

**Evaluation of respiratory muscle strength and endurance, peripheral muscle strength, and functional capacity in patients with COPD**

**Avaliação da força e resistência muscular respiratória, força muscular periférica e capacidade funcional em pacientes com DPOC**

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**ABSTRACT**

This is an analytical, observational and cross-sectional study conducted from August 2017 to February 2020 in patients with Chronic Obstructive Pulmonary Disease (COPD) that aimed to assess respiratory muscle strength and endurance, peripheral muscle strength and functional capacity in patients with COPD. Respiratory muscle function was assessed using strength and endurance, peripheral muscle strength using the handgrip test, and functional capacity using the six-minute walk test (6MWT). The sensation of dyspnea was assessed by modified Medical Research Council and risk of exacerbation/hospitalization according to the classification of the Global Initiative for Chronic Obstructive Lung (GOLD). For statistical analysis, the Kolmogorov Smirnov, Chi-square, Pearson's correlation, Student t, ANOVA, and Bonferroni tests were performed with a significance level of 0.05. Forty patients were analyzed. There was a reduction in inspiratory and peripheral muscle strength in 97.5% ( $p < 0.001$ ) and 80% of patients ( $p = 0.001$ ), respectively, in addition to a decrease in functional capacity in 97.4% ( $p < 0.001$ ) of individuals evaluated. There was a correlation between the GOLD classification with 6MWT ( $p=0.005$ ) and inspiratory muscle strength ( $p=0.041$ ), in addition to a relation between distance traveled and spirometric severity of obstruction ( $p=0.049$ ). We conclude that there was a significant reduction in respiratory and peripheral muscle strength and functional capacity.

The higher the degree of obstruction, the worse the performance on the 6MWT. In addition, patients who walked less have a higher risk of exacerbation and hospitalization, as well as those who have less respiratory muscle strength.

**Keywords:** Chronic obstructive pulmonary disease, Muscle weakness, Functionality.

## RESUMO

Este é um estudo analítico, observacional e transversal realizado de agosto de 2017 a fevereiro de 2020 em pacientes com doença pulmonar obstrutiva crônica (DPOC) que teve como objetivo avaliar a força muscular respiratória e a resistência, a força muscular periférica e a capacidade funcional em pacientes com DPOC. A função muscular respiratória foi avaliada usando força e resistência, força muscular periférica usando o teste de punho, e capacidade funcional usando o teste de caminhada de seis minutos (6MWT). A sensação de dispnéia foi avaliada pelo Conselho de Pesquisa Médica modificado e o risco de exacerbção/hospitalização de acordo com a classificação da Iniciativa Global para o Pulmão Obstrutivo Crônico (GOLD). Para análise estatística, os testes Kolmogorov Smirnov, Qui-quadrado, correlação de Pearson, Student t, ANOVA e Bonferroni foram realizados com um nível de significância de 0,05. Quarenta pacientes foram analisados. Houve uma redução na força muscular inspiratória e periférica em 97,5% ( $p < 0,001$ ) e 80% dos pacientes ( $p = 0,001$ ), respectivamente, além de uma redução na capacidade funcional em 97,4% ( $p < 0,001$ ) dos indivíduos avaliados. Houve uma correlação entre a classificação GOLD com 6MWT ( $p = 0,005$ ) e força muscular inspiratória ( $p = 0,041$ ), além de uma relação entre a distância percorrida e a gravidade espirométrica da obstrução ( $p = 0,049$ ). Concluímos que houve uma redução significativa na força muscular respiratória e periférica e na capacidade funcional. Quanto maior o grau de obstrução, pior o desempenho no TC6MW. Além disso, os pacientes que caminharam menos têm maior risco de exacerbção e hospitalização, assim como aqueles que têm menos força muscular respiratória.

