Endocrine (2018) 60:95–102
https://doi.org/10.1007/s12020-018-1533-4

ORIGINAL ARTICLE

Body composition and sarcopenia in patients with chronic obstructive pulmonary disease

Tatiana Munhoz da Rocha Lemos Costa[1] · Fabio Marcelo Costa[2] · Thaísa Hoffman Jonasson[1] · Carolina Aguiar Moreira[1] · César Luiz Boguszewski[1] · Victória Zeghbi Cochenski Borba[1]

Received: 3 November 2017 / Accepted: 14 January 2018 / Published online: 5 February 2018

Abstract

Purpose Changes in body composition are commonly present in chronic obstructive pulmonary disease (COPD). The main aim of this study were to evaluate changes in body composition and the prevalence of pre-sarcopenia and sarcopenia in patients with COPD, compared with two control groups and correlate these parameters with indices of COPD severity (VEF1 and GOLD) and prognosis (BODE).

Methods This was a cross-sectional study in COPD patients (DG) that undergone body composition assessment by DXA. Two control groups were used, smokers individuals without COPD (smokers group, SG), and healthy never smokers individuals (never smokers group, NSG).

Results DG comprised 121 patients (65 women, mean age 67.9 ± 8.6 years). The percentage of total body fat mass (TFM) was significantly lower in DG in both genders, despite no difference in BMI. Both BMI and relative skeletal muscle mass index (RSMI) decreased according to the worsening of GOLD in men and women, as well as the TFM and total lean mass (TLM) in men. As BODE get worse, BMI and RSMI decreased in both sexes, as well as TLM in men. The prevalence of pre-sarcopenia in the DG was 46.3% and no different with controls. In DG 12.4% were sarcopenic. Patients with sarcopenia were older and had worse prognosis. Higher BODE prognostic index, higher the prevalence of sarcopenia (OR 3.5, 95% CI 1.06–11.56, $p = 0.035$).

Conclusions This study showed alterations in body composition parameters in patients with COPD. A high prevalence of sarcopenia and the association with worse prognostic index.

Keywords COPD · Sarcopenia · Body composition · BODE · GOLD

Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation [1]. The prevalence of COPD is high, ranging from 7.8 to 19.7% depending on the population studied, and is associated with high morbidity and increased mortality [2]. In general, the inflammatory and structural changes in the airways increase with disease severity and persist on smoking cessation [3]. COPD is associated with several extrapulmonary disorders, including cachexia, and skeletal muscle weakness. Systemic inflammation may be present and could play a role in the multiple comorbid conditions found in patients with COPD [4].

Recent data obtained from patients with COPD have shown that changes in body composition, particularly decreases in lean mass, are associated with a low exercise capacity, worse quality of life indices, and increased mortality [5, 6]. The condition of pre-sarcopenia is characterized by a low muscle mass, while sarcopenia, a more severe spectrum of the syndrome, is defined by low muscle mass along with weakness, which results in impaired functional capacity and disability in elderly individuals [7]. Pre-sarcopenia has been demonstrated in approximately 20–40% of the patients with COPD, and sarcopenia in 10–25% of them [8, 9].

✉ Tatiana Munhoz da Rocha Lemos Costa
tatimrlemos@yahoo.com.br

[1] Endocrine Division (SEMPR), Hospital de Clinicas, Federal University of Paraná, Curitiba, Brazil

[2] Pulmonary Division, Hospital de Clinicas, Federal University of Paraná, Curitiba, Brazil

Low bone mineral density (BMD) is common in patients with COPD, with prevalence of osteoporosis varying from 9 to 69% in previous studies [10, 11]. The etiology of low BMD in these patients is multifactorial and includes low body mass index (BMI), inflammatory cytokines, and decreased lean mass [12–14].

It is still unclear whether abnormalities of body composition in patients with COPD are associated with disease severity and prognosis [15]. The main aims of this study were to evaluate changes in body composition and the prevalence of pre-sarcopenia and sarcopenia in patients with COPD.

Patients and methods

Subjects

This was a cross-sectional study involving patients with COPD treated at the pulmonary outpatient clinic of the Hospital de Clinicas at Universidade Federal do Paraná. The study was approved by the Ethics Committee on Human Research at our institution and all patients signed an informed consent form.

All participants undergone BMD and body composition analysis between January 2010 and December 2014. Patients of both sexes and older than 50 years were included in the study if they had a diagnosis of tobacco-induced COPD evaluated by spirometry (KoKo PFT Spirometer, Occupational Health Dynamics, Hoover, AL, USA) with a post-bronchodilator FEV1/FVC < 0.70, as defined by the global initiative for chronic obstructive lung disease (GOLD) [1]. Patients were excluded if they were taking any medications (as corticosteroids, steroids, nutritional supplements, and antiretrovirals) or had another disease or clinical condition known to interfere with body composition. Two control groups matched by age and sex were used for comparison with the disease group (DG). One group of smokers without COPD (smokers group, SG), who were attending an outpatient clinic in our institution to stop smoking. One group of healthy, never smoker, individuals (never smoker group, NSG), who were volunteers of both sexes from a random population invited to participate in the study. All individuals in the control groups were older than 50 years and had undergone evaluation of BMD and body composition in the same equipment as those in the DG. All individuals in the SG underwent spirometry using the same spirometer used for the patients in the DG and were excluded from the study if diagnosed with COPD.

