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Relationship between pulmonary function, maximum inspiratory pressure, oxygen saturation and exercise capacity in patients with chronic obstructive pulmonary

Relação entre função pulmonar, pressão inspiratória máxima, saturação de oxigênio e capacidade de exercício em pacientes com doença

Relación entre función pulmonar, presión inspiratoria máxima, saturación de oxígeno y capacidad de ejercicio em pacientes con enfermedad pulmonar obstructiva

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Abstract

Introduction: Exercise capacity is one of the determining factors in the prognosis of patients with COPD. Assessing exercise capacity and its relationships can contribute to understanding the factors that impact the reduction of physical activity and provide subsidies to mitigate its deleterious effects. Objective: The purpose of this study was to assess the relationship between pulmonary function, respiratory muscle strength, baseline peripheral oxygen saturation and exercise capacity. Methodology: 11 individuals diagnosed with COPD were selected for this study (5 patients in GOLD Stage 3-4; 6 patients in GOLD stage 1-2), of both genders, with a mean age of 70.73±6.19 years. All patients underwent evaluation of the distance covered in the six-minute walk test (6MWD), pulmonary function (FEV_1%pred, FVC%pred e %FEV_1/FVC), respiratory muscle strength (MIP, MEP) and baseline peripheral oxygen saturation (baseline SpO_2). Results: The results showed a positive correlation between baseline SpO2 (p=0.007), FVC%pred (p=0.02) and the 6MWD. Conclusions: The results of this study allow us to infer that there is an association between 6MWD, baseline pulse oxygen saturation, FVC and gender. Thus, this study suggests that the lower oxygenation at rest is correlated with a worsening of lung function and lower tolerance of the individual to physical exercise.
Keywords: COPD; Pulmonary function tests; Respiratory mechanics; Exercise.

Resumo

Introdução: A capacidade de exercício é um dos fatores determinantes no prognóstico de pacientes com DPOC. Avaliar a capacidade de exercício e suas relações pode contribuir para a compreensão dos fatores que impactam na redução da atividade física e fornecer subsídios para mitigar seus efeitos deletérios. Objetivo: O objetivo deste estudo foi avaliar a relação entre função pulmonar, força muscular respiratória, saturação periférica de oxigênio basal e capacidade de exercício. Metodologia: 11 indivíduos com diagnóstico de DPOC foram selecionados para este estudo (5 pacientes em estágio GOLD 3-4; 6 pacientes em estágio GOLD 1-2), de ambos os sexos, com média de idade de 70,73±6,19 anos. Todos os pacientes foram submetidos à avaliação da distância percorrida no teste de caminhada de seis minutos (DTC6), função pulmonar (VEF1%pred, CVF%pred e %VEF_1/CVF), força muscular respiratória (PImáx, PEmáx) e saturação periférica de oxigênio basal (SpO2 basal). Resultados: Os resultados mostraram correlação positiva entre SpO2 basal (p=0,007), CVF%pred (p=0,02) e DTC6. Conclusões: Os resultados deste estudo permitem inferir que existe associação entre DTC6, saturação basal de oxigênio de pulso, CVF e sexo. Assim, este estudo sugere que a menor oxigenação em repouso está correlacionada com piora da função pulmonar e menor tolerância do indivíduo ao exercício físico.
Palavras-chave: DPOC; Testes de função pulmonar; Mecânica respiratória; Exercício físico.

Resumen
Introducción: La capacidad de ejercicio es uno de los factores determinantes en el pronóstico de los pacientes con EPOC. Evaluar la capacidad de ejercicio y sus relaciones puede contribuir a comprender los factores que inciden en la reducción de la actividad física y proporcionar subsidios para mitigar sus efectos nocivos. Objetivo: El propósito de este estudio fue evaluar la relación entre la función pulmonar, la fuerza de los músculos respiratorios, la saturación de oxígeno periférico basal y la capacidad de ejercicio. Metodología: Para este estudio se seleccionaron 11 personas con diagnóstico de EPOC (5 pacientes en estadio GOLD 3-4; 6 pacientes en estadio GOLD 1-2), de ambos sexos, con una edad media de 70,73±6,19 años. A todos los pacientes se les evaluó la distancia recorrida en la prueba de marcha de seis minutos (6MWD), función pulmonar (FEV1%pred, FVC%pred y %FEV_1/FVC), fuerza muscular respiratoria (MIP, MEP) y saturación periférica de oxígeno basal (SpO2 basal). Resultados: Los resultados mostraron una correlación positiva entre la SpO2 basal (p=0,007), FVC%pred (p=0,02) y la 6MWD. Conclusiones: Los resultados de este estudio permiten inferir que existe una asociación entre la 6MWD, la saturación de oxígeno de pulso basal, la FVC y el sexo. Así, este estudio sugiere que la menor oxigenación en reposo se correlaciona con un empeoramiento de la función pulmonar y una menor tolerancia del individuo al ejercicio físico.
Palabras clave: EPOC; Pruebas de Función Respiratoria; Mecánica Respiratoria; Ejercicio Físico.