**Palavras-chave:** Doença pulmonar obstrutiva crônica, Fraqueza muscular, Funcionalidade.

## 1 INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is clinically characterized by the presence of productive cough and/or dyspnea on effort, generally progressive [1]. It presents as common manifestations changes in respiratory and peripheral muscles, reduced muscle strength, changes in muscle morphology and bioenergetics, hormonal changes, low tolerance to exercise, and changes in nutritional status [2].

The main complaints reported by patients are related to dyspnea and fatigue when exercising. The cause of these symptoms is the result of a complex interaction of ventilatory, cardiovascular, metabolic, and muscular impairments. Thus, low tolerance to exercise is one of the factors capable of causing a direct impact on the activities of daily living and the quality of life of these patients [3].

One of the instruments used to measure the degree of dyspnea in these daily activities [4] is the modified Medical Research Council scale (mMRC), which relates the increase in the dyspnea index to

disease progression [5]. The impairment of functional capacity in these patients is directly related to the frequency of exacerbations and hospitalizations [6] and mortality [7].

The decrease in the functional capacity of patients with COPD is closely associated with a reduced respiratory muscle strength [8,9] and strength and endurance of upper and lower limbs compared to healthy individuals [10]. Such changes may be related to neuromechanical dysfunction, thoracoabdominal desynchrony, respiratory muscles, diaphragms and accessory muscles, and changes in lung volumes and capacity [11].

Therefore, one of the main treatment objectives for these patients is to improve symptoms, especially reducing dyspnea, consequently improving the ability to exercise and the quality of life. There are pharmacological and non-pharmacological treatments, such as aerobic exercise, strength and resistance training of respiratory and peripheral muscles, and neuromuscular electrical stimulation, as the most effective therapeutic possibilities for pulmonary rehabilitation in this population [12].

The objective of the present study is to evaluate respiratory muscle endurance and strength, peripheral muscle strength, and functional capacity in patients with COPD to verify possible changes and analyze factors that may be affecting these changes.

## **2 METHODS**

### **2.1 STUDY DESIGN**

This is an analytical, observational, cross-sectional study carried out from August 2017 to February 2020. This study was approved by the Research Ethics Committee of the Lauro Wanderley University Hospital (HULW) in accordance with the Declaration of Helsinki. All volunteers informed their consent to participate in the research. The present study is an integral part of the research project entitled "Prevention, evaluation and treatment of rehabilitation in cardiovascular, respiratory, and metabolic disorders." The study protocol is registered at the Brazilian Registry of Clinical Trials (ReBEC) under the number RBR-89QMHC.

### **2.2 SAMPLE**

Inclusion criteria were patients over 40 years of age [13], with clinical and spirometric diagnosis of COPD, of both genders, already admitted to the HULW pulmonology clinic during the study period. Patients who had difficulty in understanding spirometric assessment and strength and endurance ventilatory muscle evaluation, patients with neurodegenerative diseases, clinical instability marked by signs of uncontrolled infection, any type of heart disease diagnosed and proven through imaging or

laboratory tests, orthopedic problems and/or influencing gait, patients with body mass index (BMI) > 35 kg/m<sup>2</sup>, psychic crises, and those who refused to participate in the research were excluded.

### 2.3 EVALUATIONS

Two evaluators attended the pulmonology service where they screened all patients with COPD and then contacted them so that they could attend the Laboratory of Physiotherapy in Cardiorespiratory Research at the Federal University of Paraíba. They were evaluated according to the inclusion and exclusion criteria. Once selected, patients were subjected to assessment of respiratory muscle endurance and strength, peripheral muscle strength, functional capacity, dyspnea sensation, and risk of exacerbation/hospitalization.

### 2.4 ASSESSMENT OF RESPIRATORY MUSCLE FUNCTION

To evaluate respiratory muscle function, an electronic computerized device (KH2; PowerBreathe International Ltd. UK) was used along with a feedback Breathelink software. The inspiratory muscle strength was evaluated through MIP and respiratory musculature endurance. During the test, patients remained seated with supported arms and nasal clip to prevent air leakage outside the device.