Weight (kg) was measured on a digital electronic scale with a maximum capacity of 200 kg and accuracy of 50 g while the participants wore light clothes. Height (m) was measured while the individuals kept their backs straight, heels together, and arms extended alongside the body. Their BMI was determined by dividing the weight (kg) by the squared height (m^2). According to the BMI results, the groups were classified as underweight (BMI < 22 kg/m^2), normal weight (BMI ≥ 22 and <27 kg/m^2), or overweight/obese (BMI ≥ 27 kg/m^2) following the recommendation by Lipschitz et al. [16], which are more suitable for elderly individuals.

All participants underwent a total body assessment for evaluation of body composition and BMD using dual energy X-ray absorptiometry (DXA) on a Lunar Prodigy whole-body scanner (GE Medical Systems, Madison, WI, USA) equipped with the software Encore. The software provides data about lean body mass (bone mass plus fat-free mass), bone-free lean mass (lean mass minus fat-free mass), fat mass, and BMD. The regions evaluated in the test were the lumbar spine (LS), total femur (TF), and femoral neck (FN). The BMD results were expressed as g/cm². The precision, accuracy and stability of the equipment were constantly tested, and its coefficient of variation was 0.010 g/cm^2 for the LS, 0.012 g/cm^2 for the TF and 0.010 g/cm^2 for FN. The body composition data were analyzed separately according to gender.

Patients in the DG underwent the 6-min walk test for evaluation of exercise capacity and gait speed. Patients with a gait speed ≤0.8 m/s were considered to have a slow walking speed [7].

Definition of sarcopenia

Pre-sarcopenia was defined as the occurrence of a low lean body mass, which was diagnosed according to the criterion proposed by the Foundation for the National Institute of Health (FNIH), as follow: appendicular lean mass (ALM) divided by the BMI (ALM/BMI). A ALM/BMI ratio below 0.789 in men and 0.512 in women was used to define low body lean mass [17]. The diagnosis of sarcopenia was made in patients with a low lean mass associated with a gait speed ≤0.8 m/s [17].

COPD severity and prognosis was evaluated according to several clinical parameters, including lifetime smoking exposure (pack-years) [18], history of exacerbations, post-bronchodilator forced expiratory volume in the first second (FEV1), modified Medical Research Council (mMRC) dyspnea scale [19], COPD Assessment Test (CAT) [20], and 6-min walk test [21]. Patients in the DG were classified according to the degree of airflow obstruction (FEV1) into categories 1 (≥80%), 2 (50–79%), 3 (30–49%), and 4 (<30%) (1). The COPD severity was determined according to the GOLD index, which is based on the postbronchodilator FEV1, history of exacerbations in the previous year, and symptoms such as dyspnea (measured with the mMRC or CAT), and classified the study groups into categories A, B, C, and D (1). The COPD prognosis was evaluated with the

BODE index (B, body mass index; O, airway obstruction; D, dyspnea; E, exercise capacity), and the patients were classified into four quartiles, with the first being the least severe and the fourth the most severe one [22].

Statistical analysis

Data are presented as mean ± standard deviation (SD). All analyses were performed using IBM SPSS Statistics, v.20.0 (Armonk, NY: IBM Corp.). The normality of the distribution of the variables was evaluated with the Kolmogorov–Smirnov test. The comparison between two groups of quantitative variables was performed with Student's *t* test for independent samples or using the nonparametric Mann–Whitney test. When comparing more than two groups, we used analysis of variance (ANOVA) with one factor and the least significant difference (LSD) test for multiple comparisons or the nonparametric Kruskal–Wallis test. For the preliminary statistical analysis, we used Fisher's exact test and the chi-square test to assess the association between two qualitative variables. *p* values below 0.05 were considered statistically significant.

We performed univariate analysis and adjusted a logistic regression model considering sarcopenia as the response (dependent) variable and age, gender, GOLD index, and BODE index as explanatory variables. For each variable and for the presence of the other variable included in the model, we tested the null hypothesis that the probability of sarcopenia was equal for any classification of the variable (lack of association between the variable and sarcopenia), versus the alternative hypothesis of different probabilities. The significance (*p*) values of the statistical tests and the odds ratio (OR) with a confidence interval of 95% were calculated.

Results

Subjects

Of the 758 COPD patients screened, one hundred twenty six accepted to participate in the study, but five were excluded for not having the body composition exam. Thus, the final DG comprised 121 patients (65 women, mean age 67.9 ± 8.6 years, mean BMI 26.5 ± 6.2 kg/m^2). Of these, 34 (28%) had normal weight, 32 (26.4%) were underweight, and 55 (45.5%) were overweight. The mean tobacco consumption was 58.9 ± 40.8 pack-years and 23 (19.1%) patients were still smoking at the time of the study. According to the degree of obstruction evaluated by the FEV1, 21 (17.3%) patients were classified as group 1, 48 (39.6%) as group 2, 39 (32.2%) as group 3, and 13 (10.7%) as group 4. Based on the GOLD classification, GOLD A, B and D groups had the same number of 29 patients each, while 34 patients were classified as GOLD C. According to the BODE index, 55 (45.4%) patients were in the first quartile, 37 (30.5%) in the second quartile, 18 (14.8%) in the third quartile, and 11 (9%) in the fourth quartile.

