

## Cardiovascular adaptation in the six-minute walk test in COPD patients: transversal study

### Adaptação cardiovascular no Teste de Caminhada dos Seis Minutos em pacientes com DPOC: estudo transversal

José Reinaldo Oliveira Silva<sup>1</sup>, Julia Ribeiro Santana<sup>2</sup>, Carolina Correia da Silva<sup>3</sup>, Daniel França Seixas Simões<sup>4</sup>, Aquiles Assunção Camelier<sup>5</sup>, Fernanda Warken Rosa Camelier<sup>6</sup>

<sup>1</sup>Corresponding author. State University of Bahia. Salvador, Bahia, Brazil. ORCID: 0000-0003-4617-9328. reinaldooliveira17@hotmail.com

<sup>2</sup>State University of Bahia. Salvador, Bahia, Brazil. ORCID: 0000-0002-7571-2083. julia\_ribeiro.s@hotmail.com

<sup>3</sup>State University of Bahia. Salvador, Bahia, Brazil. ORCID: 0000-0002-4944-7538. carolcorreia0504@gmail.com

<sup>4</sup>Pulsar Salvador. Salvador, Bahia, Brazil. ORCID: 0000-0002-4002-3704. francasdaniel@gmail.com

<sup>5</sup>State University of Bahia. BAHIANA – School of Medicine and Public Health. Salvador, Bahia, Brazil.

ORCID: 0000-0001-5410-5180. aquilescamelier@yahoo.com.br

<sup>6</sup>State University of Bahia. Salvador, Bahia, Brazil. ORCID: 0000-0003-2540-0142. fcamelier@uneb.br

**RESUMO | OBJETIVO:** Avaliar o comportamento da adaptação cardiovascular e da saturação periférica de oxigênio em indivíduos com DPOC submetidos no teste de caminhada dos seis minutos (TC6). **MATERIAL E MÉTODOS:** Trata-se de um estudo de corte transversal, que foram incluídas pessoas com diagnóstico de DPOC, confirmado pela espirometria e de ambos os sexos. A magnitude de sintomas foi avaliada pela escala de dispneia *Medical Research Council* (MRC) e questionário *COPD Assessment Test* (CAT). Aplicou-se o TC6 para avaliar a tolerância ao esforço. Para mensurar a frequência cardíaca máxima (FC máx) prevista para a idade foram utilizadas equações específicas para população brasileira. **RESULTADOS:** Avaliou-se 34 indivíduos com DPOC, 20 (58,8%) homens; relação VEF1/CVF foi  $56,7\% \pm 10,2\%$  pós broncodilatador (BD). Quatorze 14 (41,2%) indivíduos apresentaram impacto clínico moderado; 16 (47,2%) dos avaliados apresentou grau 2 na escala do MRC. As médias das distâncias percorridas no primeiro e segundo TC6 foram  $383,5 \pm 13,6$ ;  $408,6 \pm 85,7$  metros, correspondendo a 70,7%; 75,1% em relação ao valor previsto ( $p=0,001$ ). As médias da FC máx ao final do primeiro e segundo TC6, foram  $94,1 \pm 21,9$ ;  $92,3 \pm 17,9$  bpm e a FC pós percentual da FC máx prevista pré e pós TC6 foram  $61,1\% \pm 17,7\%$ ;  $59,7\% \pm 21,5\%$  e 14 (41,2%) pacientes apresentaram dessaturação de  $O_2$  no primeiro TC6; 9 (26,5%) no segundo teste. **CONCLUSÕES:** Pacientes com DPOC, apresentam aumento da FC identificado pelo esforço submáximo, por meio do percentual da FC max. Indivíduos com maior comprometimento da função pulmonar apresentaram dessaturação de  $O_2$ .

**PALAVRAS-CHAVE:** Doença Pulmonar Obstrutiva Crônica. Frequência cardíaca. Dessaturação de oxigênio. Teste de Caminhada dos Seis Minutos.

**ABSTRACT | OBJECTIVE:** To evaluate the behavior of cardiovascular adaptation and peripheral oxygen saturation in individuals with COPD submitted to the six-minute walk test (6MWT). **MATERIAL AND METHODS:** It was performed a descriptive study with person with a diagnosis of COPD confirmed by spirometry of both sexes. The *Medical Research Council* (MRC) dyspnea scale and the *COPD Assessment Test* (CAT) questionnaire were used to assess the magnitude of symptoms. The 6MWT was used to assess effort tolerance. To measure the maximum heart rate (HRmax) predicted for age, specific equations were used for the Brazilian population. **RESULTS:** 34 individuals with COPD were evaluated, 20 (58.8%) men; FEV1 / FVC ratio was  $56.7\% \pm 10.2\%$  after BD. Fourteen (41.2%) were classified as grade 2 and were classified as grade 2 (MRC scale). The means of the distances covered in the first and second TC6 were  $383.5 \pm 13.6$ ;  $408.6 \pm 85.7$  meters, corresponding to 70.7%; 75.1% in relation to the predicted value ( $p = 0.001$ ). The mean maximum heart rate at the end of the first and second 6MWT were  $94.1 \pm 21.9$ ;  $92.3 \pm 17.9$  bpm and the heart rate post-percentage of the predicted maximum heart rate before and after the 6MWT were  $61.1\% \pm 17.7\%$ ;  $59.7\% \pm 21.5\%$  and 14 (41.2%) patients presented  $O_2$  desaturation on the 6MWT; 9 (26.5%) in the second test. **CONCLUSIONS:** Patients with COPD throughout the 6MWT show increased heart rate and  $O_2$  desaturation in exercise activity.

