

Sarcopenia in patients with chronic obstructive pulmonary disease: A study of prevalence and associated factors in Western Greek population

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is associated with a progressive loss of muscle mass and function and a systemic inflammatory process that can cause sarcopenia. **Objective:** The objective of this study is to estimate the prevalence rate of sarcopenia in COPD patients and to determine the factors associated with sarcopenic patients living in Western Greece. **Methods:** European Working Group on Sarcopenia in Older People criteria were applied to 69 outpatients with stable COPD. Body composition, exercise capacity, functional performance, physical activity, and health status were also assessed. COPD disease severity (COPD stage) was evaluated with the Global Initiative for chronic obstructive lung disease. The study protocol was approved by the Ethical Committee of the Technological Educational Institute of Western Greece. **Results:** The sample comprised 69 patients (59 women and 10 men), with a mean age of 71.33 ± 7.48 years. The prevalence of sarcopenia was 24.6% ($n = 17$). A high percentage (82.6%; $n = 57$) of the 69 Greek participants did not perform any regular exercise. The findings of this study demonstrated that sarcopenia was positively associated with COPD, age, body mass index, skeletal muscle mass, hand grip strength, and 4 m test. **Conclusions:** In conclusion, there is a 24.6% prevalence of sarcopenia in patients with COPD. Further research with larger samples would be indicated to clarify the precise association of specific characteristics of patients with sarcopenia and COPD.

KEY WORDS: Airway obstruction, lung disease, sarcopenia, skeletal muscle mass

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major public health problem^[1] and a leading cause of morbidity and mortality worldwide.^[2] It is characterized by persistent progressive limitations in airflow and the presence of emphysema and/or bronchitis.^[1,3]

Inhaled particles (from cigarette smoke and other sources) cause lung inflammation. Chronic inflammation leads to structural changes and narrowing of the small airways, and these changes increase with disease severity.^[3] Systemic inflammation is now a recognized factor for other complications commonly observed in COPD patients,

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including atherosclerosis, osteoporosis, cachexia, and muscle wasting.^[2,4] Sarcopenia is a disease which describes age-related muscle mass loss and muscle strength decline^[5,6] and is comprised multiple factors, including inflammation and chronic illness.^[2,7] A substantial body of the literature has demonstrated that inflammation cytokines activate many of the molecular pathways involved in skeletal muscle wasting leading to an imbalance between protein synthesis and catabolism.^[8] COPD can be considered a risk factor for sarcopenia in response to increased catabolism, elevated proinflammatory cytokines, and increased oxidative stress.^[1,9]

COPD prevalence varies across countries and across different population groups. Few studies in the literature have examined the association between the prevalence of sarcopenia and indices of COPD severity. The prevalence of COPD in sarcopenic patients ranged from 4.4% to 86.55%,^[1,10] due to variability in the various diagnostic tools, different reference values, and cutoffs presented in the literature. The prevalence and burden (economic and social) of COPD are expected to increase in the coming decades due to the continuous risk factors (tobacco smoking and air pollution) and aging of the world's population.^[3] Although recognizing the prevalence and diagnostic methods of COPD and sarcopenia is a very important effort in the search of effective strategies of prevention and intervention, no studies have been conducted with Greek sample. Thus, the objective of this study was to investigate the prevalence of sarcopenia in COPD Greek patients and determine the risk factors associated with sarcopenia in patients with COPD.

METHODS

Study design and population

This was a cross-sectional study involving 69 consecutive COPD patients, all over 50 years of age. Participants were recruited from the region of Achaia and Ilia, mainlands in Western Greece. The assessment procedure was all carried out at the University of Patras (University Hospital of Patras and Physiotherapy department) between March and December of 2018.

All measurements were completed in a single visit for each participant. The exclusion criteria included (a) cognitive impairment, (b) pacemaker fitted, (c) lower leg trauma and/or amputation, (d) medical or other musculoskeletal problems that could affect ability to complete objective assessments, (e) lung rejection or transplantations, and (f) body mass index > 50.

