

The Relationship Between Exercise Capacity and Different Clinical Outcomes in Patients with Interstitial Lung Diseases

A Relação Entre Capacidade de Exercício e Diferentes Desfechos Clínicos de Pacientes com Doenças Pulmonares Intersticiais

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Abstract

Interstitial lung diseases (ILD) are associated with various extrapulmonary complications, often leading to reduced exercise capacity. However, the relationship between exercise capacity and other clinical outcomes is not well established in the literature. To evaluate the association between exercise capacity and clinical outcomes in patients with ILD. This cross-sectional observational study included 42 patients aged 40 to 75 years who were diagnosed with ILD and were clinically stable. Patients were divided into two groups based on the median distance covered in the 6-minute walk test (6MWT): Group 1 (G1) included those who covered < 457 meters, while Group 2 (G2) comprised those who covered \geq 457 meters. Participants underwent lung function tests, assessed their activities of daily living (ADL), measured global and peripheral muscle strength, and completed questionnaires evaluating quality of life, disease severity, sleep quality, sleepiness, and symptoms of anxiety and depression. The G1 covered 385 [327-415] meters on the 6MWT, while G2 covered 514 [490-590] meters. Statistical analysis showed significant differences between the groups in terms of daily steps, global muscle strength, upper limb strength, lower limb strength, and quality of life ($p < 0.05$ for all). However, no differences were found between the groups concerning lung function, including FVC, FEV1, DLCO, symptoms of anxiety and depression, sleep quality, or sleepiness. Exercise capacity influences global and peripheral muscle strength, quality of life, and activities of daily living (ADL). However, there were no statistically significant differences in lung function, sleep quality, sleepiness, disease severity, or symptoms of anxiety and depression.

Keywords: Lung Diseases. Interstitial. 6-minute Walk Test. Quality of Life.

Resumo

As doenças pulmonares intersticiais (DPI) estão associadas a várias complicações extrapulmonares, frequentemente levando à redução da capacidade de exercício. No entanto, a relação entre a capacidade de exercício e outros desfechos clínicos não é bem estabelecida na literatura. O objetivo do estudo foi avaliar a associação entre a capacidade de exercício e os desfechos clínicos em pacientes com DPI. Este estudo observacional transversal incluiu 42 pacientes com idades entre 40 e 75 anos, diagnosticados com DPI e clinicamente estáveis. Os pacientes foram divididos em dois grupos com base na distância mediana percorrida no teste de caminhada de seis minutos (6MWT): o Grupo 1 (G1) incluiu aqueles que percorreram < 457 metros, enquanto o Grupo 2 (G2) compreendeu aqueles que percorreram \geq 457 metros. Os participantes passaram por testes de função pulmonar, avaliaram suas atividades de vida diária (AVD), mediram a força muscular global e periférica, e completaram questionários avaliando qualidade de vida, gravidade da doença, qualidade do sono, sonolência e sintomas de ansiedade e depressão. O G1 percorreu 385 [327-415] metros no 6MWT, enquanto o G2 percorreu 514 [490-590] metros. A análise estatística mostrou diferenças significativas entre os grupos em termos de passos diários, força muscular global, força dos membros superiores, força dos membros inferiores e qualidade de vida ($p < 0,05$ para todos). No entanto, não foram encontradas diferenças entre os grupos em relação à função pulmonar, incluindo FVC, FEV1, DLCO, sintomas de ansiedade e depressão, qualidade do sono ou sonolência. A capacidade de exercício influencia a força muscular global e periférica, a qualidade de vida e as atividades de vida diária (AVD). No entanto, não houve diferenças estatisticamente significativas na função pulmonar, na qualidade do sono, na sonolência, na gravidade da doença ou nos sintomas de ansiedade e depressão.

Palavras-chave: Doenças Pulmonares Intersticiais. Teste de Caminhada. Qualidade de Vida.

1 Introduction

Interstitial lung diseases (ILD) comprise a group of over 300 chronic conditions characterized by inflammation in the lung parenchyma, which includes the interstitium, lung filling, and distal airways^{1,2}. This inflammation in the interstitial space gradually leads to the replacement of lung tissue with

scar tissue, impairing gas exchange (hematosis)³. As a result, patients often experience symptoms such as dyspnea, fatigue, and decreased exercise tolerance, which tend to worsen as the disease progresses. Consequently, these patients frequently encounter limitations in their physical activities of daily living (PADL), further exacerbating exercise intolerance and contributing to a decline in physical fitness. Over time,

these adaptations can lead to loss of muscle mass, functional dependence, social isolation, and increased symptoms of anxiety and depression^{1,4}.