**KEYWORDS:** Chronic Obstructive Pulmonary Disease. Heart rate. Oxygen desaturation. Six-minute Walk Test.

## Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable frequent disease. Is characterized by chronic and persistent inflammation of small and medium caliber airways, usually progressive. The inflammatory pulmonary reaction is associated to exposure to cigarette smoke, occupational fumes and biomass combustion. The clinical presentation of COPD consists of dyspnea, cough and sputum production, pulmonary exacerbations and exercise capacity reduction<sup>1,2</sup>. Beyond the respiratory system pathophysiological modifications, there are systemic alterations as muscle weakness, inferior limbs dysfunction, and muscular fatigue, leading to exercise intolerance and reduction in functional capacity<sup>3</sup>.

Due to those pathophysiological characteristics, a functional evaluation then becomes imperative, not only to determinate the functional status but also to design therapeutic actions, including pulmonary rehabilitation<sup>4</sup>. The six minute walk test (6MWT) has the objective of evaluate a subject functional capacity, being a low cost, safe, fast and cheap test, being not necessary any specific or complicated technology, and also correlates well with the activities of daily living (ADL), being considered a good predictor of COPD patients mortality. The distance walked in six minutes is the main outcome of the 6MWT, because it permits to evaluate and stage severity and prognosis of COPD<sup>5</sup>.

Furthermore, 6MWT provides a submaximal effort cardiac frequency variation and oxygen desaturation in COPD patients, specially when compared to other functional tests described in the literature. Several factors contribute to the pattern of exercise modification of cardiac variables during this field test, specially exercise-induced hypoxemia, dynamic hyperinflation, and systemic inflammation, than can contribute to the submaximal response to exercise, which also correlates to prognosis in COPD<sup>6</sup>.

Peripheral oxygen desaturation pattern, induced by 6MWT, provides not only useful clinical information associated to the reduction of ADL, but also correlate to the decline of Forced Expiratory Volume in 1 second (FEV1) linked to a worsening in COPD prognosis<sup>7</sup>.

It is quite common that COPD patients experience dyspnea during ADL. Once those subjects are limited in performing such ADL, it becomes necessary to describe the level of functional limitation in order to tailor therapeutic interventions, giving the 6MWT a relevant role in clinical practice. The objective of the present study is to describe the pattern of cardiovascular and peripheral SpO<sub>2</sub> adaptation of COPD patients when performing the 6MWT.

## Material e methods

A cross – sectional, descriptive study was conducted in COPD subjects participating in the Chronic Respiratory Diseases Assistencial Program (Programa Assistencial a Pessoa com Doenças Respiratórias Crônicas), a public practical care and educational program of the Phisiotherapy Department of State University of Bahia- UNEB (Curso de Fisioterapia do Departamento de Ciências da Vida (DCV) da Universidade do Estado da Bahia – UNEB), ubicada in Salvador – Bahia, a northwestern city of Brazil, between February to June, 2018. Inclusion criteria were stable COPD diagnosis (according to Global Initiative for Chronic Obstructive Lung Disease- GOLD Guidelines) and spirometry containing a post bronchodilator FEV1/FVC ratio < 0,71.

Exclusion criteria were: 1- Any clinical condition, verified by a physician evaluation, that precluded performing the 6MWT (including uncontrolled systemic hypertension, unstable angina, myocardial infarction in the preceding three months, unstable cardiac or any orthopedic condition that limited the performance in the test; 2- Any technical incapacity to detect SpO<sub>2</sub> and HR monitoring signals on the pulse oximeter during the 6MWT; 3-Withdrawal of the Free and Informed Consent Form.

The present study used primary and secondary data sources, and the data collection was performed at the Laboratory of Exercise Physiology, DCV / UNEB, Salvador-Bahia. Individuals were submitted to single day evaluation by a member of the research trained team. Sociodemographic characteristics were collected: age in years; sex (male and

female); color (white, mulatto, black, yellow); weight (kg); height (meter); body mass index (BMI) (kg / m<sup>2</sup>); social status (married, single, widowed). Clinical variables collected were: spirometry, stage of the disease, prognosis, degree and frequency of respiratory symptoms, and 6MWT (in two times, with an intervals of up to 30 minutes between them). The data of recent pulmonary function were obtained in the patient's chart of the outpatient clinic that they were located.

Patients were then divided into groups according to the severity of the airflow limitation, determined by GOLD 2017, taking into account spirometry parameters such as forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), and FEV1/FVC ratio<sup>1</sup>.

The COPD Assessment Test (CAT), a questionnaire validated for the Portuguese language / Brazil, was used to evaluate symptoms of respiratory magnitude, which is composed of eight items, called cough, phlegm, chest tightness, shortness of breath, limitations in home activities, confidence in leaving home, sleep and energy. The results varied according to the range of the obtained scores, classified as follows in relation to the clinical impact: 6-10 points, mild; 11-20, moderate; 21-30, severe; and 31-40; very severe and varying the score between 0 (best) and 40 (worse)<sup>8</sup>.