The SG comprised 63 individuals (29 women) with a mean age of 65.5 ± 8.9 years and a mean BMI 27.6 ± 3.6 kg/m^2. All individuals were current smokers at the time of the study. The mean tobacco consumption was 38 ± 28.2 pack-years. The NSG comprised 81 individuals (47 women) with a mean age of 66 ± 8.5 years and a mean BMI of 26.1 ± 2.6 kg/m^2.

There were no differences in gender ($p = 0.612$), age ($p = 0.147$), or BMI ($p = 0.143$) among the groups, except for the mean tobacco consumption in the DG, which was greater than that in the SG ($p < 0.001$).

Body composition

Body composition parameters are shown in Table 1. The percentage of total body fat mass (TFM) was significantly different among the groups in both genders, despite no difference in BMI. In DG women, TFM was 38.3 ± 9.6%, a value significantly lower than 41.9 ± 5.3% observed in SG women and 40.3 ± 5.7% observed in the NSG women ($p = 0.048$). Similarly, DG men exhibited a TFM of 27.2 ± 10.4% that was significantly lower than 30.5 ± 6.0% observed in SG group and 30.5 ± 5.6% observed in the NSG group ($p = 0.043$).

Both BMI and relative skeletal muscle mass index (RSMI: ALM/height^2) decreased according to the worsening of GOLD in men and women, as well as the TFM and TLM in men (Table 2).

As BODE get worse, BMI and RSMI decreased in both sexes, as well as TLM in men (Table 3).

Lean mass (TLM) and BMD

There was a positive correlation between BMD values in all three measured sites with lean mass results in all study groups, but the FN in SG. The correlations observed in DG are shown in Fig. 1. SG presented a positive correlation in LS $r = 0.39$ ($p = 0.002$), FN $r = 0.16$ ($p = 0.217$) and TF = 0.39 ($p = 0.02$) and in the NSG the correlations were LS $r = 0.59$, FN $r = 0.36$ and TF $r = 0.46$, all $p < 0.001$.

Pre-sarcopenia

The prevalence of pre-sarcopenia in the DG was 46.3% ($n = 56$), 39.7% ($n = 25$) in the SG and 29.6% in the NSG ($n = 24$) ($p = 0.06$). In the DG, the gait speed significantly decreased as disease severity and prognosis impaired according to the GOLD classification and BODE index (Table 4 and Fig. 2).

Sarcopenia

A total of 15 (12.4%) patients in the DG presented sarcopenia. Age was the only difference observed between patients with (73.4 ± 8.8 years) and without (67 ± 8.2 years) sarcopenia ($p = 0.006$). Patients with and without sarcopenia did not differ in relation to BMI, gender, current tobacco use, mean tobacco use, osteopenia or osteoporosis, LS BMD, FN BMD, TF BMD, number of MVF, %TFM, TLM, A/G, FMI, and RSMI. The higher the BODE prognostic index, the higher the prevalence of sarcopenia ($p = 0.035$) (Table 5).

Table 1 Body composition parameters between groups

Variable	Women				Men			
	DG ($n = 121$)	SG ($n = 63$)	NSG ($n = 81$)	p	DG ($n = 121$)	SG ($n = 63$)	NSG ($n = 81$)	p
BMI (kg/m²)	27.2 ± 6.6	28 ± 3.7	25.6 ± 2.3	0.088	25.6 ± 5.3	27.3 ± 3.5	26.7 ± 2.7	0.180
TFM (%)	38.3 ± 9.6	41.9 ± 5.3	40.3 ± 5.7	0.048	27.2 ± 10.4	30.5 ± 6	30.5 ± 5.6	0.043
A/G	0.98 ± 0.1	0.99 ± 0.1	0.98 ± 0.1	0.839	1.15 ± 0.2	1.18 ± 0.2	1.27 ± 0.2	0.070
TFM (kg)	24.7 ± 11.4	28.2 ± 7.1	24.7 ± 5.1	0.165	20.5 ± 11.7	23.2 ± 7.1	22.8 ± 5.6	0.295
FMI	10.5 ± 4.7	11.3 ± 2.5	10.1 ± 2	0.344	7.3 ± 4	8.0 ± 2.3	8.1 ± 2.2	0.392
TLM (kg)	36.2 ± 7.7	37.9 ± 4.4	35.9 ± 5.4	0.329	48.4 ± 8.3	51.4 ± 5.5	50.3 ± 5.9	0.108
RSMI	6.2 ± 0.9	6.2 ± 0.6	6.1 ± 0.7	0.812	7.2 ± 1.1	7.7 ± 0.8	7.7 ± 0.7	0.069

DG disease group, *SG* smoking group, *NSG* never smoked group, *BMI* body mass index, *TFM* total body fat mass, *A/G* android/gynoid fat mass ratio, *TFM* total fat mass, *FMI* fat mass index (TFM/height^2), *TLM* total lean mass, *RSMI* relative skeletal muscle mass index ALM/height^2; statistical significance $p < 0.05$

Table 2 Body composition according to the global initiative for chronic obstructive lung disease (GOLD) classification in women and men with chronic obstructive pulmonary disease (COPD)