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a chronic respiratory disease characterized by persistent respiratory symptoms and airflow limitation initially associated with an inflammatory response in the airways and lungs (Global; Vaes et al., 2021; Li et al., 2020; Mansour et al., 2019). Although it primarily affects the lungs, its extrapulmonary consequences, including reduced exercise tolerance, are well established (Vaes et al., 2021).

Currently, Chronic Obstructive Pulmonary Disease (COPD) is a major health problem that negatively impacts the quality of life of patients (Hulya et al., 2020). In addition to a poor quality of life, COPD accompanies physical, psychological and social problems, with dyspnea as the main limiting symptom (de Souza et al., 2022; Hulya et al., 2020; Amaral et al., 2020).

Patients with COPD are involved in a vicious cycle of dyspnea, physical deconditioning and exercise intolerance, which considerably reduces activities of daily living, leading to inactivity, inability to work and/or take care of themselves, and social isolation with consequent onset of anxiety and depression (Hulya et al., 2020; Zeng et al., 2018) (Klein et al., 2021).

Dyspnea on exertion is considered multifactorial, reflecting the imbalance between the load on the respiratory system and the capacity of the respiratory muscles (Kofod, 2020), peripheral muscle dysfunction (Casaburi, 2000), dynamic hyperinflation (O'Donell; Webb, 2008), stimulation of chemoreceptors (hypoxemia, hypercapnia) (Kofod, 2020), body composition with high fat level, among others.

Thereby, patients with COPD often have reduced tolerance to physical exercise and difficulties in performing activities of daily living. Skeletal muscle dysfunction causes repercussions that lead to poor exercise performance, poor quality of life, and early mortality (Mansour et al., 2019). This reduced activity in COPD patients can be mitigated with the introduction of incorporated exercises as a key component of a rehabilitation program (Zeng et al., 2018). Therefore, the pulmonary rehabilitation program can alleviate dyspnea and fatigue, improve exercise tolerance and quality of life, also generating positive impacts in reducing the number of hospitalizations (Zeng et al., 2018).

Thus, the assessment of exercise capacity is essential practice, especially in a pulmonary rehabilitation program. There are tools that contribute to this assessment, such as the six-minute walking test (6MWT), a simple, reproducible and inexpensive field test widely used in clinical practice to assess functional capacity, being able to objectively reflect the ability to perform activities of daily living (Klein et al., 2021).

It has been described that a worse performance on the 6MWT portrayed by a shorter distance covered is associated with a larger number of exacerbations and hospitalizations, with a consequent increase in mortality (Aarli et al., 2017; Celli et al., 2016). In addition, there is evidence that exercise capacity is related to impairment of respiratory muscles (Loiseau et al., 1989).

Therefore, understanding the factors that impact exercise capacity can contribute to a better understanding of how to act in a rehabilitation program to mitigate the deleterious effects of reduced exercise tolerance. Thus, the purpose of this study was to evaluate the relationship between pulmonary function, respiratory muscle strength, peripheral oxygen saturation and exercise capacity.

2. Methodology

Eleven individuals diagnosed with COPD were selected for this study (5 patients in GOLD Stage 3-4; 6 patients in GOLD stage 1-2), of both genders, with a mean age of 70.73±6.19 years old.

As inclusion criteria were considered participants aged between 61 and 80 years old, with a medical diagnosis of COPD, medical referral to a Pulmonary Rehabilitation Program and without an exacerbation for at least 30 days. Patients with complex cardiac arrhythmias, unstable angina, uncontrolled systemic arterial hypertension, myocardial ischemia and patients using cardio depressant or cardio stimulating medications were excluded. This study was carried out at the Cardiopulmonary Rehabilitation Laboratory belonging to the Faculty of Health Sciences (FCS) of the University of Vale do Paraíba (Univap) after approval by the Ethics Committee under protocol 36117020.0.0000.5503. It was conducted in accordance with resolution 466/2012 of the National Health Council (CNS). All participants were previously informed and oriented about the procedures and signed a Free and Informed Consent Form.