For the assessment of dyspnea, the mMRC (Modified Medical Research Council) scale was used, an instrument that assesses the degree of dyspnea from strenuous physical activity to simple activities of daily living. This scale is divided into five groups: grade 0 indicates that the patient refers to shortness of breath when performing intense physical activity as running, giving, practicing sport. Grade 1 indicates that the patient refers to shortness of breath when walking in a plane or when climbing a raised surface. Grade 2 states that the patient walks more slowly than people of the same age from lack of air; or when the patient walking on the plane, at the same pace, has to stop to breathe. Grade 3 indicates that the patient, after walking a few meters or a few minutes in the plane, has to stop breathing. Grade 4 states that the patient experiences shortness of breath when he or she performs a simple daily life activity (ADL) or when this shortness of breath has come a time to stop him from leaving the house<sup>9</sup>.

The BODE index was used to assess the systemic COPD impairments that reflect the limitations to perform ADLs<sup>10</sup>. This instrument is considered a multidimensional graduation system composed of four domains, namely: the degree of impairment of pulmonary function (FEV1) after bronchodilator use; the perception of dyspnea on the MRC scale; body mass index (BMI) and exercise capacity (6MWT) by the distance traveled in meters. The BODE index comprises a score ranging from zero to ten points, divided into four quartiles. Quartile 1 score varies from 0 to 2 points; quartile 2, from 3 to 4 points; quartile 3, from 5 to 6 points and quartile 4, from 7 to 10 points. Such division in quartiles makes possible to functionally classify the COPD individuals and, the higher the score, the greater not only the limitation in the ADLs but also the mortality risk of each subject<sup>10</sup>.

The 6MWT is simple field test, well tolerated and reproducible, requiring low cost equipment<sup>11,12</sup>. Each subject had his vital signs recorded twice by the researcher, before and after the test. Systolic and diastolic blood pressure (BP) and heart rate (HR) were measured using an aneroid sphygmomanometer (Premium®, G-TECH). Peripheral oxygen saturation (SpO<sub>2</sub>) was measured with the individual in a sitting position while breathing room air (using a pulse oximeter - Rossmax®, model Palpus1 SA210). Dyspnea and lower limb fatigue were evaluated by applying the Modified Borg scale immediately after performing the 6MWT<sup>11,12</sup>. A practice 6MWT was performed before the test that was considered for the research, as the literature states<sup>13</sup>. There was a 10-minute rest interval, and then the investigator timed the time to perform the test. To predict the distance traveled during the established time, healthy adult reference values, both sexes, were used based on a study described by Britto et al<sup>12</sup>. To calculate the predicted maximum heart rate for age equations were used for the Brazilian population, where FC max = 211 - (0.87 \* age) for men and FC max = 212 - (0.89 \* age) for women<sup>13,14</sup>. To evaluate the behavior of cardiovascular adaptation, the equations  $\Delta CF = (\text{peak HR} - \text{rest HR})$  and  $\text{HR reserve} = (\text{HR peak} - \text{HR rest}) / (220 - \text{age} - \text{HR rest}) \times 100$  were used<sup>14,15</sup>. Regarding the SO<sub>2</sub> percentage drop in clinical practice the peripheral O<sub>2</sub> desaturation is considered in the effort when SpO<sub>2</sub> occurs a variation of 4%<sup>16</sup>.

The study used a convenience sample, and the sample of 34 individuals was able to detect, in terms of accuracy, a variation of 8 mmHg in systolic or diastolic blood pressure, or 5 bpm in heart rate, based on data from the literature and from the sample calculation table described in Hulley SB et al<sup>4,17</sup>.

Data were stored in an Excel© data sheet and in the SPSS (v.22.0) database. The data were expressed as a measure of central tendency, dispersion and proportions. Normality of data were tested with a Shapiro-Wilk test. Comparisons of continuous data were done using paired T – test. A p value <0.05 was considered statistically significant.

The study was approved by the Ethical and Research Committee of Universidade do Estado da Bahia (UNEB).

