

Sarcopenia in Chronic Obstructive Pulmonary Disease

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ABSTRACT

Objective: To investigate the frequency of sarcopenia in patients with chronic obstructive pulmonary disease (COPD) and in the Control group, and to compare the 6-minute walk test (6MWT), handgrip strength (HGS) measured by a dynamometer, pulmonary function test (PFT) parameters, and bioimpedance analysis (BIA) parameters among the COPD GOLD A, B, and E subgroups.

Study Design: Cohort study.

Place and Duration of the Study: Department of Pulmonary Disease, Faculty of Medicine, Tokat Gaziosmanpasa University, Tokat, Turkiye, from February to August 2022.

Methodology: Sarcopenia rates were compared between the COPD group and the Control group. Patients diagnosed with COPD according to the GOLD 2022 criteria by pulmonologists were included in the COPD group. Volunteers without any neuromuscular and pulmonary disease were included in the Control group.

Results: The study included 43 patients with COPD and 40 volunteers without respiratory disease. The incidence rate of sarcopenia was found to be 39.5% in the COPD group. Group E patients had the highest rate of sarcopenia (70%). It was found that the COPD group had lower HGS, as measured by dynamometer, and age and gender-corrected HGS measurements compared with the Control group ($p = 0.019$ and $p = 0.005$, respectively).

Conclusion: Sarcopenia was found to be higher in the COPD group compared to the Control group. The highest rate was observed in Group E. Sarcopenia should definitely be taken into consideration in the follow-up of COPD patients, and treatment of sarcopenia (nutritional supplement, exercise, and pulmonary rehabilitation etc.) should be evaluated in those patients.

Key Words: Chronic obstructive pulmonary disease, Sarcopenia, Inflammation, Muscle mass.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a systemic disease characterised by an inflammatory response of the lungs to harmful particles and it gases, and it develops as a result of both congenital and acquired risk factors inherent in the affected individual.¹ The inflammatory response affects all organ systems, especially the cardiovascular and musculoskeletal systems, besides the lungs.² Sarcopenia is defined by the criteria of low muscle strength, reduced muscle mass, and impaired performance and is mostly associated with systemic and chronic diseases.³

Sarcopenia, which is known to be associated with chronic diseases and contributes significantly to mortality, is often overlooked in the treatment and follow-up of COPD patients. The loss of muscle strength and mass due to immobilisation and systemic inflammation in COPD naturally weaken the respiratory muscles, thereby worsening pre-existing dyspnoea.

Moreover, a decrease in exercise capacity leads to prolonged immobilisation and muscle atrophy in the extremities.² The presence of sarcopenia secondary to COPD is thought to directly decrease the quality of life by increasing exacerbations, hospitalisations, and treatment costs.^{4,5} In the literature, the reported prevalence of sarcopenia in COPD patients varies due to the diagnostic methods and threshold values used.⁶⁻⁸

This study aimed to investigate the frequency of sarcopenia in patients with COPD and in the Control group, and to compare six-minute walk test (6MWT), hand grip strength (HGS) measured by a dynamometer, pulmonary function test (PFT) parameters, and bioimpedance analysis (BIA) parameters among the COPD GOLD A, B, and E subgroups.

METHODOLOGY

The study was conducted as a prospective cohort study. Stable COPD patients who presented to the Department of Pulmonary Disease, Faculty of Medicine, Chest Diseases Outpatient Clinic between February and August 2022, as well as volunteer participants without any respiratory disease, were included. Ethical approval was obtained from the Tokat Gaziosmanpasa University Hospital Clinical Research Ethics Committee, and informed consent was obtained from all patients before this inclusion in the study.

Power analysis was performed before the study using the G-power (version 3.1.9.4).⁹ Based on a 5% error level, 80% power,

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and an effect size of 0.7, the minimum required sample size was calculated as 26 patients per group.

