Cardiovascular changes during the six-minute walk test in COPD patients

Alterações cardiovasculares durante o teste de caminhada de seis minutos em pacientes com DPOC

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Abstract

Introduction: Specialised literature demonstrates that chronic obstructive pulmonary disease (COPD) has pathophysiological changes that impair cardiac autonomic function and the ability of the cardiovascular system to respond to stimuli. **Objective:** To analyze the correlation between heart rate (HR), peripheral oxygen saturation (SpO_2), functional and pulmonary capacity in patients with COPD during the six-minute walk test (6MWT) before and after the pulmonary rehabilitation program (PRP). **Methods:** This is a descriptive and retrospective study, with collection carried out in the PRP database of a university in Vale dos Sinos, Brazil. **Results:** The sample consisted of 216 patients, classified as having severe COPD, with a predominance of males (57.4%), with a mean age of 65.4 ± 7.9 years. The results showed that at the pre-PRP moment, the HR at the end of the test showed a strong negative correlation ($p < 0.01$) with SpO_2 obtained at the end of the test, and forced expiratory volume in the first second (FEV_1). At the post-PRP moment, the HR at the end of the test was strongly negatively correlated with SpO_2 and FEV_1 positively, weakly ($p < 0.05$) with the sensation of dyspnea at the end of the test, and strongly with the distance covered in the 6MWT (6MWD). **Conclusion:** *T*he correlations between HR, FEV_1, 6MWD, dyspnea and SpO_2 were confirmed, making it evident that as the variables change, HR changes occur to meet the metabolic, oxygenation and ventilatory demands.

Keywords: Cardiovascular system. Chronic obstructive pulmonary disease. Heart rate. 6-minute walk test.

Resumo

Introdução: *A literatura evidencia que a doença pulmonar obstrutiva crônica (DPOC) possui características fisiopatológicas que prejudicam a função autonômica cardíaca e a capacidade do sistema cardiovascular em responder aos estímulos.* ***Objetivo:*** *Analisar a correlação entre a frequência cardíaca (FC), saturação periférica de oxigênio (SpO_2) e capacidade funcional e pulmonar em pacientes com DPOC durante o teste de caminhada seis minutos (TC6), antes e após programa de reabilitação pulmonar (PRP).* ***Métodos:*** *Trata-se de um estudo descritivo e retrospectivo, com coleta realizada no banco de dados do PRP de uma universidade do Vale dos Sinos.* ***Resultados:*** *A amostra foi composta por 216 pacientes com DPOC grave, com média de idade de 65,4 ± 7,9 anos e predominância do sexo masculino (57,4%). Os resultados evidenciaram que no momento pré-PRP, a FC ao final do teste apresentou correlação negativa forte ($p < 0,01$) com a SpO_2 obtida ao final do teste e volume expiratório forçado no primeiro segundo (VEF_1). No momento pós-PRP, a FC ao final do teste se correlacionou negativamente de maneira forte com a SpO_2 e VEF_1, positivamente de forma fraca ($p < 0,05$) com a sensação de dispneia pós-teste e forte com a distância percorrida no TC6 (DTC6).* ***Conclusão:*** *As correlações entre FC, VEF_1, DTC6, dispneia e SpO_2 foram confirmadas, ficando evidente que à medida que ocorrem alterações das variáveis, acontecem modificações na FC para suprir a demanda metabólica, ventilatória e de oxigenação.*

Palavras-chave: *Sistema cardiovascular. Doença pulmonar obstrutiva crônica. Frequência cardíaca. Teste de caminhada de 6 minutos.*

Introduction

Chronic obstructive pulmonary disease (COPD) is a heterogeneous disease characterized by respiratory symptoms resulting from airways and/or alveoli abnormalities, which cause persistent and often progressive airflow obstruction.[1]

Data reveal that the clinical manifestations of COPD, including low values of forced expiratory volume in one second (FEV_1), systemic inflammatory process, and hypoxemia, negatively affect cardiac autonomic function. In a recent systematic review, Alqahtani et al.[2] indicated that COPD is associated with autonomic nervous dysfunction, and with changes in heart rate variability (HR). Heartbeat fluctuations in healthy hearts are aligned with a complex mechanism of adaptation to sudden physical and psychological changes that alter homeostasis.[3] Although healthy systems present physiological temporal complexities, disease-related mechanisms can influence a loss or increase in complexity, reducing the ability to maintain a stable state.[2,3]