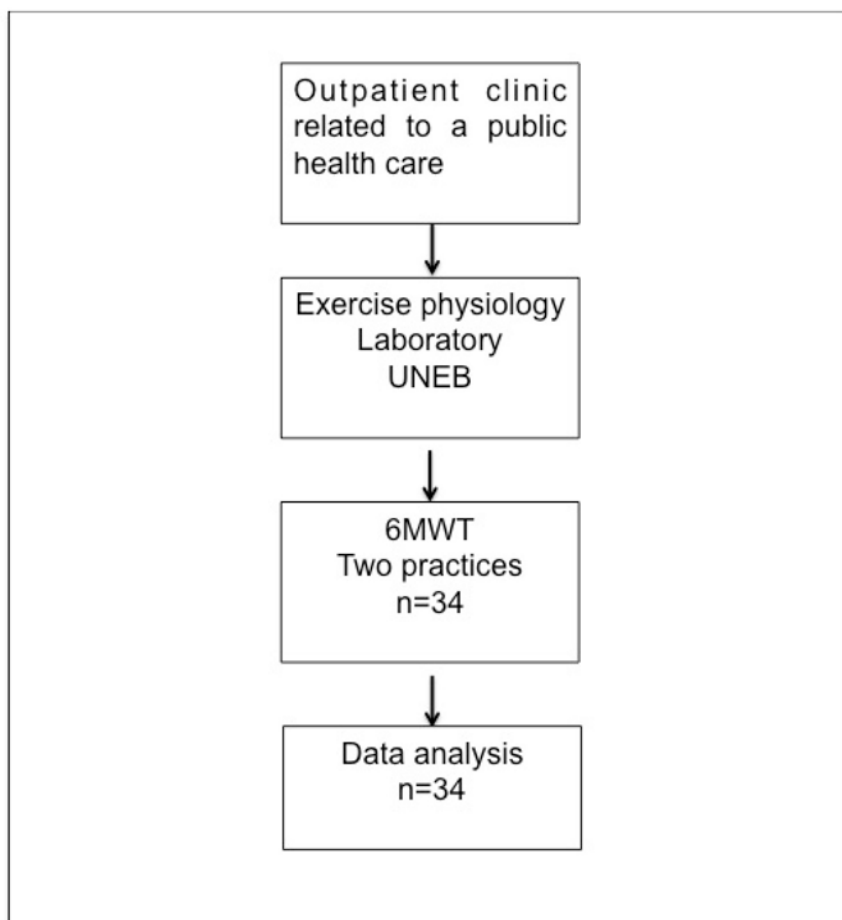
The English version of this study was translated from the original portuguese by an English speaker but not native speaker, using, after translating, the 1

Checker Online software (available from : <http://www.1checker.com>), a free online software designed and developed by SchoolPal Online Co., Ltd., powered by Artificial Intelligence (AI) and Natural Language Processing (NLP) Technologies.

## Results

Thirty-four individuals with a diagnosis of COPD were examined according to the eligibility criteria and included in the final analysis of the study (Figure 1). Twenty (58.8%) were male and 19 (55.9%) had less than or equal to 60 years. It was observed that 31 (92.7%) individuals were classified as having black skin color and 21 (61.8%) were married and in relation to the school status, 17 (50.0%) of those had completed elementary education. According to nutritional status (BMI), 17 (50.0%) were eutrophic (Table 1).

Figure 1. Participants flowchart



**Table 1.** Sociodemographic characteristics of COPD subjects, from a public university Exercise Physiology Laboratory, Salvador, BA, Brasil, 2018 (n= 34)

<b>Caracteristics</b>	<b>n</b>	<b>%</b>
<b>Gender</b>		
Male	20	58.8
Female	14	41.2
<b>Age</b>		
≤ 60 years	19	55.9
> 60 years	15	44.1
<b>Social status</b>		
Married / Stable relationship	21	61.8
Single	13	38.2
<b>Scholarity</b>		
No scholarity	4	11.8
Fundamental	17	50.0
High School	12	35.3
University	1	2.9
<b>Skin colour</b>		
Black	31	92.7
Non-black	3	7.1
<b>Nutritional Status</b>		
Low weight	4	11.8
Eutrophic	17	50.0
Overweight	13	38.2

Table 2 shows the clinical characteristics of patients with COPD. It was observed that pulmonary function had a mean post bronchodilator (BD) of FVC of  $66.6\% \pm 14.6$  of predicted, FEV1 of  $46.5\% \pm 13.1\%$  of predicted and FEV1 / FVC was  $56.7\% \pm 10.2\%$ . More than 70.0% of the individuals were classified as having a moderate degree of disease according to FEV1. According to the BODE index, 13 (38.2%) patients were classified in quartile one and two. Regarding the symptoms, cough, phlegm, chest tightness, shortness of breath, limitations in home activities, confidence in leaving home, sleep and energy evaluated by the COPD Assessment Test (CAT) 14 (41.2%) had moderate to severe clinical impact. Sixteen (47.2%) patients had shortness of breath during ADLs.

**Table 2.** Clinical characteristics of COPD subjects, from a public university Exercise Physiology Laboratory, Salvador, BA, Brasil, 2018 (n= 34)

Variables	Mean	SD
<b>Pulmonary function</b>		
FVC (L) , post BD	2.3	0.6
FEV <sub>1</sub> , (L) , post BD	1.2	0.4
FVC (%) , post BD	66.6	14.6
FEV <sub>1</sub> , (L) , post BD	46.5	13.1
FEV <sub>1</sub> / FVC , post BD	56.7	10.2
	<b>n</b>	<b>%</b>
<b>COPD GOLD Stages</b>		
A (mild)	6	17.6
B (moderate)	9	26.5
C (severe)	2	5,9
D ( very severe)	17	50.0
<b>COPD Spirometry GOLD Stages (FEV<sub>1</sub>)</b>		
Moderate	24	70.6
Severe	10	29.4
<b>CAT Score (COPD Clinical Impact)</b>		
Mild	6	17.6
Moderate	14	41.2
Severe	14	41.2
<b>mMRC Dyspnea Scale</b>		
Grade 0	1	2,9
Grade 1	6	17.6
Grade 2	16	47.2
Grade3	5	14.7
Grade4	6	17.6
<b>BODE COPD Prognosis Score</b>		
Quartile 1	13	38.2
Quartile 2	13	38.2
Quartile 3	7	20.6
Quartile 4	1	2.9

FVC L: Forced Vital Capacity, Liters; FVC %: Forced Vital Capacity, % Predicted; FEV<sub>1</sub> L: Forced Expiratory Volume 1 second, , Liters; FEV<sub>1</sub> %: Forced Expiratory Volume 1 second,, % Predicted; BD: Bronchodilator; SD: Standard Deviation and GOLD: Global Initiative for Chronic Obstructive Lung Disease.

