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# RESEARCH ARTICLE 8 Open Access

# Risk of malnutrition in pulmonary fibrosis outpatients

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## **ABSTRACT**

**Background:** Literature is sparse regarding disease related malnutrition (DRM) among patients with pulmonary fibrosis. We aimed to investigate the prevalence of unintended weight loss (UWL) within three months, reduced food intake (RFI) within the past week, and associations to nutrition impact symptoms (NIS), in an outpatient population of patients with pulmonary fibrosis.

**Methods:** The prevalence of UWL and NIS were sought in a cross-sectional questionnaire study, consecutively including a convenience sample of 100 patients, as they visited the outpatient clinic. Medical records were sought for time from diagnosis and comorbidities. Associations were examined through Chi square and simple logistic regression analysis.

**Results:** Among the 100 included patients, 66% were male, mean age was 68.1(SD 12.9), and BMI was 27.9 (SD 5.9). UWL was found in 18 (18%) with a mean weight loss of 6.2 Kg (SD 3.9), 16% had RFI and 7% had both UWL and RFI. Patients with RFI and NIS had higher odds for UWL. Women, no education and living alone were the most associated risk factors for UWL.

**Conclusion:** UWL was seen in almost one fifth of pulmonary fibrosis outpatients. Patients with NIS and RFI had higher odds for UWL. UWL seems feasible for initial nutritional risk screening in pulmonary fibrosis outpatient clinics, and may serve as an indication for the need for full screening and assessment.

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Pulmonary fibrosis, Disease related malnutrition, Weight Loss, Nutritional screening, Nutrition Impact Symptoms, Cross sectional investigation, Questionnaire.

# Introduction

Malnutrition is common in acute and chronic diseases and is known to have severe consequences for the individual and the society [1]. Malnutrition is defined as a condition due to lack of intake or absorption of nutrition, leading to altered body composition, decreased physical and mental function, hospitalizations and mortality [2]. Weight loss among patients with pulmonary fibrosis is not uncommon and may occur as a consequence of decreased caloric intake, protein-energy malnutrition and gastrointestinal side effects from anti fibrotic therapy [3]. It has been shown that 44% of patients with pulmonary fibrosis lost 5% of their body weight while 15% lost 10% of their body weight after 12 months of anti-fibrotic medicine care [4]. A similar association was found in a study that showed a significant prevalence of unintended weight loss (UWL) in 15-20% of patients with pulmonary fibrosis [5]. Furthermore, another study found that 28% of patients with pulmonary fibrosis in general practice and hospital, suffered from malnutrition, using a bioimpedance analysis for assessment [6]. They also found that the male gender, smoking and high body mass index (BMI) was significantly associated with lower risk of malnutrition [6]. In a Danish context, the prevalence of UWL was 26% among 713 patients visiting five different outpatient clinics [7]. In the outpatient clinic for pulmonary diseases, 28% of the 124 included patients had UWL, with a mean UWL of 5.5 kilos [8]. The study however did not differentiate between diagnosis, and thus gave no indication of whether or how UWL appears in pulmonary fibrosis outpatients. No Danish studies have investigated nutritional risk in pulmonary fibrosis. Even though literature is sparse, it seems that there may be a relation between a negative prognosis for pulmonary fibrosis and the presence of malnutrition. Nutritional risk is found by screening, and specific screening tools are validated towards indication for indication for nutritional intervention in those at nutritional risk by screening [9-11]. Most screening tools include the aspect of UWL, which has also been used as a primary marker for nutritional risk in former studies regarding pulmonary fibrosis and outpatient clinics [3-5,8,12]. Nutrition impact symptoms (NIS) [13-15], are commonly associated to UWL, however not reported in pulmonary fibrosis.

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The aim of this study was to examine the prevalence of UWL, in an outpatient clinic for pulmonary fibrosis patients in Denmark, and to identify possible associations between UWL and risk factors for UWL as NIS. We furthermore aimed to find if UWL within three months, is feasible and may serve as relevant measure for the indication of need for full screening of nutritional risk in the busy outpatient clinic.