In COPD, HR may present an inadequate response to exercise due to autonomic dysfunction.[4] Therefore, HR obtained during standardized tests - performed in clinical or laboratory environments - has become a well-established physiological biomarker. Such an aspect echoes the ability of the cardiovascular system to respond appropriately to an abrupt transition in physical load, reflecting on how an important indicator of cardiovascular and physical functioning in patients with COPD.[5]

The six-minute walk test (6MWT) is a standardized test that significantly reproduces the cardiovascular changes induced by submaximal effort,[6] showing the heart's functional capacity through the distance covered in the 6MWT (6MWD).[7] Also, the 6MWT provides relevant data on the clinical course of COPD, such as exercise-induced hypoxemia and the need for supplemental oxygen, symptoms that affect physical performance and induce low exercise tolerance, and changes in walking capacity, providing important bases for appropriate clinical interventions.[8]

Thus, the present study aimed to analyze the correlation between HR, peripheral oxygen saturation (SpO_2), FEV_1, 6MWD, and sensation of dyspnea in patients with COPD during the 6MWT, before and after the pulmonary rehabilitation program (PRP).

Methods

This study is quantitative, cohort, descriptive, and retrospective. It collected data from the PRP database at Feevale University in Novo Hamburgo, Rio Grande do Sul, and it was approved by the Research Ethics Committee of the same institution (number 4.08.01.10.1630). This being a study with database collection, the researchers signed a data use consent form.

The investigation included all patients who joined Feevale University's PRP from May 2003 to December 2018. Adult patients of both sexes with a diagnosis of COPD confirmed by spirometry according to the criteria of the Global Initiative for Chronic Obstructive Lung Disease (GOLD)[1] [FEV_1/forced vital capacity (FVC) < 0.7]

were participants. They performed the 6MWT pre- and post-PRP, which in their medical records included the variables HR, SpO_2, 6MWD and sensation of dyspnea by the Modified Borg Scale (MBS), collected during the 6MWT in the pre- and post-PRP, and whose clinical profile was complete. Upon joining the PRP, all patients signed the informed consent form. Then, they did the initial interview in which the clinical profile was described.

The severity of COPD was measured according to GOLD,[1] recommendations, being estimated according to the degree of airflow obstruction. It is based on FEV_1 values after the use of a bronchodilator and classified as GOLD 1 (mild: $FEV_1 \geq 80\%$ of predicted), GOLD 2 (moderate: $50\% \leq FEV_1 < 80\%$ predicted), GOLD 3 (severe: $30\% \leq FEV_1 < 50\%$ predicted) or GOLD 4 (very severe: $FEV_1 < 30\%$ predicted).

The 6MWT's performance followed international guidelines.[6] Patients walked down a 30-meter-long corridor for six minutes with standardized verbal encouragement. The patients walked alone, with the instructor only observing, and received instructions they could stop the test at any time. After six minutes, they were asked to stop at their location. The remaining distance was measured with a tape measure (WESTERN 20 m – China). To predict the 6MWD, the reference value for healthy adults of both sexes was used, based on the formula described by Britto et al.,[9] being: predicted distance (6MWD) = 890.46 - (6.11 × age) + (0.0345 × age 2) + (48.87 × sex) - (4.87 × body mass index).

Blood pressure (BP) was measured only at one point, 15 minutes before the start of the activity, with a sphygmomanometer and stethoscope from P.A. MED, model 3222009, with the patient sitting and with the upper limb resting on a table. HR was measured using the Polar FT1 cardiac monitor (cardiac monitor and transmission belt) and SpO_2, by non-invasive oximetry (SENSE 10 oximeters – ALFAMED, CMS50C – Contec, Palpus 1 – Rossmax), being checked before the start of the walk and after the sixth minute. The predicted maximum heart rate (HRMP) was calculated using the Karvonen equation (HRMP = 220 – age years) for each participant. The sub-maximal HR was 85% of the maximum HR.[10] Desaturation was considered when the variation in SpO_2 (ΔSpO_2), that is, the difference between the final SpO_2 and initial SpO_2, decreased (≥ 4%).[11] The sensation of dyspnea and fatigue were assessed at the beginning and the end of the test using EBM (0-10).