Mean distance walked in the first and second 6MWTs were, respectively,  $387.5 \pm 85.6$  and  $411.3 \pm 87.3$  meters. None patient stopped the test and the tests were not interrupted. According to predicted 6MWT values<sup>12</sup>, participants walked 70.7 5 % meters in the first test and 75.10 % in the second test ( $p < 0.001$  between the predicted value and the performed test). There were no statistical difference between the first and the second distance walked in the 6MWT. When comparing pre and post-test, there was a statistically significant increase in heart rate (HR), respiratory rate (RR), blood pressure (BP), dyspnea and lower limb fatigue, as well as decreased peripheral oxygen saturation, without clinical repercussion of this parameter. Mean HR

variation and mean reserve HR, pre and post tests were, respectively,  $20.2 \pm 15.8$  bpm;  $18.8 \pm 10.7$  bpm;  $26.2 \pm 20.4$  bpm;  $24.6 \pm 15.3$  bpm and no statistical difference were found. Mean maximum predicted HR for age was  $153.7 \pm 8.8$ . Mean maximum HR at the end of the first and second 6MWT were, respectively,  $94.1 \pm 21.9$  and  $92.3 \pm 17.9$  bpm ( $p = 0.875$  between them), corresponding to  $61,1\% \pm 17,7\%$  e  $59,7\% \pm 21,5\%$ , respectively, of the age and sex percentual of predicted, being those predicted values statistically different between them ( $p < 0,05$ ). In addition, the  $SpO_2$  desaturation observed in the present study was evidenced in individuals with greater impairment of pulmonary function.

**Table 3.** Distance walked and predicted and clinical variables of First (6MWT1) and Second (6MWT2) of COPD subjects, from a public university Exercise Physiology Laboratory, Salvador, BA, Brasil, 2018 (n= 34)

Variables	Mean /SD				
HR max pred age (pm)	$153.7 \pm 8.8$				
6MWT pred (m)	$547.7 \pm 45.7$				
	6MWT 1	p	6MWT2	p	p*
6MWT pred (m)	$387.5 \pm 85.6$	-	$411.3 \pm 87.3$	-	<b>0.001</b>
HR pre (bpm)	$73.7 \pm 11.2$		$73.8 \pm 12.6$		0.405
HRpost (bpm)	$94.1 \pm 21.9$	<b>&lt;0.001</b>	$92.3 \pm 17,9$	<b>&lt;0.001</b>	0.875
HR post % HR max pred (pm)	$61.1 \pm 17.7$		$59.7 \pm 21.5$		<b>&lt;0.001</b>
$\Delta$ HR post x pre (pm)	$20.2 \pm 15.8$		$18.8 \pm 10.7$		0.620
HR reserve (pm)	$26.2 \pm 20.4$		$24.6 \pm 15.3$		0.627
RR pre (ipm)	$19.2 \pm 4.4$		$21.8 \pm 10.9$		0.144
RR post (ipm)	$23.4 \pm 5.4$	<b>&lt;0.001</b>	$25.8 \pm 18.9$	<b>0.023</b>	0.472
SBP pre (mmHg)	$127.1 \pm 14.3$		$128.1 \pm 16.4$		0.913
SBP post (mmHg)	$138.2 \pm 22.8$	<b>0.003</b>	$137.3 \pm 26.3$	<b>0.026</b>	0.833
DBP pre (mmHg)	$83.1 \pm 20.3$		$86.1 \pm 14.7$		0.498
DBP post (mmHg)	$81.5 \pm 20.9$	0.697	$88.1 \pm 12.4$	0.489	0.069
SpO <sub>2</sub> pre (%)	$95.9 \pm 2.1$		$95.3 \pm 2.1$		0.195
SpO <sub>2</sub> post (%)	$92.4 \pm 4.9$	<b>&lt;0.001</b>	$91.5 \pm 6.2$	<b>0.023</b>	0.192
$\Delta$ SpO <sub>2</sub> post 6MWT (%)	$- 3.4 \pm 4.1$		$- 3.8 \pm 5.3$		<b>&lt;0.001</b>
Borg IL pre	$0.6 \pm 1.1$		$0.7 \pm 1.5$		0.705
Borg IL post	$2.6 \pm 2.9$	<b>&lt;0.001</b>	$2.3 \pm 2.7$	<b>0.001</b>	0.231
Borg dyspnea pre	$0.6 \pm 1.1$		$0.6 \pm 1.1$		0.951
Borg dyspnea post	$2.5 \pm 2.9$	<b>&lt;0.001</b>	$2.8 \pm 2.5$	<b>0.001</b>	0.657
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
Desat SpO <sub>2</sub>	14	41.2	9	26.5	

p – p value pre vs post; p\* - p value first vs second practice; HR, Heart Rate ; RR Respiratory Rate; SpO<sub>2</sub> Pulse Oxygen Saturation; IL – Inferior Limbs; SBP- Systolic Blood Pressure; DBP-Diastolic Blood Pressure; Borg – Borg Scale. Pre – pre 6MWT, Post – post 6MWT.