Definition

Patients diagnosed with COPD on the basis of past history and spirometric data according to the Global Initiative for chronic obstructive lung disease were eligible for this study. These criteria were characterized by persistent airflow limitation and a postbronchodilator

force-expiratory volume in 1 s (FEV1) < 70% of forced vital capacity.^[3]

Sarcopenia was identified using a combination of Hand Grip Strength (HGS), skeletal muscle mass index (SMMI), and gait speed measurements according to the criteria presented in the European Working Group on Sarcopenia in Older People (EWGSOP).^[6] The EWGSOP presented a European consensus on the definition and diagnosis of sarcopenia in 2010,^[5] which was updated in 2018 by EWGSOP2.^[6] In EWGSOP2, low muscle strength is defined as the first parameter of sarcopenia, and the diagnosis is confirmed by the presence of decreased muscle mass (quantity and quality). The following cutoff values were used to identify sarcopenia: Handgrip strength of < 27 kg for men and < 16 kg for women and either SMMI of ≤ 7 kg/m² for men and ≤ 5.5 kg/m² for women, and or a gait speed of < 0.8 m/s.^[6]

Assessments – Procedure

After consent, baseline patient data were collected by trained clinical researcher (MT). Each participant was interviewed face-to-face to assess his/her history of smoking, lifestyle habits, exercise habits, and medication use. Participants also completed a Mini-Mental State Examination (MMSE), which consisted of a 30-point questionnaire to assess their cognitive function. MMSE has been validated and extensively used in both clinical practice and research.^[11]

Severity of COPD was measured through spirometry. Patients were asked to inhale as deep as they could and then exhaled into the sensor as hard as possible, for 6 s. Spirometry was repeated at least three times and up to a maximum of eight times to ensure the reproducibility and validity of results.^[12] Spirometry was performed according to the 1994 American Thoracic Society recommendations using the same type of dry rolling-seal spirometer (model SP10; CONTEC Medical Systems Co., LTD) for all of the participants.

HGS strength was measured using a hand-held dynamometer (Saehan corporation, Seoul, Korea).^[6] The researcher asked the patient to squeeze the dynamometer with maximal isometric strength for 5s. The procedure was carried out with the elbow flexed and by the side of the body. The best of three attempts was recorded.

Body composition was estimated using bioelectrical impedance analysis (BIA), with a Tanita BC 601 model body analysis monitor. Participants removed their socks, stood on two metallic electrodes on the floor scale barefoot, and held two metallic grip electrodes placed in the palm of their hand with their fingers wrapped around the handrails.

Skeletal muscle mass (SMM, kg) was estimated using whole body BIA and SMMI calculated as $SMM/height^2$.^[12,13] Fat free mass (FFM) was extracted by BIA and SMM values,

using the following equation: $SMM (kg) = 0.566 \times FFM$. Participants were recommended to empty their bowel within 30 min before the measurement, and also not consume any meals and alcoholic beverages for at least 48 h before the tests.^[12,13]

Gait speed was measured with the 4 m test. Participants were informed to walk 4 m with their maximal speed. The procedure was fully explained before the assessment followed by a familiarization attempt. For the 4 m test, time in seconds was the recorded variable.

Statistical analysis

Descriptive statistics were reported using means, standard deviations, and frequencies for patients' characteristics. The effects of factors associated with sarcopenia were evaluated using the regression analysis. *T*-test for independent samples was used to determine the differences between the participants with sarcopenia and participants with no sarcopenia. Statistical significance was accepted at $P \leq 0.05$ and adjusted odds ratio and 95% confidence interval were reported to consider the strength of association between the variables. Statistical analysis was performed with the SPSS Statistics Software Package, version 20.0 (IBM Corporation, Armonk, NY, USA).

