 had higher OR for being offered pulmonary rehabilitation (OR = 5.99 [1.11−32.27]). Furthermore, patients with sarcopenia risk (SARC-F ≥ 4) had higher OR of

Table 2
Clinical outcomes at the time of follow-up

Variable	Follow-up, *n* = 91 *n* (%)
Dead	2 (2.2), *n* = 93
Offered pulmonary rehabilitation	11 (12.1)
Participating in pulmonary rehabilitation	4 (36.4)
Risk of sarcopenia, SARC-F (≥ 4)	19 (20.9)

SARC-F, strength, assistance with walking, rising from a chair, climbing stairs, and falls questionnaire.

being admitted at follow-up (OR = 1.90 [0.52−6.85]), but the association was not significant ($P > 0.05$) (Table 5).

Patients with risk of sarcopenia (SARC-F ≥ 4) and patients obese at follow-up had higher OR for being referred to pulmonary rehabilitation (OR = 6.51 [1.19−35.71] and OR = 5.10 [1.18−22.10]). Furthermore, patients offered pulmonary rehabilitation had lower OR for having a BMI <18.5 kg/m² and UWL at follow-up; however, these associations were not significant (OR = 0.19 [0.01−2.78] and OR = 0.86 [0.07−9.73]). The results are presented in Table 6.

Discussion

In this study, we aimed to investigate the association between IPF outpatients with and without UWL regard to mortality and hospital admissions in ≤1 y after inclusion. Furthermore, we aimed to investigate the referral to and participation in pulmonary rehabilitation and the prevalence and associations of sarcopenia risk measured by self-reported SARC-F (≥ 4). Patients with UWL were found to be at significant higher risk of mortality and hospital admissions. However, the small sample and only two deaths within the year may indicate a bias, even though the *P* value indicates otherwise.

The study suffered a loss to follow-up of seven patients (7%), of whom two declined further participation, and five patients never replied to follow-up phone calls. The five patients who did not reply may have died outside the hospital. Unfortunately, we did not have access to the data system in the municipality.

Two patients were registered as dead before follow-up. According to Dettori et al. [26], a rule of thumb is that < 5% loss minimizes the risk of bias, whereas > 20% poses serious threats to validity. In our study, the group lost to follow-up made no changes to the composition of the group, because the groups in-between are still comparable, because sex and age are practically the same, including an age increase of the past year, and because 70.4 % had a BMI >25 kg/m² at both time points. This higher BMI may be slightly higher than that seen in similar studies of IPF in Western countries [18].

In our study, only 13% of our patients had a UWL >5% after 1 y, which is much less than that found in the study of Perelas et al. [27], who found that 44% of their patients lost >5% of their baseline body weight. However, our populations might not be quite comparable, because they only included patients at the start of IPF treatment; however, they excluded 148 of 228 patients. We included all patients in our cohort consecutively and only excluded those not willing to participate at baseline (*n* = 9) (see initial prevalence

Table 3
The association between unintended weight loss at baseline and follow-up regarding mortality, hospital admission, and risk of sarcopenia

Variable	Unintended weight loss at baseline			
	OR (95% CI) (unadjusted)	P value	OR (95% CI) (adjusted)	P value
Dead (yes)	9.67 (0.56−168.04)	0.119	29.81 (1.22−728.00)	0.037*
Admission (yes)	6.99 (1.40 − 34.99)	0.018*	14.68 (1.94−110.68)	0.009*
	Unintended weight loss at follow-up			
	OR (95% CI) (unadjusted)	P value	OR (95% CI) (adjusted)	P value
Sarcopenia, SARC-F (≥ 4) (yes)	5.08 (1.41−18.23)	0.013*	4.00 (0.99−16.16)	0.052
Admissions (yes)	2.41 (0.70−8.30)	0.162	3.26 (0.61−17.44)	0.168
Unintended weight loss at baseline (yes)	0.94 (0.11−8.35)	0.952	0.43 (0.03−5.50)	0.515

CI, confidence interval; OR, odds ratio; SARC-F, strength, assistance with walking, rising from a chair, climbing stairs, and falls questionnaire.
*$P < 0.05$.