	Women gold					Men gold				
Variable	A ($n = 15$)	B ($n = 18$)	C ($n = 20$)	D ($n = 12$)	p	A ($n = 14$)	B ($n = 11$)	C ($n = 14$)	D ($n = 17$)	p
BMI (kg/m^2)	28.6 ± 7	27.6 ± 7.1	26.4 ± 6.9	26.1 ± 4.7	0.032	28.7 ± 4.8	27.1 ± 3.8	23 ± 4.5	24.1 ± 6	0.015
TFM (%)	40.2 ± 9.2	37.8 ± 11.6	37.4 ± 8.5	38 ± 9.1	0.883	30.2 ± 8.9	31.7 ± 7.6	22.2 ± 9.8	25.7 ± 12.2	0.08
A/G	1.04 ± 0.1	0.98 ± 0.2	0.98 ± 0.1	0.88 ± 0.1	0.688	1.19 ± 0.1	1.25 ± 0.1	1.15 ± 0.2	1.07 ± 0.2	0.115
TFM(kg)	26.6 ± 11.8	26.2 ± 13.1	23 ± 11.3	22.8 ± 8.6	0.690	25.4 ± 11.5	24.5 ± 9.5	18.1 ± 9.7	15.3 ± 12.8	0.049
FMI	11.5 ± 5.2	10.7 ± 5.3	9.7 ± 4.5	9.9 ± 3.5	0.07	9.2 ± 4.4	8.5 ± 2.9	5.28 ± 3.1	6.4 ± 4.3	0.06
TLM (kg)	36.8 ± 6.2	38.2 ± 6.4	34.3 ± 9.7	35.2 ± 4.3	0.345	53.5 ± 9.9	49.1 ± 6.8	47.6 ± 7.4	44.4 ± 6.6	0.02
RSMI	6.4 ± 1	6.2 ± 0.9	6 ± 1	6 ± 0.6	0.004	8.2 ± 1.3	7.4 ± 0.8	6.8 ± 0.8	6.5 ± 0.7	<0.001

BMI body mass index, *TFM* percentage of total fat mass, *A/G* android/gynoid fat mass ratio, *TFM* total fat mass, *FMI* fat mass index (TFM/height^2), *TLM* total lean mass, *RSMI* relative skeletal muscle mass index

Table 3 Body composition according to the BODE index in women and men with chronic obstructive pulmonary disease (COPD)

	Women BODE quartiles					Men BODE quartiles				
Variable	1 ($n = 31$)	2 ($n = 22$)	3 ($n = 8$)	4 ($n = 4$)	p	1 ($n = 24$)	2 ($n = 15$)	3 ($n = 10$)	4 ($n = 7$)	p
BMI (kg/m^2)	28.2 ± 6.9	26.6 ± 6.2	26.3 ± 7.9	24.4 ± 4.7	0.002	27.4 ± 4.3	26.4 ± 6.2	21.6 ± 3.3	23.2 ± 6.3	0.001
TFM (%)	39.4 ± 10	36.9 ± 9.2	36.5 ± 10.5	39.5 ± 6.4	0.754	30 ± 8.4	27.4 ± 10.5	22 ± 9.3	24.4 ± 16	0.196
A/G	1.02 ± 0.1	0.92 ± 0.1	0.99 ± 0.2	0.92 ± 0.1	0.08	1.23 ± 0.1	1.14 ± 0.2	1.1 ± 0.2	1.03 ± 0.2	0.07
TFM (kg)	26.3 ± 11.5	23.6 ± 11.6	23.4 ± 12.9	20.5 ± 5.5	0.694	23.6 ± 10.2	21.6 ± 12.5	12.9 ± 7.8	18.2 ± 15.7	0.09
FMI	11.2 ± 5	9.8 ± 4.4	9.8 ± 5.1	9.4 ± 3.2	0.645	8.5 ± 3.8	7.4 ± 4.1	4.8 ± 2.6	6.1 ± 5	0.08
TLM (kg)	36.9 ± 6	36.7 ± 5.8	37.8 ± 9	30.9 ± 3.3	0.335	50.8 ± 8.1	50.5 ± 8.9	42.1 ± 4.7	44.7 ± 6.9	0.014
RSMI	6.3 ± 0.9	6.2 ± 0.	6.1 ± 1.1	5.4 ± 0.5	0.001	7.7 ± 1.2	7.3 ± 0.9	6.3 ± 0.6	6.3 ± 0.6	0.001

BMI body mass index, *TFM* percentage of total fat mass, *A/G* android/gynoid fat mass ratio, *TFM* total fat mass, *FMI* fat mass index (TFM/height^2), *TLM* total lean mass, *RSMI* relative skeletal muscle mass index