Thus, assessing exercise capacity is crucial for patients with respiratory diseases. One of the most cited tests in the literature for this evaluation is the six-minute walk test (6MWT). This test is widely used as a predictor of mortality across various pathologies and is recommended as a complementary tool for assessing and monitoring pulmonary and cardiovascular diseases. The 6MWT has also proven useful in preoperative and postoperative evaluations in both physiotherapy and medicine, aiding decision-making processes for lung transplantation⁵. Therefore, the aim of the present study was to evaluate the impact of exercise capacity on clinical outcomes in patients with ILD.

2 Material and Methods

This cross-sectional observational study included patients aged 40 to 75 years, of both genders, with a diagnosis of chronic obstructive pulmonary disease (COPD) according to internationally accepted criteria established by the American Thoracic Society/European Respiratory Society (ATS/ERS)⁶. The patients included in the study demonstrated clinical stability for the four weeks preceding the evaluation and had no comorbidities that could interfere with the tests. Exclusion criteria included the presence of severe or unstable heart disease identified during the cardiopulmonary exercise test conducted at the start of the study, cognitive impairments that prevented patients from performing the tests, and patients who developed lung cancer or were placed on the waiting list for a lung transplant.

Exercise capacity was assessed using the six-minute walk test (6MWT), in which patients walked as far as possible in a 30-meter corridor for six minutes, with two attempts separated by a 30-minute interval or until vital signs returned to baseline values. Vital functions, including blood pressure (BP), oxygen saturation (SpO₂), heart rate (HR), and subjective measures of dyspnea and fatigue, were monitored before and after the test using the modified BORG scale.

Patients were divided into two groups based on the median distance covered during the 6MWT: Group G1, which indicated poorer exercise capacity, and Group G2, which indicated better exercise capacity. Lung function was assessed through pre- and post-bronchodilator spirometry and evaluation of carbon monoxide diffusion capacity (DLCO)⁸. Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI), while daytime sleepiness was assessed with the Epworth Sleepiness Scale (ESE).

Health-related quality of life was evaluated using the Saint George Respiratory Questionnaire (SGRQ-I), designed specifically for patients with COPD, and symptoms of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS). Grip strength was measured bilaterally using a hand-held hydraulic dynamometer (Jamar

– Medical Ibérica), and the strength of the biceps brachii and quadriceps femoris of the dominant limb was quantified through maximal voluntary isometric contraction using a portable dynamometer². Daily physical activity levels were assessed by tracking the number of steps taken throughout the day using a triaxial accelerometer (Actigraph®, model GT3X).

The severity of the disease was evaluated using the GAP index, which is calculated based on clinical and physiological variables such as sex, age, forced vital capacity (FVC), and DLCO₉.

Statistical analysis was performed using SAS® Studio 9.4 software. The normality of data distribution was assessed using the Shapiro-Wilk test. For comparing outcomes between the two groups, the Mann-Whitney test and chi-square test were employed.

3 Results and Discussion

The 42 patients with interstitial lung disease (ILD), whose characteristics are outlined in Table 1, were divided into two groups: G1 and G2. The cutoff point for this division was established based on the median distance covered in the 6-minute walk test (6MWT), which was found to be 457 [380-513] meters. Patients in Group G1 were characterized by covering a shorter distance in the 6MWT, with a median distance of 380 [324-412] meters, achieving approximately 76 [63-82]% of the predicted value for the walking test based on sex, age, and BMI. In contrast, Group G2 achieved a median distance of 513 [487-579] meters, reaching about 97 [91-105]% of the predicted value for the walking test according to the same demographic factors. These data are detailed in Table 1.

Table 1 - Characteristics of patients, according to the cutoff point established by the median distance covered in meters during the six-minute walk test

Outcomes	Group 1 (6MWT < 457m) N = 22	Group 2 (6MWT > 457m) N = 20	p
Sex, female (%)	73	55	0,12
Age, years	64 [58-70]	65 [46-67]	0,17
Weight, Kg	65 [61-74]	69 [60-79]	0,46
BMI, Kg/m²	28 [23-32]	26 [24-29]	0,11
FVC, % of predicted	74 [49-87]	75 [67-85]	0,32
D_LCO, % of predicted	46 ± 21	55 ± 20	0,11
FEV₁, % of predicted	74 ± 22	78 ± 15	0,30
GAP	1 [1-2]	1 [1-2]	0,54

Legend: Data expressed as mean ± standard deviation and median [25th-75th percentile]; F = female sex; meters (m); Kg = kilogram; BMI = body mass index; m² = square meter; 6min walk test = six-minute walk test; FVC = forced vital capacity; % = percentage of predicted; DLCO = diffusing capacity of the lungs for carbon monoxide; FEV₁ = forced expiratory volume in the first second.