Patients over 40 years of age with a history of smoking for more than 10 years, biomass exposure, or occupational smoke exposure, whose FEV1/FVC ratio was measured as <70% by PFT and diagnosed with COPD according to the GOLD 2023 criteria by pulmonologists, were included in the COPD group. Volunteers who applied to the outpatient clinic with nonspecific symptoms and without any known lung disease were included in the Control group. Patients with bronchiectasis, cystic fibrosis (CF), COPD exacerbation in the previous month, or those who did not provide consent were excluded from the study. In addition, individuals with known muscle disease, malignancy, or those receiving treatment that affects muscle mass, such as steroids or protein supplements, were excluded from the study. Additional exclusion criteria are presented in the flow diagram (Figure 1).

Demographic characteristics (age, gender, smoking history), comorbidities, nutritional status (evaluated with the Mini Nutritional Assessment Short-Form [MNA-SF]), and SARC-F questionnaire score (strength, assistance in walking, rise from a chair, climbing stairs, and falls) as well as MRC (modified Medical Research Council) dyspnoea scale scores of the patients included in this study were recorded. Besides, spirometry parameters, GOLD combined staging, and 6MWT results were evaluated in the outpatient clinic. BIA was performed using the TANITA BC = 420MA body analyser, HGS was measured with a TAKEI brand HGS digital dynamometer, and a measuring tape

was used for the measurements of the diameters of upper arms and calves of the participants. Diagnostic parameters proposed by the Sarcopenia Definition and Outcomes Consortium (SDOC) in 2020, including HGS (<35.5 kg in men and <20 kg in women) and low walking speed (<0.8 m/sec), were used as the two main diagnostic criteria for sarcopenia to evaluate physical performance.¹⁰

Statistical analysis was performed using SPSS version 20.0 (SPSS, Inc., Chicago, Illinois). The Kolmogorov-Smirnov test was used to test the distribution pattern of the variables. Categorical variables (gender, comorbidities etc.) were expressed as frequencies and compared with the Chi-square test. All parametric data were expressed as mean $\pm$ standard deviation (SD). Analysis of variance (ANOVA) was used to examine the association between the GOLD A-B-E stages and sarcopenia parameters in patients with COPD. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 83 participants, comprising 43 patients diagnosed with COPD and 40 individuals in the Control group, were included in the study. The mean age of the patients with COPD was 63.93 ± 8.10 years, and 95.3% (n = 41) of the patients were male. In addition, the mean smoking rate of the patients was 42.09 ± 12.09 pack/year, which was significantly higher compared to the Control group. The general characteristics of COPD patients and their comparative evaluation with the Control group are summarised in Table I.

Table I: General characteristics and laboratory findings of the COPD and Control groups.

Parameters (mean $\pm$ SD)	COPD group (n : 43)	Control group (n : 40)	p-values
Age (years)	63.93 ± 8.10	54.67 ± 11.60	<0.001
Gender (M/F)	41/2	29/11	0.004
Cigarette pack / years	42.09 ± 12.09	8.20 ± 9.68	<0.001
Comorbid diseases (yes/no)			
HT	35/8	31/9	0.660
IHD	32/11	35/5	0.131
DM	37/6	34/6	0.892
MNA-SF	13.54 ± 1.21	13.84 ± 0.33	0.090
SARC-F	1.53 ± 0.27	0.17 ± 0.07	<0.001
Hb g/dL	13.8 ± 1.8	14.1 ± 1.5	0.660
Hct %	41.6 ± 4.9	41.6 ± 4.1	0.980
BUN mg/dL	17.3 ± 7.3	18.1 ± 8.7	0.710
Creatinine mg/dL	0.84 ± 0.24	0.90 ± 0.19	0.320
AST U/L	18.7 ± 10.2	18.9 ± 6.4	0.930
ALT U/L	16.4 ± 7.1	18.5 ± 9.5	0.400
CRP mg/dL	5.6 ± 4.6	2.4 ± 1.7	<0.001

HT: Hypertension; IHD: Ischaemic heart disease; DM: Diabetes mellitus; MNA-SF: Mini nutritional assessment short form; SARC-F: Sarcopenia assessment questionnaire; Hb: Haemoglobin; Hct: Haematocrit; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CRP: C-reactive protein; SD: Standard deviation. *Independent Student's t-test was used for parametric data, and the Chi-square test was used for categorical data.