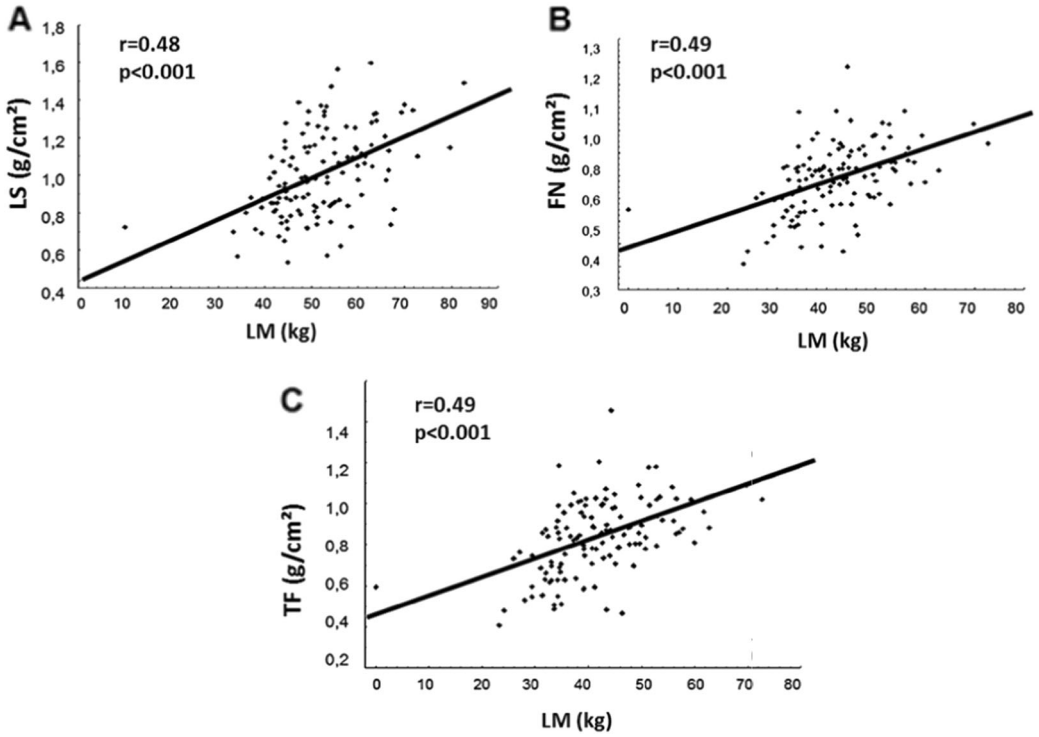

Fig. 1 Correlation of bone mineral density at **a** lumbar spine, **b** femoral neck, and **c** total femur with lean mass in the disease group (DG). LS lumbar spine, FN femoral neck, TF total femur, LM lean mass, r = coefficient correlation

Table 4 Gait speed in the disease group (DG) distributed according to disease severity (GOLD classification) and prognosis (BODE index)

	Gait speed (*m/s*)				
	1/A	2/B	3/C	4/D	*p*
FEV1	1.16 ± 0.2	1.07 ± 0.2	0.96 ± 0.2	0.85 ± 0.3	0.001
GOLD	1.12 ± 0.2	1.10 ± 0.2	0.99 ± 0.3	0.90 ± 0.2	0.004
BODE	1.14 ± 0.2	1.00 ± 0.2	0.92 ± 0.3	0.75 ± 0.3	0.000

FEV1 postbronchodilator forced expiratory volume in the first second, *BODE B* body mass index, *O* airway obstruction, *D* dyspnea, *E* exercise capacity, *GOLD* global initiative for chronic obstructive lung disease

On univariate analysis, sarcopenia was associated with age and BODE index. Logistic regression analysis using these two explanatory variables showed an increased risk of sarcopenia with age (OR 1.10, 95% CI 1.02–1.18, p = 0.012) and BODE index (OR 3.5, 95% CI 1.06–11.56, p = 0.035).

Discussion

This study evaluated the body composition, pre-sarcopenia, and sarcopenia in patients with COPD, and correlated them with criteria of severity and prognosis of the disease. The evaluation also included a comparison of these results with those obtained in two control groups, one with smokers and another with never smokers. The smoking load was higher in the DG when compared with the SG, which was expected considering that the number of pack-years is related to the development of COPD, although other factors are also involved in this process [23, 24].

Patients in the DG had a lower body fat percentage compared with those in the control groups, as previously described [25, 26]. A negative energy balance mainly influencing the individual's body composition accompanies frequent exacerbations of the disease. These changes in body composition may contribute to the low-grade chronic systemic inflammation present in these patients and indirectly stimulate COPD progression. The reasons for a progressive loss of weight, lean mass, and fat mass in patients with COPD include an increased catabolic demand from the respiratory muscles, elevated levels of proinflammatory cytokines, increased oxidative stress, and smoking [25]. The absence of changes in body composition in the SG reinforces the hypothesis that the disease itself, rather than smoking, is responsible for these changes, besides the smoking load could have an effect too.

The parameters of body composition in the DG varied according to the GOLD and BODE indices. Levels of BMI < 21 kg/m² are described as a risk factor for exacerbations and worse prognosis in patients affected by the disease [27]. In addition to lower BMI, lower lean mass is associated

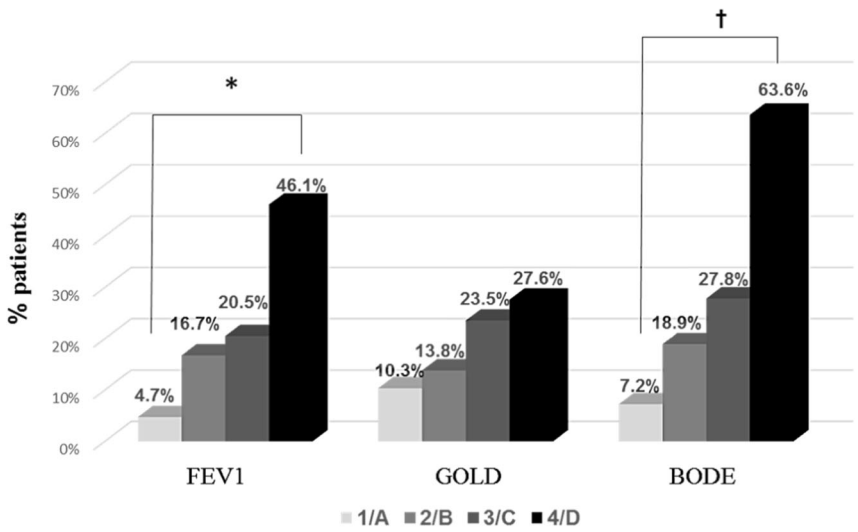

Fig. 2 Percentage of patients with abnormal gait speed (<0.8 m/s) according to disease severity (FEV1 and GOLD classification) and prognosis (BODE index). *$p < 0.026$ (FEV1), † $p < 0.001$ (BODE) ANOVA FEV1 forced expiratory volume in first second-post-bronchodilator, GOLD global intiative for chronic obstructive lung disease, BODE (B body mass index, O airway obstruction, D dyspnea, E exercise capacity).