Pulmonary rehabilitation is a comprehensive intervention that aspires to improve the physical and psychological conditions of people with chronic respiratory diseases through physical exercise, education, and behavioral changes. The PRP is made up of a multidisciplinary team.[12] The program occurred three times a week (12 weeks minimum). The patients underwent physical training through the following techniques: warm-up, aerobic, and resistance training. The warm-up consisted of functional diagonals of the upper and lower limbs. The aerobic consisted of a flat treadmill, with a progressive increase in speed and distance based on the 6MWT and perception of dyspnea according to the Borg scale. Lastly, the resistance training was performed on weight training equipment, with free exercises with load and free exercises without load, with two series of 8-10 repetitions and a gradual increase in load, estimated through the one maximum repetition test, starting with 50% of the estimated load and reaching 85% of the maximum load obtained in the test). Concomitantly, the participants' vital signs were monitored, and supplementary oxygen was offered if SpO_2 fell below 90%.

The results were presented using absolute (n) and relative frequencies (%) or using minimum and maximum values, arithmetic average, and respective standard deviation. Performance between the moments before and after the 6MWT and pre- and post-PRP was analyzed using the non-parametric Wilcoxon statistical test in the variables: HR, SpO_2, systolic blood pressure (SBP), diastolic blood pressure (DBP), 6MWD and perception of dyspnea. Analysis of cause-effect relationships based on HR, correlating with the variables 6MWD, dyspnea, and FEV1, was carried out using Spearman's rho correlation coefficient (ρ). All statistical procedures used the Statistical Package for Social Sciences (SPSS, version 26.0) software, adopting a significance level of $p > 0.05$.

Results

There was a selection of 216 patients, 124 males (57.4%) and 92 females (42.6%), with an approximate age of 65.4 ± 7.9 years. Regarding the degree of airflow obstruction, the average FEV_1/FVC presented was 52.4 ± 17.3, confirming the diagnosis of COPD, and the average FEV1% was 43.5 ± 18.7%, classifying the study collaborators as GOLD 3 (severe COPD). As a result, 39.4% (n = 85) of patients have systemic arterial hypertension (SAH), with 74% (n = 63) of these reporting the use of antihypertensive medication. Other sample characteristics are displayed in Table 1.

Table 1 - Clinical profile of study participants (n = 216)

Variables	Results
Male*	124 (57.4)
Female*	92 (42.6)
Age (years)	65.4 ± 7.9
Body mass index (kg/m^2)	25.9 ± 4.7
Smoking habit*	199 (92.0)
Comorbidities *	127 (58.8)
Systemic hypertension *	85 (39.4)
Diabetes mellitus*	27 (12.5)
Cardiovascular disease*	25 (11.6)
Antihypertensive medication use*	63 (74.0)
Lung function	
FVC (l/min)	2.4 ± 0.9
FVC (% predicted)	68.3 ± 22.7
FEV_1 (l)	1.7 ± 6.6
FEV_1 (% predicted)	43.5 ± 18.7
FEV_1/FVC	52.4 ± 17.3

Note: FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second. *n (%); other data expressed as arithmetic average ± standard deviation.

The initial and final variables found in the 6MWT before and after the PRP are shown in Table 2. The average time of participation in the PRP was 18.9 ± 6.4 weeks. When comparing the variables before and after the 6MWT, there was a statistically significant increase in HR, dyspnea, and fatigue, both before and after the PRP ($p < 0.05$). Likewise, the average values indicate an eminent drop in SpO_2 compared to baseline values at the sixth minute, pre- and post-PRP ($p < 0.05$). Also, there was peripheral oxygen desaturation. Regarding the maximum HR predicted for age, the average was 154.6 ± 7.9 beats per minute (bpm). In the first and second tests, the average percentages of predicted maximum HR were 66.9 ± 10.9% and 67.5 ± 12.9% (respectively), characterizing submaximal effort. The predicted 6MWD mean was 542.5 ± 37.1 meters. The 6MWD mean in the pre- and post-PRP tests were, respectively, 400.3 ± 106.6 and 460.4 ± 103.2 meters, with an average increase of 60.5 ± 70.0 meters in the distance covered. Thus, one can observe a statistically significant difference ($p = 0.000$). When correlating the HR at the end of the 6MWT with the other variables before the PRP, the Spearman correlation coefficient exhibited a strong negative correlation between HR and FEV_1% ($\rho = -0.261$; $p = 0.000$) and HR and SpO_2 at the end of the test ($\rho = -0.280$; $p = 0.000$). As the variables decrease, the HR increases. The variables dyspnea at the end of the test and 6MWD did not correlate with HR at the end of the test in the pre-PRP moment.