Table 4
The association between obesity at baseline and follow-up regarding mortality hospital admission and risk of sarcopenia

Variable	Obesity (BMI $\geq$30 kg/m^2) at baseline			
	OR (95% CI) (unadjusted)	P value	OR (95% CI) (adjusted)	P value
Dead (yes)	—	—	—	—
Hospital admissions (yes)	0.48 (0.18−1.22)	0.123	0.58 (0.20−1.69)	0.323
	Obesity (BMI $\geq$30 kg/m^2) at follow-up			
	OR (95% CI) (unadjusted)	P value	OR (95% CI) (adjusted)	P value
Risk of sarcopenia, SARC-F (≥ 4) (yes)	2.51 (0.89−7.12)	0.083	1.96 (0.64−5.92)	0.235
Hospital admissions (yes)	0.50 (0.19−1.30)	0.156	0.53 (0.18−1.57)	0.257

—, not enough data to calculate; CI, confidence interval; OR; BMI, body mass index; OR, odds ratio; SARC-F, strength, assistance with walking, rising from a chair, climbing stairs, and falls questionnaire.
*$P < 0.05$.

study [11]). Even though only 13% of our patients suffered UWL during the year of follow-up, and, because our sample is reduced to 91 patients, the meaning of UWL at baseline is statistically significant regarding the clinical outcomes, such as mortality and hospital admissions. UWL at follow-up seems, however, affected by the small sample, because the ORs are high, but, when fully adjusted, statistical significance is not met. As found by Jouneau et al. [8,10], our baseline study confirmed that malnutrition screening should be done in all underweight patients regarding BMI [11].

In the present sample, 11 patients were referred to pulmonary rehabilitation within the past year and only four participated. Pulmonary rehabilitation was typically offered to those who were subject to sarcopenia risk by SARC-F (≥ 4), and those with BMI $\geq$30 kg/m^2. The many patients with high BMI evoke cause for concern, due to a perceived inability for clinicians to spot UWL in these obese patients, when there is no systematic approach to screening. Although clinicians more often referred patients with a high BMI to pulmonary rehabilitation, the actual attendance was low.

Table 5
The association between risk of sarcopenia and hospital admission and offered pulmonary rehabilitation

Variable	Risk of sarcopenia (SARC-F $\geq$ 4)			
	OR (95% CI) (unadjusted)	P value	OR (95% CI) (adjusted)	P value
Admission (yes)	1.5 (0.54−4.15)	0.436	1.90 (0.52−6.85)	0.330
Offered pulmonary rehabilitation	2.48 (.64−9.56)	0.188	5.99 (1.11−32.27)	0.037*

CI, confidence interval; OR, odds ratio; SARC-F, strength, assistance with walking, rising from a chair, climbing stairs, and falls questionnaire.
*$P < 0.05$.

Table 6
The association between offered pulmonary rehabilitation and hospital admission, risk of sarcopenia, obesity, BMI <25 kg/m^2 at follow-up, BMI <18.5 kg/m^2 at follow-up, and unintended weight loss at follow-up

Variable	Offered pulmonary rehabilitation			
	OR (95% CI) (unadjusted)	P value	OR (95% CI) (adjusted)	P value
Admission (yes)	1.31 (0.37−4.68)	0.671	1.78 (0.41−7.82)	0.442
Risk of sarcopenia, SARC-F (≥ 4) (yes)	2.47 (0.64−9.56)	0.188	6.51 (1.19−35.71)	0.031*
Obesity (BMI $\geq$30 kg/m^2) at follow-up	3.16 (0.88−11.42)	0.079	5.10 (1.18−22.10)	0.030*
BMI <25 kg/m^2 at follow-up (yes)	2.01 (0.41−10.17)	0.382	2.85 (0.50−16.20)	0.237
BMI <18.5 kg/m^2 at follow-up (yes)	0.39 (0.04−4.11)	0.433	0.19 (0.01−2.78)	0.224
Unintended weight loss at follow-up (yes)	0.63 (0.07−5.39)	0.671	0.86 (0.07−9.73)	0.897

BMI, body mass index; CI, confidence interval; OR, odds ratio; SARC-F, strength, assistance with walking, rising from a chair, climbing stairs, and falls questionnaire.
*$P < 0.05$.