Table 5 Diagnosis of sarcopenia in relation to disease severity (FEV1 and GOLD classification) and prognosis (BODE index)

	1/A	2/B	3/C	4/D	*p*
FEV1	1 (4.7%)	6 (12.5%)	4 (10.2%)	4 (30.7%)	0.149
GOLD	2 (6.9%)	3 (10.3%)	5 (14.7%)	5 (17.2%)	0.634
BODE	3 (5.4%)	5 (13.5%)	3 (16.6%)	4 (36.3%)	0.035

FEV1 postbronchodilator forced expiratory volume in the first second, *BODE B* body mass index, *O* airway obstruction, *D* dyspnea, *E* exercise capacity, *GOLD* global initiative for chronic obstructive lung disease

with worse lung function, greater number of exacerbations, and worse FEV1 [28]. Recent studies have pointed out that a higher percentage of fat mass, rather than a reduction in lean mass, could be the factor related to poorer physical performance in patients with COPD [29, 30]. The calculated fat mass index (FMI) showed no association with disease severity and prognosis or difference with the control groups.

In patients with COPD, poorer physical performance evaluated with the 6-min walk test was associated with worse disease severity and prognosis. A greater degree of pulmonary obstruction and worse prognosis, in turn, were associated with gait velocity <0.8 m/s, a criterion of poor performance. Andrianopoulos et al. [31] have suggested the use of a higher gait speed cutoff value (<0.9 m/s) for characterization of poor performance in patients with COPD, showing that at this level, the patients present a worse prognostic index and higher rates of hospitalization and mortality.

The prevalence of pre-sarcopenia (46.3%) in the DG was similar to that found in other studies, which range from 20 to 40%, and showed a trend towards higher values in the DG when compared with the SG and NSG [8, 32]. The frequency of sarcopenia however, was much higher in the DG when compared with the control groups, and similar to the frequency found in the literature (around 15–20%) [8, 9]. Comparing to healthy individuals seen in literature and using the same diagnostic criteria we found in our patients with COPD, much higher prevalence of sarcopenia 12.4 vs. 2.3% [33]. This finding emphasizes the importance of obtaining a physical performance test in patients with COPD since only a reduction in lean mass or a diagnosis of pre-sarcopenia is insufficient to determine the exercise capacity of these patients. However, this may also suggest that the respiratory difficult itself may be the reason to the low performance.

When we separated the patients with COPD into subgroups with and without sarcopenia, we observed that the differences between both subgroups were the mean age and BODE prognostic index. The low absolute number of patients with sarcopenia may explain the lack of difference in the other parameters. The finding that sarcopenia was unrelated to the patients' BMI in our cohort is an important one, considering the common assumption that the diagnosis of sarcopenia is present only in lean patients, assuming that it is more prevalent in this population [34]. However, recent studies have also shown that around 10–15% of normal-weight individuals have sarcopenia, as well as overweight or obese individuals [35, 36].

Some studies have shown an association between the occurrence of sarcopenia and worse obstruction index (FEV1), GOLD, and lower walking performance [8, 9]. The finding of a higher prevalence of sarcopenia in patients with a poorer BODE index was expected since the index takes into account a parameter of physical capacity that can be affected by lean mass. The reduction in lean mass leads to a decrease in exercise capacity, which in turn leads to poorer quality of life indices, high frequency of exacerbations, and increased mortality [37]. We were unable to find in the literature associations between sarcopenia and the BODE

index, as shown in the present study. On univariate analysis, the OR of this association was 3.50 showing that the presence of sarcopenia is associated with a worse prognosis of the disease.

The correlations between a lower lean mass and lower BMD values and the presence of osteopenia or osteoporosis and fractures have already been shown in different populations [38, 39]. Vondracek et al. [40] have reported specifically in patients with COPD the association between lower lean mass and lower BMD, which we have confirmed in all three groups in the present study.

One of the limitations of the present study was the lack of evaluation of muscle strength tests to compare the diagnosis of sarcopenia obtained from patients with COPD with those obtained from controls. In order to minimize this limitation, we compared the diagnoses of pre-sarcopenia between the groups. Other limitation was that the type of feeding of these subjects, in particular the protein intake was not investigated and patients with COPD may have had a worse outcome in the walking test due to a worse respiratory parameter and not a muscular limitation.