Source: research data.

Additionally, Table 1 shows no significant statistical differences between Groups G0 and G1 concerning pulmonary function measures (FVC, FEV1, and DLCO) and disease severity (GAP). However, there was a statistically significant difference in the number of steps taken daily between the groups.

In Table 2, a significant difference in quality of life, as assessed by the SGRQ-I questionnaire, can be observed, particularly in the activity and impact domains. There were also differences in muscle strength for both upper and lower limbs, as well as overall muscle strength. However, no significant differences were found between the groups with respect to symptoms of anxiety and depression, sleep quality, and daytime sleepiness.

Table 2 – Clinical outcomes of patients with ILD, according to the cutoff point established by the median and the distance covered in meters during the six-minute walk test

Outcomes	Group 1 (6MWT < 457m) N = 22	Group 2 (6MWT > 457m) N = 20	P
HandGrip Force (N)	277 [166-235]	304 [205-333]	0,003*
Quadriceps Strength (N)	245 [215-264]	402 [235-500]	0,003*
Biceps Strength (N)	156 ± 29	205 ± 68	0,012*
Steps Counts (steps/day)	3714 ± 1991	5505 ± 1929	0,003*
SGRQ-I (Symptoms)	68 [44-80]	46 [9-66]	0,08
SGRQ-I (Activity)	78 [78-89]	63 [29-78]	0,013*
SGRQ-I (Impact)	51 ± 16	34 ± 19	0,022*
SGRQ-I (total)	60 ± 16	41 ± 22	0,020*
Pittsburg	17 ± 10	15 ± 8	0,25
Epworth	7 [4 - 10]	5 [3 - 10]	0,23
HADS (A)	4 [1 - 8]	6 [2 - 8]	0,35
HADS (D)	6 [2 - 10]	6 [2 - 9]	0,29

Legend: Data expressed as mean ± standard deviation and median [25th-75th percentile]; FM = muscle strength; SGRQ-I = Saint George Respiratory Questionnaire for DPI subdivided in the table into 3 domains; HADS = Anxiety and Depression Scale; A = Anxiety D = Depression.

Source: research data.

The present study demonstrated the impact of exercise capacity on various clinical outcomes in patients with interstitial lung disease (ILD). It is noteworthy that many Brazilians tend to walk more due to demographic attributes, including climatic and geographic factors, as well as anthropometric characteristics, particularly influenced by the diverse ethnic profile of urban populations. This was highlighted in a study by Dourado¹⁰, which discussed reference values for the 6-minute walk test (6MWT) and compared normal values from the United States with those from Brazil. The study concluded that the American reference equations are not applicable to the Brazilian population.

Similarly, research involving Europeans, such as the study by Bois et al.¹¹, indicated that 822 English patients with idiopathic pulmonary fibrosis (IPF) walked a median distance of 395 (328 – 462) meters. This shows that the median distance in our study is higher compared to those in other countries. The cutoff point used in our study also differs from that proposed by Mancuzo et al.¹², who defined a Brazilian cutoff point based on the survival of patients diagnosed with IPF. Their study established an average distance of 330 meters in the 6MWT, with 7 of our patients falling below this cutoff. This highlights the importance of utilizing the 6MWT as a fundamental tool in evaluation.

There is a natural progression of respiratory dysfunction, functional limitations, disabling symptoms, and side effects from medications used in the treatment of ILD¹³. Consequently, negative effects on the activities of daily living (PADL) of these patients are expected. This is supported by a study conducted by Nishiyama⁹, which correlated PADL with the 6MWT in patients with IPF, finding that normally inactive patients tended to spend more time in sedentary activities. As a result, these individuals walked shorter distances in the 6MWT, ultimately leading to reduced survival rates. This aligns with our findings, which demonstrate that the group with lower exercise capacity also exhibits reduced levels of PADL, confirming the interdependence of these variables.

Al Ameri¹⁴ conducted a study in Saudi Arabia that observed the correlation between exercise capacity and lung function in patients with chronic lung diseases, primarily ILD, using the 6MWT as a starting point. Although their study focused on correlation while ours examined influence, they demonstrated a relationship between 6MWT results and lung function parameters-specifically FVC, FEV1, and DLCO. Applying this insight to our study, it is plausible to infer that both patient groups included individuals with significant lung function impairment, with these results manifesting independently of exercise capacity.