Assessments

Before the beginning of the procedure, the patients were evaluated in the Respiratory Physiotherapy Laboratory at a temperature of 22º C and relative humidity between 50% and 60%, where resting variables such as systolic and diastolic blood pressure (SBP and DBP), respiratory rate (RR), heart rate (HR), pulse oxygen saturation (SpO2) and clinical data such as age, gender, body mass index (BMI) and disease staging were collected.

Subsequently, pulmonary function tests, manovacuometry and the six-minute walk test were performed. Patients were instructed to wear comfortable clothes, appropriate walking shoes, eat light food beforehand and not perform physical activity in the two hours prior to the test, in addition to avoiding alcoholic beverages, stimulants, not smoking, and not performing exhaustive physical exercises the day before the assessments.

Pulmonary function test

To perform the pulmonary function test, the absence of respiratory infection in the last three weeks (i.e. cold, bronchitis, flu, pneumonia) was necessary, taking into account that these could alter pulmonary function or lead to bronchial hyperresponsiveness (Souza, 2002). Participants received the necessary guidelines so that the test could be performed (Souza, 2002). The test was performed in accordance with the Guidelines for Pulmonary Function Tests (Souza, 2002).

To carry out the spirometry test, the MicroQuark spirometer (Brazil, Cosmed®) was adjusted, and the temperature was checked. The individual was positioned seated during the examination with the head held in a neutral position. The mouthpiece was introduced over the tongue, between the teeth and closed lips, to prevent air leakage. The individual received stimulus so that the effort was maintained during the procedure for the necessary time. During the examination, the Forced Vital Capacity maneuver was performed to measure the Forced Expiratory Volume in the first second (FEV_1,%pred) and Forced Vital Capacity (FVC%pred) (Souza, 2002).

Six-minute walk test

Exercise capacity was evaluated by means of the 6-minute walk test (6MWT) in a 30-meter-long straight corridor, delimited by cones, on a rigid and flat surface with markings on the ground every 1 meter. Patients were instructed, according to the American Thoracic Society ATS/ERS guidelines, to walk at their own pace and alone as far as possible in six minutes, circling between the cones (Holland et al., 2014). Before starting the 6MWT and at the end of the sixth minute, heart rate (HR), systolic (SBP) and diastolic (DBP) blood pressure, respiratory rate (RR), peripheral oxygen saturation (SpO2 baseline) and application of Borg's perceived exertion scale. After 2 and 4 minutes of rest, a new check was performed to verify the recovery of the patients.

The participant was encouraged during the test every one minute until the sixth minute. At the end of the sixth minute, the exact point where the participant had stopped was marked and, soon after, he sat down, and the measurement of post-test vital signs and the application of the Borg's perceived exertion scale were performed.

During the 8th and 10th minutes of the chronometer during the test, a new measurement of vital signs was performed, and the Borg's perceived exertion scale was applied to assess the patient's recovery from exercise. The distance values obtained in meters were calculated using the prediction equations of Enright and Sherril (1998), which determine the level of predicted distance walked for each individual patient:

Men: 6MWD = (7.57 x height cm) - (5.02 x age) - (1.76 x weight kg) - 309m and,

Women: 6MWD = (2.11 x height cm) - (2.29 x weight kg) - (5.78 x age) + 667m.

Respiratory muscle strength measurement

The method of assessing respiratory muscle strength was through maximal inspiratory (MIP) and expiratory pressures (MEP) measurements, according to the guidelines of the European society (Laveneziana, 2019). To perform the manovacuometry test, a Ger-Ar® manovacuometer scaled from -300 to + 300cmH2O was used. The individual was instructed to follow the instructions to start the exam and immediately afterwards performed maximal respiratory efforts stimulated by verbal command. During the MIP measurement, the individual initially breathed normally through the manovacuometer, then was asked to perform a maximum expiration and soon after, he performed a maximum inspiratory effort against the occluded airway (Neder et al., 1999; Souza, 2002). For the measurement of MEP, at first, the individual breathed in until reaching their total lung capacity and, soon after, performed a maximal expiratory effort against the occluded airway (Valsalva Maneuver). The value of MIP and MEP was usually expressed in cmH2O (Neder et al., 1999; Souza, 2002). The test was repeated three times with a rest interval of at least 2 minutes between measurements. The highest value obtained was selected as MIP and MEP and also expressed as a percentage of the predicted %MIP and %MEP.