## Discussion

The present study describes the both cardiovascular and respiratory adaptation during the 6MWT in outpatients with stable COPD. The standardized, submaximal, 6MWT induced an increase in HR and a decrease in SpO<sub>2</sub> in the patients studied. At the end of the 6MWT, the participants of this study assumed around 60% of the maximum HR predicted, confirming this submaximal behavior of the assumed exercise. There was also a mean drop of SpO<sub>2</sub> in the first and second test, respectively, of  $-3.4 \pm 4.1$  and  $3.8 \pm 5.3$ , ratifying the capacity of 6MWT in identifying SpO<sub>2</sub> desaturation during this test and corroborating the findings in the literature<sup>18-22</sup>.

These physiological findings corroborate that stable COPD patients assume a spontaneous submaximal level of exercise during this field test, justifying the use of 6MWT in assessing functional capacity in individuals with chronic obstructive pulmonary disease. This study also shows that the 6MWT is an easy and feasible test to apply in a clinical practice situation, specially in a limited space and resource setting, because it is a simple to perform and there is no need to use expensive or complicated equipment<sup>5</sup>.

When comparing the initial and final HR in the pre and post 6MWT, it is possible to observe a significant increase in HR at the end of the test. The increase in HR in individuals with COPD in a submaximal effort activity can be attributed to several pathophysiological aspects: increased metabolic demand; a increase in the air trapped in the alveoli during exercise, due to an increase in the airflow resistance of smaller airways (also called dynamic hyperinflation); an increase in intrathoracic pressure (due to the dynamic hyperinflation), which consequently can produce a reduction in left ventricular ejection volume and, in turn, reflects in the increase in HR (in the intention to maintain elevation of cardiac output imposed by increased metabolic demand). Finally, an increase in HR is also mediated by the activation of baroreceptors<sup>19</sup>. Other aspects related to the cardiopulmonary dynamics in COPD also justify the elevation of the HR during the 6MWT. One of them is the stimulation of pulmonary stretch receptors, induced by the increase of tidal volume during exercise, which produces lowering of venous return, lowering of end

diastolic left ventricular pressure, and consequent tachycardia in order to maintain a higher cardiac output (during exercise)<sup>13</sup>. In addition, people with COPD have a limited increase in systolic ventricular volume ejection, which can be explained by several factors that can be present in COPD patients, such as a decrease in the reserve of right ventricular preload, reduction of the right ventricular inotropic reserve, myocardial ischemia, tricuspid insufficiency, right-to-left ventricular interaction and alteration of right ventricular diastolic function<sup>20</sup>. In addition, the increase in heart rate during the 6MWT may be related to the inability of the elevation of the cardiac output, which can reflect a worsening of prognosis<sup>18</sup>. It has also been demonstrated in the literature that, during the 6MWT, patients with COPD spontaneously adopt a level of self-determined walking speed, which, according to the pathophysiological changes imposed by the disease, is unconsciously adjusted to reach a bearable level of exercise, submaximal, which by definition corresponds to the "critical power" or "critical walking speed" described by Casas et al., thus reproducing a spontaneous daily life activity, and justifying the use of this test as a way to evaluate functional capacity using an activity quite similar to a daily activity<sup>21</sup>.

The SpO<sub>2</sub> desaturation in people with COPD, 6MWT induced in the present study is justified by the presence of the change in the ventilation - perfusion mismatch in those patients, which can be worsened by effort, a known pathophysiological feature in COPD<sup>1,13</sup>. These aspects are justified not only by the ventilatory limitation, but also by the disproportion between consumption and delivery of O<sub>2</sub>, in addition to a systemic inflammation and oxidative stress, which end up affecting peripheral muscle oxygenation<sup>22,23</sup>. Thus, there is a significant decrease in circulating levels of oxygen at both the blood and the muscle level, a factor that becomes responsible for sympathetic stimulation, causing an increase in blood pressure, peripheral vascular resistance, and, consequently, increasing the perception of dyspnea and muscle fatigue, thus reducing tolerance in the performance of submaximal exercises by these patients, and these physiopathological factors can be present both in isolation and in conjunction<sup>7</sup>. Previous studies have shown that the time of desaturation during the 6MWT is indicative of the possibility of desaturation during activities daily,



culminating in severe hypoxemia and the need for oxygen therapy<sup>7,12,14</sup>.

In the present study, a significant reduction in the distance walked in the 6MWT was seen, according to the predicted values for healthy individuals, based on the study by Brito et al<sup>12</sup>. Individuals with COPD in the present study walked around 70 to 75% of the maximum distance predicted by age, a factor that could be justified, in addition to the physiopathological aspects previously described, to the state of inactivity, common in those patients, as well as in the sedentary lifestyle adopted, described by the low frequency and intensity effort during the performance of activities of daily living, as well as by social, cultural factors, and specially the low motivation of these people because of the severity of symptoms when performing ADLs tasks<sup>1</sup>.