During MIP assessment, the patient was instructed to exhale up to the residual volume, and then perform a maximum inspiration maintained for as long as possible, neglected when shorter than 1.5 seconds. This evaluation was carried out from three to a maximum of eight repetitions seeking variations lower than 10% in the values between them. The measure of greatest value was considered.

Respiratory muscle endurance was assessed by incremental load test, where patients were instructed to perform the largest number of breaths. An initial load of 10 cmH<sub>2</sub>O was standardized for a period of two minutes. Subsequently, the patient was instructed to rest for one minute, and then a new two-minute cycle started, adding another 10 cmH<sub>2</sub>O to the equipment load. The highest load sustained for at least one minute was considered the value of sustained MIP.

The test was interrupted if the participant failed the task or was defined by the evaluator as incapable of generating the target pressure. In addition, there was an interruption in the test if the sensation of dyspnea or fatigue was described by the patient as too uncomfortable to tolerate.

MIP was evaluated before (initial MIP) and shortly after the incremental load test (final MIP) to verify the occurrence of muscle fatigue. The division between final MIP and initial MIP was called

fatigue resistance index (FRI). We consider the occurrence of reduction in respiratory muscle resistance when the FRI is lower than 88% [14].

During all tests, patients were monitored for vital signs: heart and respiratory rate and SpO<sub>2</sub>. The sensation of dyspnea and fatigue was also monitored using the Borg scale before and after the end of each test. In addition, standard words of encouragement were said to optimize the performance of participants.

## 2.5 ASSESSMENT OF PERIPHERAL MUSCLE STRENGTH

The assessment of peripheral muscle strength was performed by measuring handgrip strength using a dynamometer (JAMAR<sup>®</sup> hand dynamometer; Patterson Medical; Warrenville, USA). The measurement was performed with patients seated with the elbow flexed at 90°, with three repetitions in the dominant limb. The highest value found among the three repetitions was recorded [15]. The values obtained were compared with those recommended for age and gender of the Brazilian population [16].

## 2.6 ASSESSMENT OF FUNCTIONAL CAPACITY

Functional capacity was assessed by the six-minute walk test (6MWT). The patient should cover a 30-meter flat and rigid surface visibly delimited through two cones. The main objective of the test is to determine exercise tolerance during a submaximal exercise [17].

The patient was instructed to walk as fast as possible for six minutes without stopping. The pause during the 6MWT was neither forbidden nor limited. However, the time was counted until the end of six minutes. The test followed the recommendations of the American Thoracic Society (ATS) [18].

## 2.7 ASSESSMENT OF DYSPNEA SENSATION AND RISK OF EXACERBATION/HOSPITALIZATION

The sensation of dyspnea was assessed by mMRC, which classifies dyspnea into five degrees, associating it with different levels of physical activities (e.g., running, walking, going uphill etc.). The risk of exacerbation/hospitalization was also analyzed using the classification of Global Initiative for Chronic Obstructive Lung (GOLD) [19], which classifies this population into four groups: A: low risk (0-1 exacerbation/year without the need for hospitalization) and little symptomatic (mMRC grade 0 or 1); B: low risk (0-1 exacerbation/year, without hospitalization) and very symptomatic (mMRC > 2); C:

high risk (> 2 exacerbation/year or one or more exacerbation requiring hospitalization) and little symptomatic (mMRC grade 0 or 1); and D: high risk (> 2 exacerbation/year or one or more exacerbation requiring hospitalization) and very symptomatic (mMRC > 2) [20].

## 2.8 DATA PROCESSING AND ANALYSIS

The database was created using the software EPI INFO, version 3.5.4, by which validation was performed. After validation, the databank was exported to the software SPSS, version 18, in which the analysis was performed. Categorical variables were subjected to proportional comparison analysis using the Chi-square test. To test the assumption of normality of the variables involved in the study, the Kolmogorov Smirnov test was used. Pearson's correlation coefficient was used for correlations. For the analysis of comparison of means, unpaired Student t test and ANOVA were used. *Post hoc* was also used for pair comparisons and the Bonferroni test was used for this analysis. A significant relevance of 0.05 was taken into account.