Table II: Comparative evaluation of BIA and HGS parameters between the COPD and Control groups.

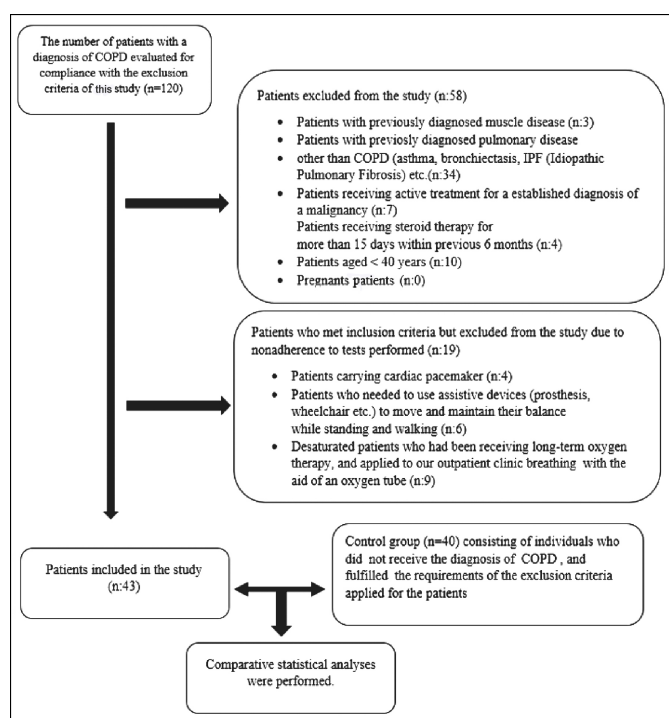
Parameters (mean $\pm$ SD)	COPD group	Control group	p-values
BMI (kg/m ²)	26.24 ± 4.39	27.86 ± 3.67	0.084
Body weight (kg)	71.52 ± 14.34	77.06 ± 9.79	0.052
Muscle mass (%)	52.29 ± 8.94	53.66 ± 7.29	0.460
Fat mass (%)	18.11 ± 8.68	20.47 ± 6.39	0.160
FFM (kg)	54.55 ± 8.71	56.68 ± 7.54	0.250
Upper extremity diameter (cm)	28.36 ± 4.45	30.07 ± 4.34	0.080
Calf diameter (cm)	32.97 ± 4.92	34.05 ± 4.01	0.280
HGS (kg)	31.31 ± 8.15	37.12 ± 13.32	0.019
AGCHGS decreased / normal (n)	30/13	13/27	0.005

HGS: Hand grip strength dynamometer; AGCHGS: Age and gender-corrected hand grip strength dynamometer; FFM: Fat-free mass; BMI: Body mass index. *Independent Student's t-test was used for the analysis.

Table III: PFT parameters, frequency of sarcopenia, and HGS data in the COPD subgroups and the Control group.