Because former studies found that more attention should be given to physical activity and rehabilitation in IPF due to the effect on outcomes [8,16,19,20], more attention should maybe be given to a systematic approach on physical performance and body composition, as argued in earlier studies [8,10]. This may serve as an argument for clinicians to refer patients more systematically to early rehabilitation programs and, even more, serve as motivation for patients to participate in rehabilitation programs, keep active, and not increase weight above a BMI ≥ 30 kg/m^2, which may have other concerns regarding comorbidities [10,18]. No consistency between UWL and offering pulmonary rehabilitation was seen. The low degree of referral to and even more participation in pulmonary rehabilitation programs, as recommended by Yu et al. [20], thus needs further attention.

Strengths and limitations

The small sample in this study makes statistical analysis a challenge. However, there are few studies regarding the effect of malnutrition as well as obesity in this diagnosis, and an even smaller number of studies seem relevant for achieving the interest of clinicians and to achieve funding for larger and more in-depth studies. This study relies on information gathered in medical records and on patient-reported outcomes and phone interviews. This suggests a bias of medical staff interpretation before reporting data in records as well as of recall and social desirability bias for patient-reported outcomes. We aimed to structure and secure our data collection as far as possible against patient-reported biases by giving as much structure to the phone call methods as possible. The SARC-F was recently used in telephone interviews, in a study of 951 older adults. This study found similar prevalence between in-person and remote assessments, which suggests that using the SARC-F by phone interview is a reliable alternative for sarcopenia and low muscle function risk assessment [25].

Conclusions

IPF outpatients with UWL had a higher risk of mortality and hospitalizations in ≤ 1 y and a higher risk of sarcopenia by SARC-F screening. Few patients were referred to pulmonary rehabilitation. Patients with BMI ≥ 30 kg/m^2 and those with risk of sarcopenia by SARC-F were referred to pulmonary rehabilitation more often; however, even for those referred to pulmonary rehabilitation, participation was low. Based on this study, UWL, high BMI, body composition, and a low degree of physical rehabilitation participation, including a systematic approach to tertiary rehabilitation, should be the focus of further investigations.

Acknowledgments

References

[1] Richeldi L, Collard HR, Jones MG. Idiopathic pulmonary fibrosis. Lancet 2017;389:1941–52.

[2] Rozenberg D, Sitzer N, Porter S, Weiss A, Colman R, Reid WD, et al. Idiopathic pulmonary fibrosis: a review of disease, pharmacological, and nonpharmacological strategies with a focus on symptoms, function, and health-related quality of life. J Pain Symptom Manage 2020;59:1362–78.

[3] Collins PF, Stratton RJ, Kurukulaaratchy RJ, Elia M. Influence of deprivation on health care use, health care costs, and mortality in COPD. Int J Chron Obstruct Pulmon Dis 2018;13:1289–96.

[4] Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017;36:49–64.

[5] Lelli D, Tolone S, Pulignano G, Tinti MD, Del Sindaco D, Dipasquale Mazzilli G, et al. Nutritional status is associated with physical function and disability in older adults with chronic heart failure. Eur J Intern Med 2020;74:73–8.

[6] Gomes F, Schuetz P, Bounoure L, Austin P, Ballesteros-Pomar M, Cederholm T, et al. ESPEN guidelines on nutritional support for polymorbid internal medicine patients. Clin Nutr 2018;37:336–53.

[7] Bosch X, Monclús E, Escoda O, Guerra-García M, Moreno P, Guasch N, et al. Unintentional weight loss: clinical characteristics and outcomes in a prospective cohort of 2677 patients. PLoS One 2017;12:e0175125.

[8] Jouneau S, Crestani B, Thibault R, Lederlin M, Vernhet L, Valenzuela C, et al. Analysis of body mass index, weight loss and progression of idiopathic pulmonary fibrosis. Respir Res 2020;21:312.

[9] Nakatsuka Y, Handa T, Kokosi M, Tanizawa K, Puglisi S, Jacob J, et al. The clinical significance of body weight loss in in idiopathic pulmonary fibrosis patients. Respiration 2018;96:338–47.