Table 2 - Description of variables obtained in the six-minute walk test (6MWT) pre- and post-PRP (n = 216)

Variables	6MWT pre-PRP		6MWT post-PRP		p-value**
	Mean ± SD	p-value*	Mean ± SD	p-value*	
Distance covered in the 6MWT (6MWD) (m)	400.3 ± 106.6	-	460.4 ± 103.2	-	**0.000**
6MWD percentage predicted (%)	73.8 ± 19.6	-	84.9 ± 19.4	-	**0.000**
Heart rate pre-test (bpm)	87.3 ± 15.7	-	88.5 ± 16.1	-	0.169
Heart rate post-test (bpm)	103.4 ± 16.9	**0.000**	104.6 ± 18.7	**0.000**	0.072
Maximum heart rate predicted (%)	66.9 ± 10.9	-	67.5 ± 12.9	-	0.095
Systolic blood pressure (mmHg)	129.3 ± 17.2	-	127.0 ± 14.0	-	**0.043**
Diastolic blood pressure (mmHg)	77.7 ± 10.1	-	76.7 ± 9.1	-	0.177
Borg dyspnea pre-test	1.1 ± 1.7	-	0.9 ± 1.3	-	**0.018**
Borg dyspnea post-test	3.0 ± 2.7	**0.000**	2.8 ± 5.1	**0.000**	**0.007**
Borg MMII pre-test	0.8 ± 1.0	-	0.78 ± 1.0	-	0.857
Borg MMII post-test	1.9 ± 1.7	**0.000**	1.6 ± 1.6	**0.000**	0.460
Peripheral oxygen saturation pre-PRP (%)	94.0 ± 4.5	-	94.3 ± 4.0	-	0.117
Peripheral oxygen saturation post-PRP (%)	92.0 ± 5.6	**0.000**	91.6 ± 6.2	**0.000**	0.267
Peripheral oxygen desaturation (> 4%) – n (%)	59 (27)	-	74 (34)	-	-

Note: PRP = pulmonary rehabilitation program; SD = standard deviation. Wilcoxon Signed Rank Test. *Association between pre- and post-test. **Association between the tests pre- and post- PRP. Aspects highlighted show statistic relevance.

After PRP, Spearman's correlation coefficient showed a strong negative correlation between HR at the end of the 6MWT with SpO_2 at the end of the 6MWT (ρ = -0.285; p = 0.000) and with FEV1 (ρ = -0.273; p =0.000), in addition to a strong positive correlation with the 6MWD' (ρ = -0.255; p = 0.000). Similarly, HR at the end of the test showed a weak positive correlation with the perception of dyspnea at the end of the test (ρ = 0.140; p = 0.041) (Figure 1).

Discussion

In the present study, one can perceive that the effort developed during the 6'MWT was capable of promoting an increase in HR and a reduction in circulating oxygen levels and precipitating the perception of dyspnea and fatigue, which confirms in clinical practice that the 6'MWT is an ideal instrument to assess the functional capacity and cardiovascular responses of people with COPD.[6]

The physiological phenomena presented in the 6MWT result from the simultaneous action between the cardiovascular, respiratory, musculoskeletal, and nervous systems. These systems provide the necessary stimuli to maintain cardiac output and ventilation during the test and sustain aerobic metabolism. These stimuli come from reflex and adaptive responses of pulmonary and cardiac activity to the levels of oxygen consumption required in response to the degree of effort undertaken.[7]

Hence, HR is observed as a variable with high sensitivity to adaptive mechanisms to efforts, being commonly used to measure the intensity of an exercise.[13] The present study evidences HR's adaptive responses through the significant increase in HR when comparing the baseline value with the sixth minute of the 6MWT before and after PRP.