## 3 RESULTS

115 patients diagnosed with COPD were recruited, 64 of whom were excluded. Of these, 30 did not participate in the research due to difficulty in locating them, eight due to inaccessibility to the place of assessment, ten because they refused to participate in the research, and 16 because they met some exclusion criteria. 51 patients were allocated. However, nine did not attend the assessment and two had physical limitations on the day of the assessment, totaling 40 patients analyzed. (Figure 1).

Figure 1: Flowchart of selection and allocation of participants.

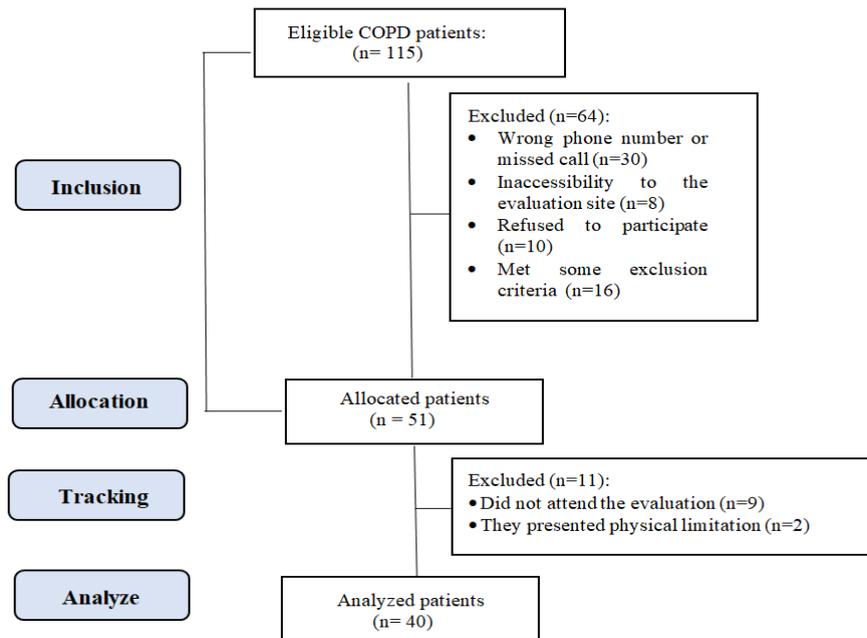


Table 1 shows the sample characterization. 82.5% of the studied population was composed of elderly people over 60 years of age (mean age  $65 \pm 10.0$  years), 42% of patients were within the ideal weight as classified by BMI, and 55% of patients were female. In addition, 47.5% were classified in the GOLD group A, which are considered low risk (0-1 exacerbation/year, without need for hospitalization). However, the sensation of dyspnea was classified as level 4 on the mMRC scale, that is, 47.5% of participants reported a great tiredness, including for leaving home or getting dressed. Regarding the degree of COPD obstruction assessed by spirometry, 15 patients were classified as mild, 11 as moderate, and 12 as severe.

Table 1. Distribution of personal profile of the patients evaluated.

Variable	N	%
<b>Age</b>		
43-59 years	7	17.5
60-87 years	33	82.5
Minimum - maximum		43.0 - 87.0
Mean±SD		65.7 ± 9.59
<b>BMI</b>		
Low weight	1	2.5
Ideal weight	17	42.5
Overweight	13	32.5
Level I obesity	3	7.5
Level II obesity	5	12.5

Level III obesity	1	2.5
<b>Gender</b>		
Female	22	55.0
Male	18	45.0
<b>GOLD</b>		
A	19	47.5
B	7	17.5
C	8	20.0
D	6	15.0
<b>mMRC</b>		
0	1	2.5
1	3	7.5
2	8	20.0
3	9	22.5
4	19	47.5
<b>Degree of Obstruction*</b>		
Low	15	39.5
Moderate	11	28.9
Severe	12	31.6

\*The total number of elements does not coincide with the sample size, as some observations do not have information on the evaluated factor.