In conclusion, this study showed an important prevalence of sarcopenia in patients with COPD. These findings serve as an alert for physicians to weight on potential musculoskeletal changes that occur in patients with this condition, in addition to changes related to aging and low body weight. In order to increase survival, improve quality of life and compress morbidity, a multi-modal approach is needed, which should targeted the factors involved in loss of lean mass in patients with COPD.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. National Heart, Lung and Blood Institutes. (2011). www.goldcopd.com
2. T.M. Eagan, P. Aukrust, T. Ueland, J.A. Hardie, A. Johannessen, T.E. Mollnes et al. Body composition and plasma levels of inflammatory biomarkers in COPD. Eur. Respir. J. **36**(5), 1027–1033 (2010)
3. N. Cielen, K. Maes, G. Gayan-Ramirez, Musculoskeletal disorders in chronic obstructive pulmonary disease. Biomed. Res. Int. **2014**, 965764 (2014)
4. M. Decramer, W. Janssens, M. Miravitlles, Chronic obstructive pulmonary disease. Lancet **379**(9823), 1341–1351 (2012).
5. M.I. Polkey, J. Moxham, Attacking the disease spiral in chronic obstructive pulmonary disease. Clin. Med. **6**(2), 190–196 (2006)
6. P. Tunsupon, M.J. Mador, The influence of body composition on pulmonary rehabilitation outcomes in chronic obstructive pulmonary disease patients. Lung **195**(6), 729–738 (2017).
7. A.J. Cruz-Jentoft, F. Landi, S.M. Schneider, C. Zúñiga, H. Arai, Y. Boirie, L.K. Chen, R.A. Fielding, F.C. Martin, J.P. Michel, C. Sieber, J.R. Stout, S.A. Studenski, B. Vellas, J. Woo, M. Zamboni, T. Cederholm, Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing **43**(6), 748–759 (2014)
8. M.K. Byun, E.N. Cho, J. Chang, C.M. Ahn, H.J. Kim, Sarcopenia correlates with systemic inflammation in COPD. Int. J. Chron. Obstruct. Pulmon. Dis. **12**, 669–675 (2017)
9. S.E. Jones, M. Maddocks, S.S. Kon, J.L. Canavan, C.M. Nolan, A.L. Clark, M.I. Polkey, W.D. Man, Sarcopenia in COPD: prevalence, clinical correlates and response to pulmonary rehabilitation. Thorax **70**(3), 213–218 (2015)
10. C.B. Franco, G. Paz-Filho, P.E. Gomes, V.B. Nascimento, C.A. Kulak, C.L. Boguszewski, V.Z. Borba, Chronic obstructive pulmonary disease is associated with osteoporosis and low levels of vitamin D. Osteoporos. Int. **20**(11), 1881–1887 (2009)
11. L. Graat-Verboom, E.F. Wouters, F.W. Smeenk, B.E. van den Borne, R. Lunde, M.A. Spruit, Current status of research on osteoporosis in COPD: a systematic review. Eur. Respir. J. **34**, 209–218 (2009)
12. Y. Yamamoto, M. Yoshikawa, K. Tomoda, Y. Fujita, M. Yamauchi, A. Fukuoka, S. Tamaki, N. Koyama, H. Kimura, Distribution of bone mineral content is associated with body weight and exercise capacity in patients with chronic obstructive pulmonary disease. Respiration **87**(2), 158–164 (2014)
13. W. Janssens, A. Lehouck, C. Carremans, R. Bouillon, C. Mathieu, M. Decramer, Vitamin D beyond bones in chronic obstructive pulmonary disease: time to act. Am. J. Respir. Crit. Care Med. **179**, 630–636 (2009)
14. L. Forli, O.J. Mellbye, J. Halse, O. Bjortuft, M. Vatn, J. Boe, Cytokines, bone turnover markers and weight change in candidates for lung transplantation. Pulm. Pharmacol. Ther. **21**, 188–195 (2008)
15. H.K. Koo, J.H. Park, H.K. Park, H. Jung, S.S. Lee, Conflicting role of sarcopenia and obesity in male patients with chronic obstructive pulmonary disease: Korean National Health and Nutrition Examination Survey. PLoS. One **9**(10), e110448 (2014)
16. D.A. Lipschitz, Screening for nutritional status in the elderly. Prim. Care **21**(1), 55–67 (1994)
17. S.A. Studenski, K.W. Peters, D.E. Alley, P.M. Cawthon, R.R. McLean, T.B. Harris, L. Ferrucci, J.M. Guralnik, M.S. Fragala, A. M. Kenny, D.P. Kiel, S.B. Kritchevsky, M.D. Shardell, T.T. Dam, M.T. Vassileva, The FNIH sarcopenia project: rationale, study description,conference recommendations, and final estimates. J. Gerontol. Ser. A **69**(5), 547–558 (2014)
18. J. Prignot, Quantification and chemical markers of tobacco-exposure. Eur. J. Respir. Dis. **70**(1), 1–7 (1987)
19. B.G. Ferris, Epidemiology standardization project (American Thoracic Society). Am. Rev. Respir. Dis. **118**(6 Pt 2), 1–120 (1978)
20. P.W. Jones, G. Harding, P. Berry et al. Development and first validation of the COPD assessment test. Eur. Respir. J. **34**(3), 648–654 (2009)
21. B. Balke, A simple field test for the assessment of physical fitness. Rep 63–6. Rep Civ Aeromed Res Inst US. 1–8 (1963)
22. B. Celli, C. Cote, J. Marin et al. The body mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N. Engl. J. Med. **350**, 1005–1012 (2004)
23. D.A. Stern, W.J. Morgan, A.L. Wright, S. Guerra, F.D. Martinez, Poor airway function in early infancy and lung function by age 22 years: a non-selective longitudinal cohort study. Lancet **370** (9589), 758–764 (2007)