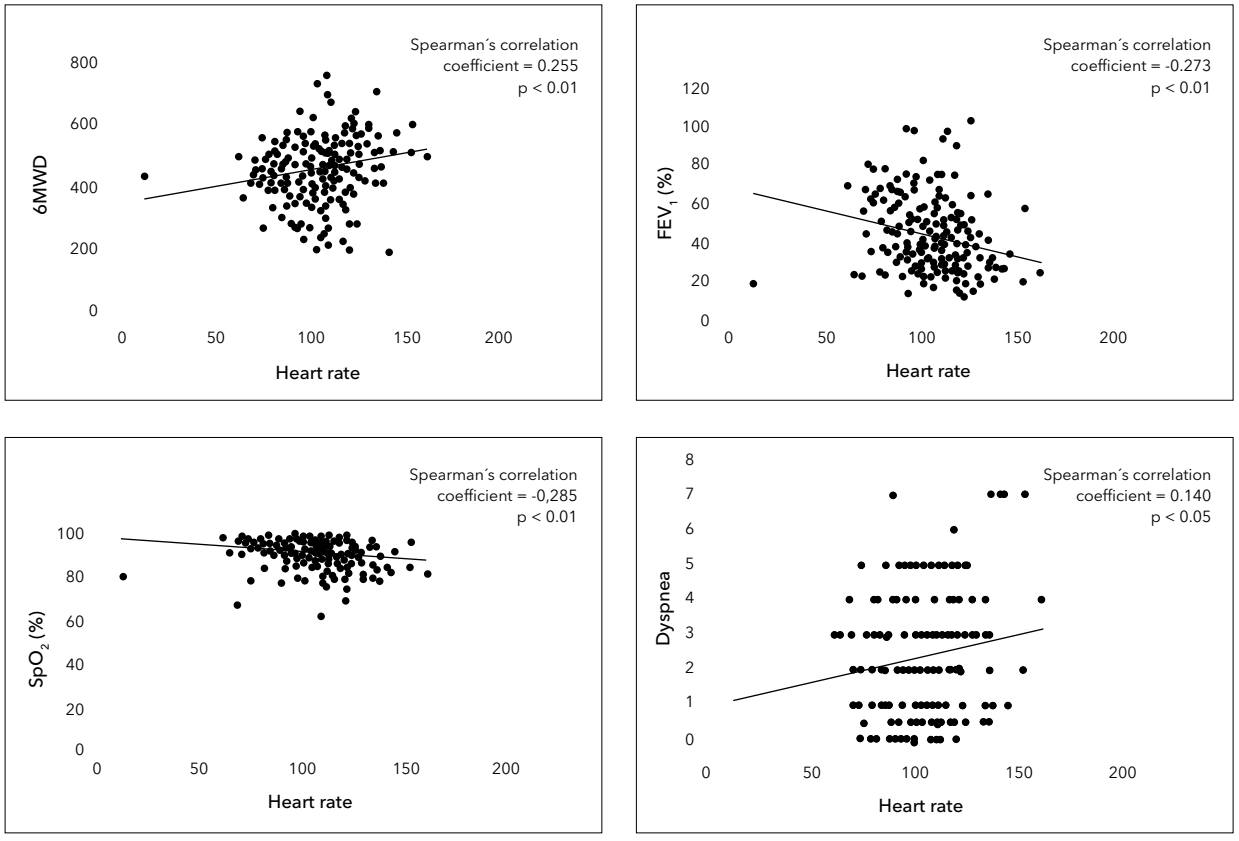

Figure 1 - Correlation between heart rate (bpm) at the end of the six-minute walk test with the distance covered in the test (6MWD), forced expiratory volume in the first second (FEV_1), perception of dyspnea, and peripheral oxygen saturation (SpO_2) at the end of the test (n = 216).

Furthermore, in the post-PRP test, HR showed a strong positive correlation with the 6MWD, indicating that, as the 6MWD increases, there is a greater demand on the HR, causing cardioacceleration. Physical exercise directs the body to temporary dysfunctions, generating the adaptive mechanisms responsible for better future functional performance,[14] such as lean body mass increase.[15] It is suggested that this cause-effect relationship can be justified by the increase in cross-sectional area of the muscle fiber and an increase in type I fibers,[16] with greater oxygen consumption after PRP. It is a greater chronotropic response to maintain adequate oxygen levels. There was also a significant increase in the 6MWD, which is another factor that can influence HR, suggesting that the effort undertaken in the second test was more significant than in the first, increasing the metabolic demand. Consequently, it requires a greater HR response.[4]

Multiple factors can cause fluctuations in HR, which may increase or decrease in the face of indirect stimuli. There are many reasons despite the intensity of the exercise.[13] There is evidence that people with COPD have a loss in autonomic modulation; as a consequence, they are susceptible to worse health conditions, greater risk of cardiovascular events[17] and inadequate HR response to exercise.[18] Hence, the significant increase in HR during submaximal efforts can be attributed to the influence of pathophysiological stimuli involved in COPD on control autonomic.