[10] Jouneau S, Kerjouan M, Rousseau C, Lederlin M, Llamas-Guttierez F, De Latour B, et al. What are the best indicators to assess malnutrition in idiopathic pulmonary fibrosis patients? A cross-sectional study in a referral center. Nutrition 2019;62:115–21.

[11] Jensen BD, Mikkelsen S, Krogh PH, Lingholm CH, Huremovic J, Holst M. Risk of malnutrition in pulmonary fibrosis outpatients. Am J Res Med Sci 2021;6:1–5.

[12] Deutz NE, Ziegler TR, Matheson EM, Matarese LE, Tappenden KA, Baggs GE, et al. Reduced mortality risk in malnourished hospitalized older adult patients with COPD treated with a specialized oral nutritional supplement: sub-group analysis of the NOURISH study. Clin Nutr 2021;40:1388–95.

[13] van Beers M, Rutten-van Mölken MPMH, van de Bool C, Boland M, Kremers SPJ, Franssen FME, et al. Clinical outcome and cost-effectiveness of a 1-year nutritional intervention programme in COPD patients with low muscle mass: the randomized controlled NUTRAIN trial. Clin Nutr 2020;39:405–13.

[14] Creutzberg EC, Wouters EFM, Mostert R, Weling-Scheepers CAPM, Schols AMWJ. Efficacy of nutritional supplementation therapy in depleted patients with chronic obstructive pulmonary disease. Nutrition 2003;19:120–7.

[15] Vermeeren MAP, Wouters EFM, Geraerts-Keeris AJW, Schols AMWJ. Nutritional support in patients with chronic obstructive pulmonary disease during hospitalization for an acute exacerbation; a randomized controlled feasibility trial. Clin Nutr 2004;23:1184–92.

[16] Nordén J, Grönberg AM, Bosaeus I, Forslund HB, Hulthén L, Rothenberg E, et al. Nutrition impact symptoms and body composition in patients with COPD. Eur J Clin Nutr 2015;69:256–61.

[17] Christensen T, Mikkelsen S, Geisler L, Holst M. Chronic obstructive pulmonary disease outpatients bear risks of both unplanned weight loss and obesity. Clin Nutr ESPEN 2022;49:246–51.

[18] Faverio P, Bocchino M, Caminati A, Fumagalli A, Gasbarra M, Iovino P, et al. Nutrition in patients with idiopathic pulmonary fibrosis: critical issues analysis and future research directions. Nutrients 2020;12:1131.

[19] Cheng L, Tan B, Yin Y, Wang S, Jia L, Warner G, et al. Short- and long-term effects of pulmonary rehabilitation for idiopathic pulmonary fibrosis: a systematic review and meta-analysis. Clin Rehabil 2018;32:1299–307.

[20] Yu X, Li X, Wang L, Liu R, Xie Y, Li S, et al. Pulmonary rehabilitation for exercise tolerance and quality of life in IPF patients: a systematic review and meta-analysis. Biomed Res Int 2019;2019:1–9.

[21] Malmstrom TK, Morley JE. SARC-F: a simple questionnaire to rapidly diagnose sarcopenia. J Am Med Dir Assoc 2013;14:531–2.

[22] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16–31.

[23] Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition − a consensus report from the global clinical nutrition community. J Cachexia Sarcopenia Muscle 2019;10:207–17.

[24] Barazzoni R, Sulz I, Schindler K, Bischoff SC, Gortan Cappellari G, Hiesmayr M. A negative impact of recent weight loss on in-hospital mortality is not modified by overweight and obesity. Clin Nutr 2020;39:2510–6.

[25] Frenzel AP, Bielemann RM, Barbosa-Silva TG, Gonzalez MC. Applicability of the SARC-F questionnaire by remote interview. Nutrition 2022;105:111871.

[26] Dettori JR. Loss to follow-up? Ann Thorac Surg 2017;103:1037.

[27] Perelas A, Glennie J, van Kerkhove K, Li M, Scheraga RG, Olman MA, et al. Choice of antifibrotic medication and disease severity predict weight loss in idiopathic pulmonary fibrosis. Pulm Pharmacol Ther 2019;59:101839.