The perception of dyspnea and fatigue in LBW is one of the main complaints reported by people with COPD, which results in decreased functionality and decline in functional independence. This information was observed in the results of the present study, in which these symptoms were able to compromise the performance of the evaluated volunteers. The main explanation for this result would be because of the physical condition, degree of instruction about disease and social factors. However, some scientific studies show that the sensation of dyspnea and fatigue in lower limbs are the main symptoms of effort intolerance<sup>14,21,22</sup>. These results are important for the understanding that not only pulmonary mechanics, but other factors are involved in exercise tolerance as well as abnormal gas exchange, cardiac dysfunction, dysfunction of the global skeletal muscle<sup>22-24</sup>.

It is also added that the abnormal nutritional status in people with COPD is a frequent complication in such patients, since they are related to the systemic inflammation and oxidative stress related to the disease, which justifies the loss of muscular mass. In this study, however, the mean BMI of the sample studied were around the normal value of reference<sup>25,26</sup>. This finding can possibly be justified by sample size and sampling limitations due to the study design, however.

Among the advantages of the 6MWT, it can be pointed out the simplicity in performing the test, the utility in evaluating the limitation of functional capacity, as well as showing the behavior of HR and SpO<sub>2</sub> in people with COPD, among with a low cost ( since it does not require high technology equipment ), good safety and good validation in the literature<sup>1,11</sup>. Another important point of the present study is the ability of the 6MWT to correlate with the ADLs, determining the functional profile of individuals with COPD, giving a practical and useful application.

The limitations of this study relates to the sample size and sampling adopted in the study design, and some limitation in the external validation of data due to the subjects become in the totality from an outpatient public university clinic, characterized by more severe and symptomatic patients, which may limit the generalization of results especially for a primary care setting where patients have milder stage and symptoms presentation.

## Conclusion

It can be concluded that the 6MWT induces an increase in HR at the level of a submaximal effort, according to the predicted value for age. In this study, subjects with COPD also presented SpO<sub>2</sub> desaturation during the 6MWT performance. The 6MWT was shown to be simple and had a low cost test, which justifies its use in the majority of COPD health care settings available.

## Author contributions

Authors Silva JRO, Camelier AA and Camelier FWR designed the initial concept and planned the work. Silva JRO, Santana JR, da Silva CC and Camelier FWR interpreted the final results. Silva JRO, Camelier AA and Camelier FWR drafted the article. Silva JRO, Santana JR, da Silva CC, France D, Camelier AA and Camelier FWR reviewed successive versions and approved the final version of the article.