#### **Material and Methods**

#### Study objects

The setting is a 900 bed university hospital in Denmark. The outpatient clinic for pulmonary fibrosis is organized and physically placed within the Department of Pulmonary Diseases. The pulmonary fibrosis population visiting the outpatient clinic is a quite heterogeneous population in terms of diagnosis and severity. It currently consists of 370 patients. Some patients receive treatment which involves steroid and sometimes also immunosuppressive treatment, and some are checked in the outpatient clinic without treatment if the disease is not quite pronounced and shows no signs of worsening. The most common diagnoses are allergic alveolitis (hypersensitivity pneumonitis), eosinophilic pneumonia, sarcoidosis, cryptogenic organizing pneumonia, connective tissue disease-associated interstitial lung disease, and respiratory bronchiolitis-interstitial lung disease. Some patients do not have a definite diagnosis if their condition does not allow this due to current state or comorbidities. Some patients need oxygen therapy and have a very limited level of function, while some get well and can quit therapy. Many have a history over a few years.

The outpatient clinic staff consists of one consultant with specialization and shifting younger doctors during their specialization. Four to five nurses are associated with the group, and take care of the different examinations, however these nurses also have tasks in other patient groups. Patients with the most severe pulmonary fibrosis (IPF) are sent to the nearest other university hospital for initiation of anti-fibrosis therapy or invasive investigations in case of uncertain diagnosis. In this study we did not differentiate within diagnosis.

All patients visiting the outpatient clinic were invited through personal contact to participate in the study. The patients were informed about the main study objective and before participating the patients were informed and asked to sign a statement of consent.

## Study design

A cross sectional, questionnaire study design using patient reported data as well as data collected through patients' medical records. The patients were recruited in November and December 2020. The sample size was pre-determined to a pragmatic convenience sample of 100 patients, as there was no identification in the literature to complete a calculation of power.

## **Methods**

The questionnaire was based on the questionnaire used for the aforementioned outpatient setting investigations [7,8]. It was however modified for this study's accurate purpose and participants by completing a pilot test on ten patients in the target group. Afterwards the questionnaire was readjusted. The data was collected at the pulmonary fibrosis outpatient clinic. UWL within three months was defined as an UWL of two kilos or more. RFI was defined as an estimated intake of less than 75% compared to usual. Before the clinical consultation the researcher approached the patient and explained the main study objective, in a quiet spot in the patient waiting room. Patients had the option to go through the questionnaire in the waiting room, or to be taken to the assigned study space. Patients then voluntarily completed the questionnaire after they had signed the statement of consent. If the patient needed help to fill out the questionnaire, the researcher stepped in to assist as needed. Data collection was shared by seven researchers.

The patient record data were extracted through the Hospital's medical record database "clinical suite". All the data was managed in the data management program REDCap, and the statistical analysis was completed in STATA.

#### **Statistics**

Data were double checked and 999 indicated missing data. Descriptive statistic was made. The data are presented as the number of filled-in-replies (N) and percent (%) or mean ± standard deviation (SD). The primary outcome of the study was malnutrition defined as UWL within the past 3 months, which was reported as a dichotomized variable "yes" or "no". UWL was handled as a dependent variable and the other variables were handled as independent variables. Reduced food intake within the past week (RFI), NIS, time from diagnosis, comorbidity and smoking were selected as potential risk factors, on the basis of the literature and with guidance from doctors in the outpatient clinic [1,8,16,17]. BMI was dichotomized according to WHO definition of normal weight and overweight/obesity, i.e. patients with "BMI ≤24,9" and patients with "BMI>25" [18].

Chi<sup>2</sup> test and a simple logistic regression analysis were performed to determine the association between the independent variables and UWL. For all analyzes a significance level of 0.05 (p<0.05) was used as well as 95% confidence interval (95%CI).

Furthermore, a simple logistic regression was used to obtain the OR for the independent variables effect on UWL. The regression describes the relationship between the dependent binary variable UWL and the independent variables.

#### **Ethics**

The North Jutland Ethical committee was approached for project review, but according to the Danish legislation, ethical approval was not required for this study. The project was approved by North Jutland data protection agency, application ID: 2020-119.

### **Results**

#### **Demographic information**

In this study, patients from the outpatient clinic for pulmonary fibrosis were included until 100 participants was reached. Nine patients declined participation, thus 109 patients were approached for participation. Of the participating patients 66% were men. The mean age was  $68.1 \pm 12.9$  years and mean BMI was  $27.9 \pm 5.9$  kg/m². Among the 100 patients 18% have had UWL and mean weight loss was  $6.2 \pm 3.9$  kg. Furthermore, 16% had RFI and 7% had both UWL and RFI. All patients with RFI also

had UWL. Only 5% of the included patients had an intended weight loss. Demographic data are presented in Table 1.