Parameters	Control (n : 40)	GOLD A (n : 20)	GOLD B (n : 13)	GOLD E (n : 10)	p-values
Sarcopenia (n)					
Yes	7 (17%)	8 (40%)	2 (15%)	7 (70%)	0.024
No	33 (82%)	12 (60%)	11 (85%)	3 (30%)	
HGS kg (mean ± SD)	37.12 ± 13.32	33.33 ± 7.03	28.27 ± 10.16	31.20 ± 6.60	0.019
AGCHGS					
Decreased	13 (32%)	12 (60.0%)	10 (77%)	8 (80%)	0.002
Normal	27 (67%)	8 (40.0%)	3 (23%)	2 (20%)	
FEV1 (lt)	1.92 ± 0.57	1.32 ± 0.36	1.57 ± 0.64	1.67 ± 0.58	0.001
FEV1 (%)	61.9 ± 14.1	50.4 ± 13.1	54.2 ± 20.0	59.2 ± 17.7	0.005
FVC (lt)	3.08 ± 0.84	2.33 ± 0.69	2.63 ± 0.75	2.82 ± 0.84	0.043
FVC (%)	79.9 ± 16.1	66.0 ± 16.0	71.0 ± 19.9	74.0 ± 17.7	0.088
FEV1/FVC (%)	61.1 ± 8.1	56.3 ± 8.2	58.4 ± 9.5	60.6 ± 9.4	0.003
NEPY	0.15 ± 0.36	0.76 ± 0.59	2.40 ± 6.96	0.86 ± 1.08	<0.001
NHPY	0.0	0.15 ± 0.10	0.60 ± 0.22	0.18 ± 0.07	0.001
mMRC scores	0.85 ± 0.36	2.05 ± 0.80	1.90 ± 1.10	1.44 ± 0.78	<0.001
6MWT (metre)	318.7 ± 72.9	369.2 ± 96.9	225.0 ± 44.2	312.2 ± 110.1	0.005

*Patients were divided into subgroups of A, B, and E according to the GOLD 2023 guidelines. In COPD patients, GOLD subgroups were evaluated with the One-way ANOVA test for the presence of Sarcopenia according to SODC criteria. The p-value was obtained by comparing all the COPD patients and the Control group. HGS: Hand grip strength dynamometer; AGCHGS: Age and gender-corrected hand grip strength dynamometer; PFT: Pulmonary function test; FEV1: Forced expiratory volume in one second; FVC: Forced vital capacity; NHPY: Number of hospitalisations in the previous year; NEPY: Number of exacerbations in the previous year; 6MWT: Six-minute walk test; mMRC: Modified medical research council dyspnoea score.

**Figure 1: Flow diagram of the study.**

According to the BIA, mean HGS dynamometer, and age and gender-corrected handgrip strength (AGCHGS) were found to be significantly lower in the COPD group than in the Control group ($p = 0.019$ and $p = 0.005$, respectively). Body mass index (BMI), muscle mass, fat mass, fat-free mass (FFM), upper arm, and calf diameters were found to be lower in the COPD group, but not statistically significant (Table II).

Sarcopenia was detected in 17 (39.5%) of 43 patients in the COPD group, while 17.5% in the Control group ($p = 0.024$). In addition, sarcopenia was found to be higher in the GOLD E subgroup than A and B groups. Moreover, it was found that the COPD group had lower hand dynamometer grip strength and AGCHGS measurements compared to the Control group ($p = 0.019$ and $p = 0.002$, respectively, Table III).

When COPD patients were divided into subgroups of A, B, and E according to the GOLD 2023 guideline criteria, all PFT parameters, number of exacerbations, hospitalisation rates, mMRC dyspnoea scores, and 6MWT results were found to be significantly different between the two groups (Table III).

DISCUSSION

The rate of sarcopenia in the COPD group was significantly higher than in the Control group. In the COPD subgroups, the incidence rate of sarcopenia was the highest (70%) in the GOLD E subgroup. This study emphasised the importance of assessing sarcopenia in the follow-up of patients with COPD.

In the previous literature, the incidence of sarcopenia in healthy individuals has been estimated at 5-13%,^{11,12} and in this study, its frequency in the Control group was 17.5%. Previous literature reports the frequency of sarcopenia in patients with COPD at 15-55%,^{13,14} and this study reports its prevalence in the COPD group at 39.5%, consistent with these findings.¹³ The highest incidence of sarcopenia in the GOLD E subgroup suggests that patients in this group should be specifically evaluated for sarcopenia.

Most COPD patients reported in the literature are elderly and predominantly male. This study showed a similar result, with male patients comprising the majority in the COPD group. This male predominance may be due to local working exposures (such as mining, farming) and higher rates of smoking in men. To ensure an unbiased assessment of sarcopenia, the Control group was also composed primarily of male participants.