## Competing interests

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

## References

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease, 2017.
2. Calik-Kutukcu E, Savci S, Saglam M, Varda-Yagli N, Arıkan H, Arıbas Z et al. A comparison of muscle strength and endurance, exercise capacity, fatigue perception and quality of life in patients with Chronic Obstructive Pulmonary Disease and healthy subjects: a cross-sectional study. *BMC Pulm Med.* 2014;14:6. doi: [10.1186/1471-2466-14-6](https://doi.org/10.1186/1471-2466-14-6)
3. Langer D, Hendriks E, Burtin C, Probst V, van der Schans C, Paterson W et al. A clinical practice guideline for physiotherapists treating patients with chronic obstructive pulmonary disease based on a systematic review of available evidence. *Clin Rehabil.* 2009;23(5):445-62. doi: [10.1177/0269215509103507](https://doi.org/10.1177/0269215509103507)
4. Ozalevli S, Ozden A, İtil O, Akkoçlu A. Comparison of the Sit-to-Stand Test with 6 min walk test in patients with Chronic Obstructive Pulmonary Disease. *Respir Med.* 2007;101(2):286-93. doi: [10.1016/j.rmed.2006.05.007](https://doi.org/10.1016/j.rmed.2006.05.007)
5. Meriem M, Cherif J, Toujani S, Ouahchi Y, Hmida AB, Beji M. Sit to stand test and 6 min walking test correlation in patients with chronic obstructive pulmonary disease. 2015;10(4):269-273. doi: [10.4103/1817-1737.165289](https://doi.org/10.4103/1817-1737.165289)
6. Richter MJ, Milger K, Tello K, Stille P, Seeger W, Mayer E. Heart rate response during 6-minute walking testing predicts outcome in operable chronic thromboembolic pulmonary hypertension. *BMC Pulm Med.* 2016;16(1):96. doi: [10.1186/s12890-016-0260-y](https://doi.org/10.1186/s12890-016-0260-y)
7. Moreira MAF, Medeiros GA, Boeno FP, Sanches PRS, Silva Júnior DP, Müller AF. Análise da dessaturação de oxigênio durante o teste de caminhada de seis minutos em pacientes com DPOC. *J Bras Pneumol.* 2014;40(3):222-228. doi: [10.1590/S1806-37132014000300004](https://doi.org/10.1590/S1806-37132014000300004)
8. Silva GPF, Morano MTAP, Viana CMS, Magalhaes CBA, Pereira EDB. Portuguese-language version of the COPD Assessment Test: validation for use in Brazil. *J Bras Pneumol.* 2013;39(4):402-408. doi: [10.1590/S1806-37132013000400002](https://doi.org/10.1590/S1806-37132013000400002)
9. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax.* 1999;54(7):581-6.
10. Celli BR, Cote CG, Marin JM, Casanova C, Oca MM, Mendez RA et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med.* 2004;350(10):1005-12. doi: [10.1056/NEJMoa021322](https://doi.org/10.1056/NEJMoa021322)
11. Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D et al. An official European Respiratory Society/ American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J.* 2014;44(6):1428-1446. doi: [10.1183/09031936.00150314](https://doi.org/10.1183/09031936.00150314)
12. Britto RR, Probst VS, Andrade AFD, Samora GAR, Hemandes NA, Marinho PEM et al. Reference equations for the six-minute walk distance based on a Brazilian multicenter study. *Braz J Phys Ther.* 2013;17(6):556-563. doi: [10.1590/S1413-35552012005000122](https://doi.org/10.1590/S1413-35552012005000122)
13. Neder JA, Nery LE. *Fisiologia Clínica do Exercício – Teoria e Prática.* São Paulo: Artes Médicas; 2003.
14. Provencher S, Herve P, Sitbon O, Humbert M, Simonneau G, Chemla D. Changes in exercise haemodynamics during treatment in pulmonary arterial hypertension. *Eur Respir J.* 2008;32(2):393-398. doi: [10.1183/09031936.00009008](https://doi.org/10.1183/09031936.00009008)
15. Azarbal B, Hayes SW, Lewin HC, Hachamovitch R, Cohen I, Berman DS. The incremental prognostic value of percentage of heart rate reserve achieved over myocardial perfusion single-photon emission computed tomography in the prediction of cardiac death and all-cause mortality: superiority over 85 % of maximal age-predicted heart rate. *J Am Coll Cardiol.* 2004;44(2):423-430. doi: [10.1016/j.jacc.2004.02.060](https://doi.org/10.1016/j.jacc.2004.02.060)
16. Lama VN, Flaherty KR, Toews GB, Colby TV, Travis WD, Long Q et al. Prognostic value of desaturation during a 6-minute walk test in idiopathic interstitial pneumonia. *Am J Respir Crit Care Med.* 2003;168(9):1084-1090. doi: [10.1164/rccm.200302-2190C](https://doi.org/10.1164/rccm.200302-2190C)
17. Browner WS, Newman TB, Cummings SR, Hulley SB. Estimating sample size and power: the nifty-gritty. In: Hulley SB, Cummings SR, Browner WS, Grady D, Hearst N, Newman TB, editors. *Designing clinical research: an epidemiologic approach.* 2nd ed. Baltimore: Ed. Williams & Wilkins; 2001. P. 65-91.
18. Larsen PD, Tzeng YC, Sin PY, Galletly DC. Respiratory sinus arrhythmia in conscious humans during spontaneous respiration. *Respir Physiol Neurobiol.* 2010;174(1-2):111-8. doi: [10.1016/j.resp.2010.04.021](https://doi.org/10.1016/j.resp.2010.04.021)
19. Marshall JM. Peripheral chemoreceptors and cardiovascular regulation. *Physiol Rev.* 1994;74(3):543-94. doi: [10.1152/physrev.1994.74.3.543](https://doi.org/10.1152/physrev.1994.74.3.543)
20. Laskey WK, Ferrari VA, Palevsky HI, Kussmaul WG. Pulmonary artery hemodynamics in primary pulmonary hypertension. *J Am Coll Cardiol.* 1993;21(2):406-412.
21. Russo R, Iamonti VC, Jardim JR. Intolerância ao exercício no paciente com DPOC. *Pneumol Paulista.* 2012;26(1):38-41.

22. Holland AE, Spruit MA, Singh SJ. How to carry out a field walking test in chronic respiratory disease. *Breathe*. 2015;11(2):128-139. doi: [10.1183/20734735.021314](https://doi.org/10.1183/20734735.021314)

23. Poulain M, Durand F, Palomba B, Ceugniet F, Desplan J, Varray A et al. Six minute walk testing is more sensitive than maximal incremental cycle testing for detecting oxygen desaturation in patients with COPD. *Chest*. 2003;123(5):1401-7.

24. Marino DM, Marrara KT, Lorenzo VAP, Jamami M. Teste de caminhada de seis minutos na doença pulmonar obstrutiva crônica com diferentes graus de obstrução. *Rev Bras Med*. 2007;13(2):103-106. doi: [10.1590/S1517-86922007000200007](https://doi.org/10.1590/S1517-86922007000200007)

25. Hamilton AI, Killian KJ, Summers E, Jones NL. Muscle strength symptom intensity and exercise capacity in patients with cardiorespiratory disorders. *Am J Respir Crit Care Med*. 1995;152(6):2021-2031. doi: [10.1164/ajrccm.152.6.8520771](https://doi.org/10.1164/ajrccm.152.6.8520771)

26. Schettino CDS, Deus FCC, Gonçalves AAV, Wallace E. Relação entre DPOC e Doença Cardiovascular. *Pulmão RJ*. 2013;22(2):19-23.