24. G.M. Hunninghake, M.H. Cho, Y. Tesfaigzi, M.E. Soto-Quiros, L. Avila, J. Lasky-Su, C. Stidley, E. Melén, C. Söderhäll, J. Hallberg, I. Kull, J. Kere, M. Svartengren, G. Pershagen, M. Wickman, C. Lange, D.L. Demeo, C.P. Hersh, B.J. Klanderman, B.A. Raby, D. Sparrow, S.D. Shapiro, E.K. Silverman, A.A. Litonjua, S.T. Weiss, J.C. Celedón, MMP12, lung function, and COPD in high-risk populations. N. Engl. J. Med. **361**(27), 2599–2608 (2009)
25. A.E. Makarevich, S. Lemiasheuskaya, Dynamics of body composition in male patients during chronic obstructive pulmonary disease (COPD) development. Pneumonol. Alergol. Pol. **83**(6), 424–430 (2015)
26. S.B. Kim, Y.A. Kang, J.Y. Jung, M.S. Park, Y.S. Kim, S.K. Kim, J. Chang, E.Y. Kim, Body mass index and fat free mass index in obstructive lung disease in Korea. Int. J. Tuberc. Lung Dis. **18**(1), 102–108 (2014)
27. M. Lainscak, S. von Haehling, W. Doehner, I. Sarc, T. Jeric, K. Ziherl, M. Kosnik, S.D. Anker, S. Suskovic, Body mass index and prognosis in patients hospitalized with acute exacerbation of chronic obstructive pulmonary disease. J. Cachex-. Sarcopenia Muscle **2**(2), 81–86 (2011)
28. N.S. Hopkinson, R.C. Tennant, M.J. Dayer, E.B. Swallow, T.T. Hansel, J. Moxham, M.I. Polkey, A prospective study of decline in fat free mass and skeletal muscle strength in chronic obstructive pulmonary disease. Respir. Res. **8**, 25 (2007)
29. B. Van den Borst, H.R. Gosker, A.M. Schols, Central fat and peripheral muscle: partners in crime in chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med. **187**(1), 8–13 (2013)
30. A.M. Abbatecola, A. Fumagalli, L. Spazzafumo, V. Betti, C. Misuraca, A. Corsonello, A. Cherubini, E.E. Guffanti, F. Lattanzio, Body composition markers in older persons with COPD. Age Ageing **43**(4), 548–553 (2014)
31. V. Andrianopoulos, E.F. Wouters, V.M. Pinto-Plata, L.E. Vanfleteren, P.S. Bakke, F.M. Franssen, A. Agusti, W. MacNee, S.I. Rennard, R. Tal-Singer, I. Vogiatzis, J. Vestbo, B.R. Celli, M.A. Spruit, Prognostic value of variables derived from the six-minute walk test in patients with COPD: Results from the ECLIPSE study. Respir. Med. **109**(9), 1138–1146 (2015)
32. R.T. Jagoe, M.P. Engelen, Muscle wasting and changes in muscle protein metabolism in chronic obstructive pulmonary disease. Eur. Respir. J. **46**, 52s–63s (2003)
33. T.T. Dam, K.W. Peters, M. Fragala, P.M. Cawthon, T.B. Harris, R. McLean, M. Shardell, D.E. Alley, A. Kenny, L. Ferrucci, J. Guralnik, D.P. Kiel, S. Kritchevsky, M.T. Vassileva, S. Studenski, An evidence-based comparison of operational criteria for the presence of sarcopenia. J. Gerontol. Ser. A **69**(5), 584–590 (2014)
34. F.M. Franssen, H.P. Sauerwein, E.P. Rutten, E.F. Wouters, A.M. Schols, Whole-body resting and exercise-induced lipolysis in sarcopenic [corrected] patients with COPD. Eur. Respir. J. **32**(6), 1466–1471 (2008)
35. F. Maltais, Body composition in COPD: looking beyond BMI. Int. J. Tuberc. Lung. Dis. **18**(1), 3–4 (2014)
36. L.W. Lee, C.M. Lin, H.C. Li, P.L. Hsiao, A.C. Chung, C.J. Hsieh, P.C. Wu, S.F. Hsu, Body composition changes in male patients with chronic obstructive pulmonary disease: aging or disease process? PLoS. One **12**(7), e0180928 (2017)
37. A.M. Schols, R. Broekhuizen, C.A. Weling-Scheepers, E.F. Wouters, Body composition and mortality in chronic obstructive pulmonary disease. Am. J. Clin. Nutr. **82**(1), 53–59 (2005)
38. J.R. Guthrie, P.R. Ebeling, J.L. Hopper, E. Barrett-Connor, L. Dennerstein, E.C. Dudley, H.G. Burger, J.D. Wark, A prospective study of bone loss in menopausal Australian-born women. Osteoporos. Int. **8**(3), 282–290 (1998)
39. K. Zhu, M. Hunter, A. James, E.M. Lim, J.P. Walsh, Associations between body mass index, lean and fat body mass and bone mineral density in middle-aged Australians: The Busselton Healthy Ageing Study. Bone **74**, 146–152 (2015)
40. S.F. Vondracek, N.F. Voelkel, M.T. McDermott, C. Valdez, The relationship between adipokines, body composition, and bone density in men with chronic obstructive pulmonary disease. Int. J. Chron. Obstruct. Pulmon. Dis. **4**, 267–277 (2009)