COPD patients often have multiple comorbidities. Camiciotoli *et al.* reported that the most common comorbidities in COPD patients are hypertension (HT), ischaemic heart disease (IHD), and heart failure (HF).¹⁵ In Soykok *et al.*'s study, the most common comorbidities were HT, IHD, and diabetes mellitus (DM), respectively.¹⁶ Eroglu *et al.* conducted a study on 826 patients treated for COPD exacer-

bations and found at least one comorbidity in 84.5% of COPD patients, with the most common being HT, HF, and DM.¹⁷ In this study, the most common comorbidities in both the COPD and Control groups were HT, IHD, and DM.

Bioimpedance data have been analysed for many chronic diseases.¹⁸⁻²⁰ Costa *et al.* investigated sarcopenia in COPD patients and found that BMI values and BIA parameters (muscle mass, fat mass, and FFM) were similar to those in the Control group.¹⁸ Likewise, in this study, BMI, BIA parameters (muscle mass, fat mass, FFM), upper arm, and calf diameter measurements were similar between the COPD and the Control groups. Dhakal *et al.* compared patients with and without COPD and found that 48% of those with COPD had a BMI ≤ 18.5 kg/m², compared with 15% in the Control group. They also evaluated MNA-SF scores in the COPD patients and determined that 55% of them were malnourished.¹⁹ In this study, using the MNA-SF scores, no malnutrition or risk was detected in COPD patients. The lower BMI values and the presence of undernourished patients reported in the study by Dhakal *et al.* may be related to the poor socioeconomic status of their study patients.

Among all laboratory tests evaluated in this study, only higher levels of C-reactive protein (CRP) were observed ($p < 0.001$). In two different meta-analyses, in which 26 and 61 articles were examined, respectively, higher CRP levels were found to be associated with early-term and higher mortality rates.^{21,22} Sin *et al.* found that CRP elevation is not a specific finding in COPD.²³ Although almost all of the patients had comorbidities, the higher CRP values detected in the COPD patient group underline the role of inflammation in the disease. Moreover, the similar comorbidities observed in both the COPD and the Control groups allowed for a more objective assessment of sarcopenia.

Martinez *et al.* followed up 272 COPD patients for approximately 2.6 years and found that lower HGS measurements were associated with lower BMI values and more frequent exacerbations, while higher HGS measurements were associated with decreased exacerbation rates.²⁴ Qaisar *et al.* performed a survey study on 1,582 participants, including individuals with and without COPD, and found that the COPD group had lower AGCHGS measurements compared to the Control group. They also observed that the AGCHGS values in the COPD subgroups decreased further from stage 1 to stage 4 when compared in terms of FEV1, which is one of the GOLD criteria for COPD.²⁵ In addition, in another study, any difference between individuals with and without COPD could not be found in terms of HGS measurements; however, HGS was found to be directly related to the quality of life of individuals with COPD. In this study, HGS and AGCHGS values were significantly lower in the COPD group compared with the Control group. This reduction in muscle strength is one of the most important parameters indicating the severity of sarcopenia in COPD patients.

The most significant limitation of this study is the small sample size of the study due to the exclusion criteria. Patients who required assistance with standing or walking, or who were unable to walk due to hypoxia, were excluded. Inclusion of these severely affected COPD patients could have provided additional insight into the burden of sarcopenia.

CONCLUSION

According to the results of this study, it is important to routinely evaluate patients in Gold group E for the presence of sarcopenia and to plan appropriate treatment (such as supplementary nutrition, exercise, and pulmonary rehabilitation) when sarcopenia is diagnosed.

ETHICAL APPROVAL:

Ethical approval was obtained from the Ethics Committee of the Tokat Gaziosman Pasa University (Approval No. 83116987-092; dated: 20.01.2022).

PATIENTS' CONSENT:

Informed consent was obtained from the patients before the conduction of the study.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

SG: Data collection and writing of the manuscript.

HIY, HIK, ACP, GA: Conception of the study, writing, revision, and correction of the acquired data.

All authors approved the final version of the manuscript to be published.

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