Chronotropic insufficiency is common in COPD,[18] increasing as lung function decreases.[4] Studies show that the pulmonary and cardiovascular systems share risk factors and physiological and pathophysiological processes.[19,20] Lung function is the most potent predictor of mortality heart rate,[21,22] as the decline in lung function results in an overload of the cardiovascular system and possible injuries.[21] In the present study, the association between lung function and greater cardiac demand was clear through the strong negative correlation between FEV_1 and HR.

Another aspect identified during the test was the drop in SpO_2 to significant levels, with precipitation reaching values ≥ 4% in both tests, characterizing oxyhemoglobin desaturation.[11] The study carried out by Waatevik et al.[11] indicated that patients who present desaturation of oxygen in the 6MWT have higher HR in both the first and sixth minutes of the 6MWT, when compared to patients who do not desaturate.[11] Such association was evidenced in the present research through the strong negative correlation between HR and SpO_2, indicating that as oxygen levels decrease, HR increases.

Oxygen desaturation in people with COPD can occur during physical activities[23] or even while resting. Both in acute events and in chronic situations, hypoxemia can generate cardiovascular changes and result in dysfunctions of autonomic control. In acute events, sympathetic nervous activity increases, leading to tachycardia and the risk of ischemic coronary events.[24] Chronic hypoxemia causes constriction and hyperplasia in the pulmonary vascular bed. The increase in afterload reflects in right ventricular hypertrophy, which can lead to the displacement of the ventricular septum to the left, compromising left ventricular filling, systolic volume, and cardiac output.[19,25]

Furthermore, people who experience early desaturation during the 6MWT are at greater risk of hospitalization and death.[26,27] Exercise-induced hypoxemia can also result in a higher rate of symptoms and more severe dyspnea.[23] Dyspnea and muscle fatigue are the symptoms that lead the pneumopathy patient to functional limitation and physical deconditioning,[28] and the precipitation of such symptoms is observed during the execution of both tests, as well as the significant reduction in dyspnea after PRP. There is vast documentation of this aspect in literature, with the main benefit of physical exercise being the reduction of symptoms, leading to greater independence in activities of daily living and quality of life,[29,30] also leading to increased exercise tolerance and reduced cardiovascular risks.

In addition to reducing symptoms, this research showed that PRP was able to provide a significant increase in the 6MWD and in the percentage of 6MWD predicted for age, which is a factor of extreme clinical relevance. Studies show that the 6MWD is associated with functional impairment and quality of life indices, with a 6MWD equal to or less than 350 meters determining the risk of hospitalizations and survival in patients with COPD.[6,7,31] A change in 35 meters on the 6MWD' represents a discovery with a clinically significant impact on moderate or severe COPD.[8,32]

Additionally, this study demonstrated that PRP contributed to reducing blood pressure levels. It is observed that there was a prevalence of comorbidities that can lead to cardiovascular risk, hypertension being the most common. The association between COPD and hypertension has been gaining more and more attention,

as it has often been found to be the most common comorbidity in these patients. The pathophysiological mechanisms of COPD may be the precursor to high blood pressure levels, which are responsible for an unfavorable prognosis for the pneumopathy patient.[33,34]

It is noteworthy that there were limitations of the present study, such as the convenience sample. Also, the research was carried out in a single center, and BP obtaining only occurred before and after the PRP - not in the pre and post-6MWT. Such aspects may generate doubt regarding the results, although maximum care was taken in exploring these data to obtain the most accurate information possible. However, despite the limitations found, the present study made vital contributions, as HR is an easy-to-measure and low-cost variable, pointing to a field of research that needs engagement so that there is a greater understanding of responses to stimuli about its usage in clinical practice. Due to its relevance, new studies in the area are suggested.

Conclusion

The correlations between HR, FEV_1, 6MWD, dyspnea, and SpO_2 were confirmed. As changes occur in variables, changes occur in HR to meet metabolic, ventilatory, and oxygenation demands. Hence, it promotes body homeostasis.

Authors´ contributions

MN and CCC participated in the elaboration of the research question and methodological design. MN was responsible for the search and analysis of the data, and CCC was responsible for the statistical analysis. The results' interpretation was carried out by all authors, and the manuscript was written by MN and LDS. All authors approved the final version.

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