The data were presented as N (%) or mean  $\pm$  SD.

BMI: Body mass index; GOLD: Global Initiative for Chronic Obstructive Lung; mMRC: Medical Research Council.

Table 2 shows the performance of patients in evaluations by analyzing the values obtained together with reference values established in the literature. There was a reduction in MIP in 97.5% of patients ( $p < 0.001$ ). Regarding the fatigue resistance index (FRI), only 22.5% ( $p = 0.001$ ) of the patients showed a reduction in respiratory muscle resistance. Similar to respiratory muscle strength, peripheral muscle strength assessed by handgrip was reduced in 80% of COPD patients ( $p = 0.001$ ), in addition to the fact that 97.4% of those assessed did not achieve what was expected in the 6MWT, demonstrating an important decrease in the functional capacity of these individuals ( $p < 0.001$ ).

Table 2. Characterization of patients in relation to respiratory and peripheral muscle function, and functional capacity.

Variable	N	%	p-value <sup>1</sup>
<b>MIP (cmH20)</b>			
Strength reduction	39	97.5	<0.001
Normal	1	2.5	
<b>FRI (%)</b>			
	31	77.5	0.001
	9	22.5	
<b>Handgrip (kg/force)</b>			
Strength reduction	32	80.0	<0.001
Normal	8	20.0	
<b>6MWT distance (min)</b>			
Normal functional capacity	1	2.6	<0.001*
Limited functional capacity	38	97.4	

\*p-value of the Chi-square test for comparison of proportions. \*The total number of elements does not match the sample size because one participant refused to perform the 6MWT.

The data were presented as N (%).

MIP: maximum inspiratory pressure; FRI: fatigue resistance index; 6MWT: six-minute walk test.

Figure 2A shows the comparison of different degrees of spirometric changes with the 6MWT. The patients with the highest degree of obstruction classified as severe evolved with a shorter distance covered in the 6MWT (p=0.049) compared to patients with moderate changes in spirometry. Figure 2B, on the other hand, shows the comparison of exacerbation degree assessed by the GOLD classification with the distance covered by 6MWT. The greater the distance covered in the 6MWT, the lower the risk of exacerbating the disease, as evidenced in groups classified as GOLD A and B. Consequently, the risk of hospitalization is lower (p=0.005).

Figure 2A and 2B: Comparison between the classification of spirometry (obstruction degree) and the six-minute walk test (6MWT) (Fig. 2A), and the classification of GOLD and the 6MWT (Fig. 2B). \*ANOVA and Bonferroni tests = difference between 6MWT and moderate and severe spirometry (p=0.049) and ANOVA = difference between the GOLD classification (A and B) and (C and D) (p=0.005) and values found in the 6MWT (Fig. 2B). 6MWT: six-minute walk test; GOLD: Global Initiative for Chronic Obstructive Lung.

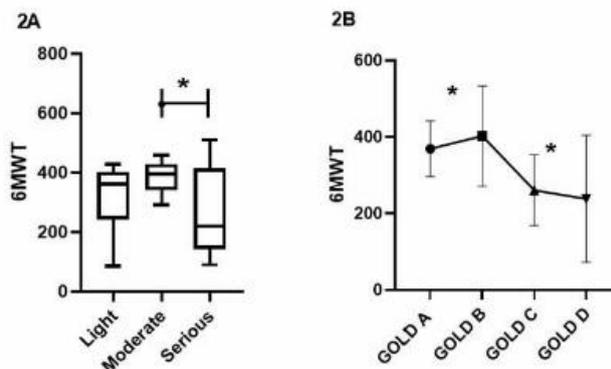
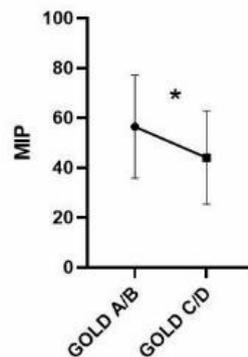