The study protocol was approved by the Ethical Committee of the Technological Educational Institute of Western Greece.

RESULTS

The sample consisted of 69 patients (59 women and 10 men), with a mean age of 71.33 ± 7.48 years and a mean BMI of 26.09 ± 4.13 kg/m². Most of the participants were ex-smokers (79.7%; $n = 55$). Four patients (5.8%) were current smokers at enrollment in the study. The characteristics of the study population are shown in Table 1.

Table 1: Differences between chronic obstructive pulmonary disease with sarcopenia and no sarcopenia

Variable	Sarcopenia ($n=17$)	No sarcopenia ($n=42$)	<i>P</i>
	<i>n, SD</i>		
Age (years)	71.82±6.31	71.17±7.87	NS
Drug (<i>n</i>)	3.35±1.32	2.3±1.6	0.01
Comorbidities (<i>n</i>)	2.58±1.12	2.11±1.13	NS
BMI (kg/h ²)	21.67±2.32	27.54±3.52	≤0.001
HGS (kg)	16.27±3.1	21.86±6.35	≤0.001
SMMI	5.51±0.21	7.4±1.74	≤0.001
4 m test (s)	4.68±0.86	3.97±1.11	0.02
Smoking status, <i>n</i> (%)			
Smokers	2 (11.8)	8 (15.4)	NS
Ex-smokers	14 (82.4)	41 (78.8)	
Nonsmokers	1 (5.9)	3 (5.8)	
Regular physical activity, <i>n</i> (%)			
Yes	2 (11.8)	10 (19.2)	NS
No	15 (88.2)	42 (80.8)	

NS: Nonsignificant differences, BMI: Body mass index, SMMI: Skeletal Muscle Mass Index, HGS: Hand Grip Strength, 4 m test: 4 m test, COPD: Chronic Obstructive Pulmonary Disease, SD: Standard deviation

On the basis of the FEV1 values, the degree of obstruction was classified as mild in 14 (20%) of the patients, moderate in 31 (55.7%), severe in 14 (20%), and very severe in 10 (14.3%).

The prevalence of sarcopenia among COPD patients is 24.6% ($n = 17$). The mean SMMI was 5.51 ± 0.21 in the patients with sarcopenia (5.51 ± 0.21 in women and 6.65 ± 0.25 in men), compared with 7.4 ± 1.74 in those without (6.89 ± 1.2 in women and 9.57 ± 2.05 in men), the difference between the two groups being statistically significant ($P < 0.001$).

The comparison of the risk factors between sarcopenic and nonsarcopenic patients with COPD is shown in Table 2. The findings of this study demonstrated that sarcopenia was positively associated with BMI, SMMI, HGS, 4 m test, and negatively associated with smoking, age, regular physical activity, gender, comorbidities, and falls.

DISCUSSION

To our knowledge, this is the first study to examine sarcopenia in COPD in Greece. The overall prevalence of sarcopenia was 24.6%, which is consistent with the literature on COPD patients, in which the most reported prevalence is 20%–40%.^[4,14,15] As observed, the prevalence of sarcopenia in COPD patients is higher than that in the normal elderly people. According to the Korean National Health and Nutrition Examination Survey, 13.4% of the population aged 40 years or older has COPD.^[16] Sarcopenia is frequently observed in COPD patients, with varying prevalence across populations.^[17] This variation is likely to be due to the differences in the criteria used for the assessment of sarcopenia. In the present study, the diagnosis of sarcopenia was performed using the EWGSOP criteria. Considering that the prevalence of sarcopenia in COPD patients is higher than that in normal elderly people,^[16] and that the loss of muscle strength, muscle mass, and function may lead to decreases in physical activity and energy consumption, COPD may be among the possible causes of sarcopenia.^[16-20] However, sarcopenia in COPD should be assessed using standardized tests and cutoff points from sarcopenia consensus criteria for clinical practice and international comparisons.^[17] Estimating the overall prevalence of sarcopenia in line with the contemporary operational definitions will provide further insight into its burden in COPD.