Variable	N (%) or mean ± SD	
Sex (men %), N=100	66 (66.0)	
Age, years (Mean, SD), N=100	68.1 ± 12.9	
BMI, kg/m <sup>2</sup> (Mean, SD), N=100	27.9 ± 5.9	
Unintended weight loss(%), N=100	18 (18)	
Unintended weight loss(Mean, SD), kg	$6.2 \pm 3.9$	
Reduced food intake (%), N=100	16 (16.0)	
Reduced food intake + unintended weight loss (%)	7 (7.0)	
Intended weight loss (%), N=100	5 (5.0)	

**Table 1:** Demographic data.

# **Nutrition impact symptoms (NIS)**

Among the included patients, 32 patients had reported NIS regarding UWL and RFI. The most common NIS were lack of appetite (76.2%), shortness of breath (40.6%), pain (25.0%), nausea (21.9%) and worries (21.9%) (Table 2).

Nutrition impact symptoms (NIS), N=32	N (%)
Nausea	7 (21.9)
Worries	7 (21.9)
Lack of appetite	16 (76.2)
Shortness of breath	13 (40.6)
Lack of help to cook and inlet	1 (3.1)
Pain	8 (25.0)
Chewing / swallowing problems	3 (9.4)
Constipation	2 (6.3)
Oral and throat discomforts e.g. fungus	5 (15.6)
Do not like eating alone	0 (0.0)

Table 2: Nutrition impact symptoms.

#### **Social indicators**

Most of the patients had a short or vocational education (56%). Living status and smoking were sought in patients' medical records, and only found in 69 patients. Of the 69 patients, 72.5% lived together with another person. Two thirds of the patients had minimum one comorbidity (67.0%). A large proportion of the patients were smokers or had previously smoked (78.3%). Social indicator data are presented in Table 3.

Variable	N (%)	
Education, N=100		
Non or shorter courses	29 (29.0)	
Short or Vocational (1-3 years)	56 (56.0)	
Medium long or long (>3 years)	15 (15.0)	
Living status, N=69		
Alone	19 (27.5)	
Together	50 (72.5)	
Diagnose time, N=100		
0-2 years	75 (75.0)	
>2 years	25 (25.0)	
Comorbidity, N=100		
No	33 (33.0)	
Yes	67 (67.0)	
Smoking, N=69		
No	15 (21.7)	
Yes	54 (78.3)	

Table 3: Social indicators.

## Associations and exposures for UWL

Patients with NIS had higher OR for UWL (OR=8.621 [2.72;27.28]). Patients with RFI had a higher OR of having UWL (OR=5.162 [1.60;16.69]). Men had lower OR for UWL compared to women. All education above 1 year had lower OR for having UWL compared to patients with both no education and shorter courses. Patients living together with another person had lower OR for UWL, giving a higher risk for having UWL among patients living alone. No significant difference was shown between UWL and age (p=0.565), BMI (p=0.090), diagnose time (p=0.549), comorbidity (p=0.603), or smoking (p=0.854).

The results are presented in Table 4.

#### **Discussion**

In this study we aimed to examine the prevalence of malnutrition, measured by UWL, in an outpatient clinic for pulmonary fibrosis patients in Denmark, and to identify possible associations between UWL and risk factors for UWL as NIS. We furthermore aimed to find if UWL within three months, may serve as a relevant measure for early screening of nutritional risk in the outpatient clinic. The main results show that 18% of the patients have had an UWL, where women, patients with no education and patients living alone had higher odds for having UWL (p<0.05). Furthermore, patients with RFI and NIS had higher odds for having UWL (p<0.05). The firm association between RFI and UWL found in this population as in others, indicate that UWL may be used as initial screening for disease related malnutrition [16].

Considering the previous results from other studies, the prevalence of UWL in the present study is slightly lower, which could be explained by the possible methodological underestimation. Nakatsuka et al. (2018) support the prevalence of UWL in pulmonary fibrotic patients in this study (18%), as they found a prevalence of 15-20% in the target group [5]. This is deviating from another study, which found a prevalence of 28% [6]. Holst et al. found a prevalence of 28% in pulmonology outpatients in general. This study however included all patients including COPD and cancer patients, and data were collected before Coronavirus [8]. This may however also indicate a lower prevalence of UWL in the outpatient clinic for pulmonary fibrosis, compared to the overall pulmonary outpatient sample. Due to the WHO standards, our patient group in general was slightly overweight. This is in line with the general population [20]. However, BMI is a quite unspecific measure, and says nothing about body-composition. Jouneau et al (2019) calculated prevalence using a bioimpedance analysis and found a prevalence of low Fat Free Mass Index (FFMI) of 28%. Using BMI, they found a prevalence of 5% (BMI < 21.5%). They did not report weight loss in the study [6]. This is however crucial, since we know that weight loss, and even more, loss of muscle mass has shown to be most compromising with regard to nutritional risk outcomes [5,21-23].