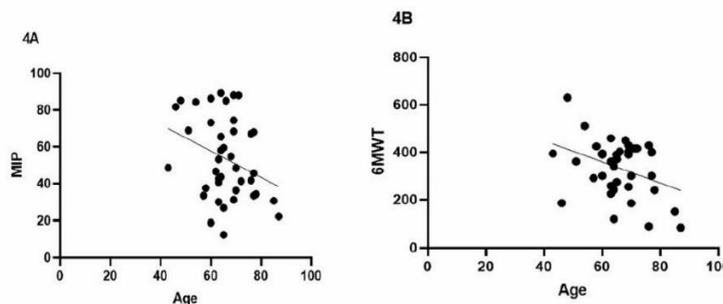
Figure 3 shows the comparison of MIP with the classification of GOLD (A and B) and (C and D). There is a difference between MIP values and GOLD classifications (A and B) and (C and D), showing that the lower the respiratory muscle performance according to the MIP, the greater the chance of exacerbation resulting in hospitalization ( $p=0.041$ ). (Figure 3).

Figure 3: Comparison between the classification of GOLD and MIP. \*Unpaired Student t test = difference between MIP and GOLD classifications (A and B) and (C and D) ( $p = 0.041$ ). MIP: maximum inspiratory pressure; GOLD: Global Initiative for Chronic Obstructive Lung.



The correlation of age with MIP and 6MWT is shown in Figures 4A and 4B, respectively. There is a negative correlation between age and respiratory muscle strength ( $r = -0.311$ ;  $p = 0.05$ ) and age with functional capacity ( $r = -0.369$ ;  $p = 0.021$ ) assessed by the 6MWT, demonstrating that the older the patient, the lower its ventilatory muscle performance and its functional capacity.

Figure 4A and 4B: Correlation between age and MIP (Fig. 4A) and comparison between age and 6MWT (Fig. 4B). \*Pearson's correlation = correlation between age and MIP ( $r = -0.311$ ;  $p = 0.05$ ) (Fig. 4 A); correlation between age and 6MWT ( $r = -0.369$ ;  $p = 0.021$ ) (Fig. 4B). MIP: maximum inspiratory pressure; 6MWT: six-minute walk test.



4 DISCUSSION

Our study confirms that COPD patients have a significant reduction in inspiratory and peripheral muscle strength. According to Neil et al. [21], in chronic inflammatory states such as COPD, there is an increase in systemic inflammatory mediators leading to oxidative muscle stress. This directly

damages muscle proteins. In addition, during the recovery from muscle fatigue, there is an injury mediated by additional reactive oxygen molecules that can develop in muscles, further impairing muscle function. There is still a reduced protein intake by these patients due to the effects of chronic inflammation on energy metabolism, leading to muscle breakdown. All these muscular changes not only affect peripheral muscles, but also respiratory muscles, imposing ventilatory restrictions and increasing the sensation of dyspnea, one of the main symptoms of the disease [22]. In addition, the association of peripheral and respiratory muscle dysfunction contributes to an increase in exacerbations and hospital admissions [22].

By analyzing only the reduction in respiratory muscle strength in these patients, studies have shown that pulmonary hyperinflation is present not only in COPD but also in other lung diseases. It causes biomechanical disadvantage of the diaphragm and inspiratory muscles, directly affecting the pressure generated by this musculature [23]. Analyses carried out by means of muscle biopsies obtained from inspiratory muscles of individuals with COPD show an important reduction in the capacity to generate strength by cross-sectional area, predisposing to weakness and directly affecting lung capacity, reflected by the displaced volume and peak flow [24].