According to EWGSOP, sarcopenia is “secondary” when another factor besides aging is present. EWGSOP state that secondary sarcopenia can occur due to a systemic disease such as COPD.^[6] However, there is not any distinction in the recommendations of methods and cutoffs for distinguishing primary and secondary sarcopenia. Further understanding of the main molecular and cellular mechanisms underlying the onset of sarcopenia in COPD patients could support the optimization of assessment tools for sarcopenia in COPD.^[17]

Table 2: Factors associated with sarcopenia among chronic obstructive pulmonary disease patients

Variable	OR (95% CI)	P
BMI	2.94 (1.52-5.69)	≤0.001
Age	0.9 (0.91-1.06)	NS
SMMI	28.6 (32.53-251.7)	≤0.05
HGS	1.67 (1.02-2.73)	≤0.05
4 m test	0.52 (0.29-0.93)	≤0.05
Drug	0.66 (0.46-0.94)	≤0.05
Comorbidities	0.69 (0.42-1.13)	NS
Gender	1.3 (0.98-1.72)	NS
Falls	0.39 (0.12-1.21)	NS
Regular physical activity	0.56 (0.11-2.8)	NS
Smoking	0.82 (0.23-2.88)	NS
COPD	0.8 (0.41-0.94)	≤0.05

NS: Nonsignificant, OR: Odds ratio, BMI: Body mass index, SMMI: Skeletal muscle mass index, HGS: Hand grip strength, 4 m test: 4 m test, COPD: Chronic obstructive pulmonary disease

Low muscle strength has been described as the main component of sarcopenia.^[6] As it was expected mean HGS was lower ($P \leq 0.001$) among individuals with than without COPD. HGS is infrequently used or reported as a functional measure in patients with respiratory disease, perhaps because it is commonly considered the part of a complex battery of functional tests. There are a few studies of HGS in selected COPD samples, but with contradictory results. Some previous studies have demonstrated decreased grip strength in patients with COPD.^[21-23] However, Marino *et al.*^[24] found that there was no association between HGS and spirometric lung function results, as assessed by the predicted forced expiratory volume percent in 1 s among participants with moderate-to-very severe COPD. In a Korean national survey, HGS was not significantly different between adults with and without COPD and was not associated with the degree of airflow limitation.^[25] In patients with COPD, the risk factors for decrease in muscle strength and endurance include chronic inflammation, oxidative stress, inactivity, hypoxemia, hormone abnormality, deficits of nutrients including protein and Vitamin D, and the use of systemic corticosteroid.^[18] Further studies are needed to clarify the actual status of HGS and the prevalence rates of sarcopenia in different aged groups in patients with COPD.

In the sample of COPD Greek patients, there was a high prevalence of diagnosed sarcopenia, which may be related to the poor prognosis. Recent data demonstrate that in patients with COPD, various factors such as specific unfavorable changes in body composition have been shown to be associated with a worse prognosis.^[19,16,26] Hence, a reduction in lean mass, which leads to exercise intolerance^[26] could contribute to those body composition changes. These factors may increase the frequency of exacerbations/hospital admissions and may increase mortality.^[9,26] This study supports the inclusion of body-composition assessment in COPD patients.