Limitations to this study should be considered. The most important limitation is the sample size. A convenience sample was chosen for 100 participants, since no comparable studies were available for power calculation. Nine patients declined participation. Furthermore, patients with the most severe pulmonary fibrosis were referred to another hospital for

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Variable	Unintended weight loss			
	Yes, N (%)	No, N (%)	OR [CI 95%]	P-value
Sex, N=100				
Women	10 (29.4)	24 (70.6)	Reference	0.033*
Men	8 (12.1)	58 (87.9)	0.331 [0.12;0.94]*	
Education, N=100				
Non and shorter courses	11 (37.9)	18 (62.1)	Reference	0.004*
Short or Vocational (1-3 years)	6 (10.7)	50 (89.3)	0.196 [0.06;0.61]*	0.004*
Medium long or long (≥3 years)	1 (6.7)	14 (93.3)	0.117 [0.01;1.02]	
Age, years, N=100				
Age<70	7 (15.6)	38 (84.4)	Reference	0.565
Age≥70	11 (20.0)	44 (80.0)	1.357 [0.48;3.85]	
BMI, kg/m², N=100				
BMI ≤24,9	9 (27.3)	24 (72.7)	Reference	0.090
BMI >25	9 (13.4)	58 (86.6)	0.414 [0.15;1.7]	
Reduced food intake, N=100				
No	11 (13.1)	73 (86.9)	Reference	0.008*
Yes	7 (43.7)	9 (56.3)	5.162 [1.60;16.69]	
Living status, N=69				
Alone	7 (36.8)	12 (63.2)	Reference	0.048*
Together	7 (14.0)	43 (86.0)	0.279 [0.08;0.95]	
Nutrition impact symptoms, N=100				
No	5 (7.3)	63 (92.7)	Reference	0.001*
Yes	13 (40.6)	19 (59.4)	8.621 [2.72;27.28]	
Diagnose time, N=100				
0-2 years	15 (20.0)	60 (80.0)	Reference	0.549
>2 years	3 (12.0)	22 (88.0)	0.545 [0.14;2.07]	
Comorbidity, N=100				
No	5 (15.1)	28 (84.9)	Reference	0.603
Yes	13 (19.4)	54 (80.6)	1.348 [0.44;4.16]	0.603
Smoking, N=69				
No	3 (20.0)	12 (80.0)	Reference	0.854
Yes	12 (22.2)	42 (77.8)	1.143 [0.28;4.72]	

Table 4: The association between unintended weight loss and the different exposures

BMI: dichotomized according to WHO definition of normal weight and overweight/obesity (WHO, 2020).

invasive investigations. Due to the Coronavirus, many patients chose to postpone their contacts at the hospital. These patients may have been in worse conditions than those included, however, due to lack of consent from patients, we were not able to detect this. These factors may have influenced the representativity of the population, and therefore prevalence of UWL may have been underestimated through selection bias. These underestimations may have affected the internal validity of whether the actual prevalence in the fibrosis outpatient clinic is being investigated. The study relied on patient reported data as well as patient record data. Data may thus be biased by recall problems in patient questionnaires, and by interpretation bias for the patient records.

According to Ringbæk et al. (2018) and the chief physician at the clinic, pulmonary fibrosis has many subcategories of diseases [19], and therefore the group of patients in the clinic may have a great diversity. Thus, it can be difficult to do an overall association analysis when patients may have different associations to the outcome.

A larger follow-up study including more sights, eventually including nutritional therapy for a group of those at risk, should test weight loss including FFMI by eventually bioimpedance, in order to find, if pulmonary fibrosis patients at nutritional risk by eventually the GLIM Criteria [21] will improve clinical outcomes by relevant intervention.

#### Conclusion

This study found a prevalence of malnutrition in patients with pulmonary fibrosis in the outpatient clinic of 18%. It was shown that women, patients with no education and patients living alone, had higher odds for having UWL. Patients with RFI within the past week and NIS, had higher odds for having UWL. Decreased appetite and shortness of breath during meals were the most pronounced NIS. Based on this study, it seems relevant and feasible to use UWL as an initial indicator for the need for further nutrition screening and assessment in pulmonary fibrosis in the outpatient clinic. Further and larger studies should investigate the impact of weight loss and nutrition intervention in pulmonary fibrosis.

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<sup>\*</sup>p<0.05.

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