Although we observed a decrease in respiratory muscle strength in our study, only 22.5% of the patients evaluated presented a reduction in respiratory muscle resistance. This finding is in accordance with the literature, which shows that disease chronicity and multicausal etiology of muscle dysfunction lead to a decrease in type IIb fibers and a relative increase in type I and IIa fibers in the diaphragm, resulting in a decrease in strength production and increased resistance to fatigue [18].

The present study also demonstrated that most patients had reduced functional capacity when assessed by 6MWT. According to Ho & Maa [25], about 51% of COPD patients assessed by 6MWT have a reduced functional capacity, which further worsens their ability to exercise and creates a vicious cycle that contributes to muscle dysfunction [26]. In the midst of this scenario, inactivity caused by the progress of dyspnea leads to a sedentary lifestyle, generating a deconditioning of the locomotor muscles and, consequently, a greater inactivity [26].

In our study, by comparing the degrees of changes in spirometry with the 6MWT, patients with more severe spirometry evolved with a shorter distance covered in the 6MWT compared to patients with moderate changes. This result corroborates the study by Casanova et al [27]. The authors demonstrated that 6MWT is an important prognostic factor especially in patients with severe COPD. The distance covered tends to decrease annually, indicating that these patients can use the 6MWT as a monitoring tool, which is a predictor of mortality in patients in this population.

Another important finding in our study was the relationship between functional capacity and the GOLD classification. The shorter the distance covered in 6MWT, the greater the risk of exacerbations. These findings are in agreement with Aarli et al. [28], who showed that the worst performance in the 6MWT described by the distance covered is associated with a greater number of exacerbations and hospitalizations, with a consequently higher mortality in these patients [28,29]. We also verified a correlation between inspiratory muscle strength and the GOLD classification, indicating that the more severe the patient condition, the lower the respiratory muscle performance. This result is similar to another study in which patients evaluated with COPD in GOLD stages II, III and IV, when performing the inspiratory muscle strength assessment, presented a strength about 70% of the predicted [30].

Our study also showed a correlation between age and inspiratory muscle strength, evidencing that the older the patient, the lower the ventilatory performance. The literature shows that the respiratory system of the elderly undergoes several structural and functional changes. In addition to muscle weakness, there are changes in the lungs, such as elastic recoil and decreased chest compliance. The impairment of ventilatory muscle performance in the elderly can lead to a decrease in their functional reserve, favoring a reduction in the level of physical activity [31]. In addition, MIP in the elderly decreases with advancing age between 60 and 90 years [32].

Finally, in this study, a correlation between age and the reduction in the distance covered in the 6MWT was found. It is already well elucidated in the literature that about 14.5% of patients with stable COPD have sarcopenia, leading to a loss of peripheral muscle strength, especially in the lower limb muscles [11], which is aggravated with age [16] and may justify the high prevalence of muscle weakness found in this study, since the majority of the study population comprised elderly people. Knowing that the sarcopenia process is common and natural to aging, affecting the respiratory and peripheral muscles, it is believed that a sum of muscle deterioration caused by aging and COPD could have occurred, causing a more pronounced muscle loss [33], and contributing to the reduction of functional capacity in these patients.

A limitation of this study refers to voluntary loss, since the Pulmonology outpatient clinic serves a large majority of patients who live outside the city where the evaluations were carried out. In addition, due to the profile of the patients recruited, it was not possible to carry out the walking test more than once to reduce the impacts that the learning effect may exert on the test.

In conclusion, the present study demonstrates that there is a significant prevalence of respiratory and peripheral muscle weakness and an important impact on the functional capacity and tolerance to

exercise in COPD patients. We also evidenced that patients with a higher degree of obstruction, classified as severe, evolved with a shorter distance covered in the walking test. In addition, patients who walked less have a higher risk of exacerbation and hospitalization, as well as those who had less respiratory muscle strength. The greater the age, the greater the impairment of inspiratory muscle performance and functional capacity.

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