Statistical Analysis

For statistical analysis, the Shapiro-Wilk test was used to analyze the normality of data distribution, with data description in mean and standard deviation. Correlations between pulmonary function, baseline SpO2, MIP, MEP and exercise capacity were investigated using Pearson's correlation coefficient (r). Statistical analysis was performed using *Graphpad Prism* 6.0 (*Graphpad* 6.0, Software, Inc, USA). Statistical significance was determined as $p<0.05$.

3. Results

This study included 11 COPD patients and their characteristics are shown in Table 1. Patients had varying degrees of airway obstruction, 45% had severe obstruction (Gold 3 and 4). Sixty three of patients were women.

Table 1. Characteristics of the patients with COPD (n=11).

Gender (male/female)	6/5
Age (years)	70.73±6.19
Weight, Kg	71.57± 11.68
Height, m	1.62± 0.10
Body Mass Index, (Kg/m^2)	27.28±4.35
FEV_1%pred	57,73±26,48
FVC%pred	75.40±23.90
Saturation before test (SpO_2 baseline)	94,73±2,83
Six-Minute Walking Test (m)	382.00±96.54
Borg Scale Baseline	7.90±1.22
Borg after 6MWT	12.00±2.56
FC baseline	78.27±11.07
MEP (cmH_2O)	129,09±75,43
MEP %pred	119,45±58,01
MIP (cmH_2O)	101,81±34,58
MIP %pred	107,27±29,96
GOLD	
1	3 (27%)
2	3 (27%)
3	4 (36%)
4	1 (9%)

Data are represented as mean ± SD or n (%). FEV_1%pred.: Forced expiratory volume in the first second as a percentage of predicted values; CVF%pred = vital forced capacity as a percentage of predicted values; MIP, Maximal Inspiratory Pressure; MIP%pred, Maximal Inspiratory Pressure as a percentage of predicted values; MEP, Maximal Expiratory Pressure; MEP%pred, Maximal Expiratory Pressure as a percentage of predicted values; cmH_2O = centimeters of water. Source: Authors.

Table 2 illustrates the correlations between pulmonary function parameters, respiratory muscle strength, gender and age and the distance covered in the six- minute walking test (6MWD). The results demonstrate that there is evidence of an association between baseline SpO_2, FVC and exercise capacity.

Table 2. Correlation between 6MWD expressed in meters and respiratory muscle strength and pulmonary function in individuals with COPD (n=11).

	Six- Minute Walking Test (m)	
Variables	R	significancy
Six-Minute Walking Test (m)	--	--
SpO_2 before test (%)	0.750	*Yes (0.007)
MIP (cmH_2O)	0.331	No (0.31)
%MIP pred	0.489	No (0.12)
MEP (cmH_2O)	0.223	No (0.50)
%MEP pred	0.336	No (0.31)
FEV_1 pred (%)	0.515	No (0.10)
FVC (%)	0.651	*Yes (0.02)
FEV_1/ FVC (%)	0.193	No (0.56)
Age	-0.073	No (0.82)
Gender	0.344	*Yes (0.30)

All values were expressed as mean and standard deviation. *$p \leq 0.05$; MIP, Maximal Inspiratory Pressure; MIP%pred, Maximal Inspiratory Pressure as a percentage of predicted values; MEP, Maximal Expiratory Pressure; MEP%pred, Maximal Expiratory Pressure as a percentage of predicted values; FEV_1%pred., Forced expiratory volume in the first second as a percentage of predicted values; CVF%pred = vital forced capacity as a percentage of predicted values; FEV_1/FVC = FEV_1/FVC relation/Tiffeneau index. Source: The authors.

4. Discussion

Patients with COPD often have reduced exercise capacity, which is associated with a greater number of exacerbations and hospitalizations with a consequent increase in mortality (Amaral et al., 2020; Li et al., 2020). Thus, it is of paramount importance to place great emphasis on the assessment and rehabilitation of exercise capacity in COPD patients (Li et al., 2020).

The reduction in functional capacity worsens the ability to exercise and creates a vicious circle that contributes to muscle dysfunction. In this scenario, the inactivity caused by the progress of dyspnea leads to a sedentary lifestyle generating deconditioning of the locomotor muscles and consequently greater inactivity (Ho & Maa, 2016).

Field tests such as the shuttle walking test and the six-minute walking test (6MWT) are popular in the assessment of exercise capacity because they are practical, simple, reproducible, and their validation is well established (Amaral et al., 2020) (Bozdemir, 2021). In addition, these tests can help in the assessment and monitoring of the response to pulmonary rehabilitation and contribute to the identification of determinants associated with reduced distance covered. Thus, they can be useful for prognostic assessment and to identify a risk of reduced physical activity (Sing et al., 2014) (Perez et al., 2019;Watz et al., 2014).