There were the six factors associated with sarcopenia using the regression analysis: COPD, BMI, number of

drugs, SMMI, HGS, and 4 m test. As it had been expected, sarcopenia has significant associations with HGS, SMMI and 4 m test because they are the diagnostic criteria. In the literature, review factors associated with sarcopenia in COPD patients included nutritional status, exercise capacity, severity of COPD, functional performance, smoking status, comorbid diseases, and self-reported hospital admission. The positive association of sarcopenia with COPD indicates that early diagnosis of sarcopenia can facilitate the implementation of interventions aimed at preventing the deterioration of lean body mass and improving the quality of life in patients with COPD.^[9,17] A more holistic approach of COPD is essential rather than focusing only on airflow limitations.^[16,27] Future work should also address how sarcopenia can be optimally managed within respiratory disease.^[27,28]

A high percentage (82.6%; $n = 57$) of the 69 Greek participants answered that they did not performed any regular exercise. As the amount of activity decreases, muscle mass may decrease and eventually oxygen cannot be used effectively, resulting in a vicious cycle of deterioration of exercise capacity.^[18] Exercise could have beneficial effects in muscle quantity and quality (strength, mass, and functional performance) in patients with sarcopenia.^[13,26] It seems important to choose the exercise method according to the COPD status and help those patients.^[18] Although there is no significant association of regular exercise with sarcopenia among Greek participants, it is important to notice that physical activity was not measured with either accelerometer of a validated instrument, but it was based on a simple answer, whether they exercised or not. Certainly, addressing this would be beneficial for future studies.

Due to the high prevalence of COPD and sarcopenia, exercise and pulmonary rehabilitation programs should be performed aimed at maintenance or improvement of physical and nutritional condition of individuals with COPD. The assessment of patients' muscle strength and body composition is important to provide them an appropriate treatment and follow-up their progress during pulmonary rehabilitation programs.^[29] Our results agree with, the recommendation of the Asian Working Group for Sarcopenia, that people with COPD are recommended for sarcopenia screening and assessment.^[30]

In this study, the main percentage of participants were ex-smokers (79.7%) and 4 (5.85%) were current-smokers. Although tobacco smoking is the main cause of COPD,^[31] it is also a known risk factor for many nonpulmonary diseases. It is well-known that even nonsymptomatic smokers can exhibit fatigability and reduced muscle resistance.^[31,32] This can be well explained by the anorectic effects of tobacco, which may lead to the loss of muscle mass, as well as inducing inflammation, oxidative stress, an imbalance between protein synthesis, and degradation in the muscle.^[31,33] In the present study, no significant association between smoking history and sarcopenia was recorded. In

support of a negative association, two studies did not find the differences in smoking across COPD patients with and without sarcopenia.^[10,15] One possible explanation for the present finding is that the majority of patients with COPD had a mild obstruction. Although there is controversy in the literature, one study demonstrated an association between smoking history and a loss of lean mass in COPD patients,^[34] whereas others do not confirm this finding.^[9,35]

Limitations of this study initially include the relatively small size of our sample. Further research with larger samples would be indicated. Future studies must also include age-matched controls to see the effect of COPD on sarcopenia. Second, muscle mass was assessed with BIA, a widely adopted method, but not the “gold standard.” However, BIA is a noninvasive, quick, safe, and inexpensive method of measuring body composition. It has been reported in an increasing number of studies over the past decade.^[13,36-40] In addition, the European Group on Sarcopenia in Older People accepts BIA as an option for sarcopenia assessment.^[5,6] In this study, the formula which was used ($SMM [kg] = 0.566 \times FFM$) was validated on individual and group data and has been compared with SMM data calculated from 24 h creatinine excretion in a group of healthy participants as well.^[12,41] The European Working Group on Sarcopenia in Older Persons (EWGSOP) criteria accept the use of BIA and has been reported in an increasing number of studies over the past decade.^[16,20] Third, the vast majority of patients were women, and hence, the results might not be representative of the population. More research is needed to clarify the precise association of specific characteristics of patients with sarcopenia and COPD.

CONCLUSIONS

In conclusion, there is a 24.6% prevalence of sarcopenia in patients with COPD. Sarcopenia is associated with reduced muscle strength, skeletal muscle mass, gait speed, BMI, and COPD. Further large-scale research, including aged-matched groups, is needed to confirm the results of this study aiming to improve our understanding of determinants of sarcopenia in patients with COPD.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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