Previous studies describe that exercise capacity in COPD patients with severe airway obstruction is apparently influenced by impairments in pulmonary function and inspiratory muscle strength (Wijkstra et al., 1994). Based on these observations, we investigated whether there is a correlation between respiratory muscle strength parameters (Maximal Inspiratory -MIP and Expiratory Pressure-MEP), pulmonary function (FEV_1, FVC), resting oxygen saturation values (SpO_2 baseline) and the capacity of exercise measured by the distance covered in the six-minute walking distance (6MWD) test.

Although there are indications that inspiratory muscle weakness may limit exercise tolerance in COPD patients (de Souza et al., 2022; Charususin et al., 2018; Wijkstra et al., 1994), Our study did not demonstrate this association. Similarly, correlations between 6MWD and MIP%pred or MEP%pred were not observed in a study by Kyomoto et al. (2019).

In fact, some studies have shown a significant correlation between respiratory muscle function and 6MWD (Giua et al., 2014; Gosselink, Troosters & Decramer, 1996) although others have described that impaired respiratory muscle function in COPD patients does not affect exercise capacity (Kyomoto et al., 2019; Charusin et al., 2018). Thus, because of these conflicting results, the relationship between respiratory muscle strength and 6MWD remains unclear.

On the other hand, our study found a positive and strong correlation between baseline oxygen saturation and the distance covered on the 6MWT. This indicates that low oxygen saturation may be correlated with poorer physical performance and underscores the role of hypoxia in the functional capacity of COPD patients. Apparently, hypoxia is related to an increase in the release of free radicals, which leads to physical damage to muscles and brain tissue and consequent functional and cognitive impairment (Chuthirds et al., 2021).

Significant associations were also found between oxygen saturation, cognitive performance, and muscle quality, confirming previous findings that hypoxia is an important systemic factor in functional performance in COPD (Kim et al., 2008). Perez et al. (2019) demonstrated that in stable patients with COPD, FVC, mMRC scale and baseline SpO_2 were the main determinants of poor functional performance.

Furthermore, low oxygen saturation, but not disease severity (e.g. FEV_1, BODE), has been linked to an increased risk of muscle dysfunction and cognitive impairment in COPD patients (Chuthirds et al., 2021). This is relevant to note since in our study we did not find a relationship between FEV_1 and 6MWD, but we did find it with baseline SpO_2.

Although our results showed no relationship with FEV_1, they pointed to a moderate correlation between 6MWD and the spirometric variable %FVC. The muscle-respiration-circulation axis is essential to physical activity, and thus, significant correlations between ventilation parameters (e.g., %FVC and %FEV_1) and diffusion (e.g., %DLCO) and exercise capacity are to be expected. These findings are consistent with previous reports which confirm that parameters such as %FVC and $\%FEV_1$ significantly correlated with 6MWD in COPD patients (Vinod et al., 2019; Kyomoto et al., 2019).

In addition, previous studies reported that the decline in 6MWD was greater in patients with severe outflow obstruction (Amaral et al., 2020; Vinod et al., 2019). Vinod et al. (2019) demonstrated a linear correlation of the six-minute walk test (6MWT) with the absolute values of pulmonary function tests and stated that 6MWD could predict COPD severity.

Amaral et al. (2020) compared the degrees of changes in spirometry with 6MWT and reported that patients with spirometry with a more severe degree of obstruction walked a shorter distance compared to those with moderate alterations. These results corroborate the study by Casanova et al. (2008) which demonstrated that 6MWT is an important prognostic factor, especially in patients with severe COPD. Thus, this author states that 6MWD seems to be more related to $\%FEV_1$, rather than %FVC (Amaral et., 2020), which differs from our findings that observed a correlation with %FVC but not with $\%FEV_1$.

Furthermore, these clinical correlates of pulmonary function and 6MWD were relatively poor predictors, insufficient to estimate the presence of low 6MWD in a single patient (Perez et al., 2019).

5. Conclusions and Final Considerations

The results of this study allow us to infer that there is an association between 6MWD, baseline pulse oxygen saturation, FVC and gender. Thus, this study suggests that the lower oxygenation at rest is correlated with a worsening of lung function and lower tolerance of the individual to physical exercise. Future studies may include a greater number of participants segmented by degree of obstruction to better understand the impacts of the disease and its severity on respiratory muscle performance and functional capacity. In addition, submitting these patients to a long-term pulmonary rehabilitation process and monitoring the effects of treatment can help to visualize the effects that exercise can have on these functional losses.

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