Our study revealed compelling results that align with the findings of Watanabe et al.¹⁵, which aimed to elucidate the significance of peripheral muscle dysfunction and its contribution to exercise intolerance, particularly measured by the 6-minute walk test (6MWT). Stude established a strong relationship between quadriceps femoris muscle strength and the distance walked during the 6MWT. In contrast, our findings indicate that patients with better exercise capacity not only demonstrated enhanced lower limb muscle strength but also exhibited improved overall muscle function and upper limb strength.

It is widely reported in the media that engaging in regular physical activity leads to improved quality of life, enhanced sleep quality, reduced symptoms of anxiety and depression, and decreased daytime sleepiness for the general population. However, it is crucial to note that a patient's ability to perform exercise does not necessarily equate to actual exercise participation, as several factors can influence this. The study

by Amorim et al.¹⁶ identifies the barriers that patients with chronic obstructive pulmonary disease (COPD) face in adopting exercise. The lack of access to structured exercise programs was identified as the primary barrier, followed by factors such as lack of motivation and social influences related to encouragement among patients.

3 Conclusion

Exercise capacity significantly affects both global and peripheral muscle strength in the upper and lower limb muscles. Additionally, patients who walked a greater distance in the 6-minute walk test (6MWT) exhibited a higher number of daily steps compared to those who walked shorter distances. These patients also reported better quality of life. Furthermore, it is noteworthy that individuals with better exercise capacity tended to have a taller stature than those who walked shorter distances.

References

1. Cabral M, Mueller P. Sono e doenças pulmonares crônicas: pneumopatias intersticiais difusas, asma brônquica e DPOC. *J Bras Pneumol* 2010;39:1-7.
2. Kendall FP, McCrary EK, Provance PG. *Músculos: provas e funções*. São Paulo: Manole; 1995.
3. Du Bois RM, Richeldi L. Interstitial lung diseases. *Eur Respir Monogr* 2009.
4. Travis WD, Costabel U, Hansell DM, King JR TE, Lynch DA, Nicholson AG, et al. An Official American Thoracic Society/European Respiratory Society Statement: update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2013;188(6):733-48. doi: 10.1164/rccm.201308-1483ST
5. Blanco I, Cuerda C, Miravittles M. Consumo máximo de oxígeno durante la prueba de marcha de 6 minutos en la enfermedad pulmonar intersticial difusa y en la hipertensión pulmonar. *Arch Bronconeumol* 2010;46(3):122-8.
6. Souza T, Jardim J, Jones P. Validação do questionário do hospital Saint George na doença respiratória (SGRQ) em pacientes com doença pulmonar obstrutiva crônica no Brasil. *J Pneumol* 2000;26:1-6.
7. Baddini-Martinez JÁ. Teste da caminhada de seis minutos em pacientes com fibrose pulmonar idiopática. *J Bras Pneumol* 2018;44(4):257-8. doi: <https://doi.org/10.1590/S1806-37562018000040001>
8. Faro A. Análise fatorial confirmatória e normatização da Hospital Anxiety and Depression Scale (HADS). *Psic Teor Pesq* 2015;31(1):23-30. doi: <https://doi.org/10.1590/0102-37722015032072349353>
9. Ley B, Ryerson CJ, Vittinghoff E, Ryu JH, Tomassetti S, Lee JS, et al. A multidimensional index and staging system for idiopathic pulmonary fibrosis. *Ann Intern Med* 2012;156:684-91.
10. Dourado VZ, Godoy I. Alterações musculares na doença pulmonar obstrutiva crônica. *Fisioter Pesq* 2006;13(3):59-67. doi: <https://doi.org/10.1590/fpusp.v13i3.76324>
11. Du Bois RM, Weycker D, Albera C, et al. Six-minute walk test in idiopathic pulmonary fibrosis: test validation and minimal clinically important difference. *Am J Respir Crit Care Med* 2011;183(9):1231-37.
12. Mancuzo EV, Soares MR, Pereira CAC. Six-minute walk distance and survival time in patients with idiopathic pulmonary fibrosis in Brazil. *J Bras Pneumol* 2018;44(4):352-7. doi: 10.1590/S1806-37562018000000049
13. Coelho AC. Fatores preditores da qualidade de vida relacionada à saúde física e mental em pacientes com doença pulmonar intersticial: uma análise multifatorial. *J Bras Pneumol* 2010;36(5):607-14.
14. Al Ameri HF. Six minute walk test in respiratory diseases: a university hospital experience. *Ann Thorac Med* 2006;1(1):16-9.
15. Zanchet RC, Viegas CAA, Lima T. A eficácia da reabilitação pulmonar na capacidade de exercício, força da musculatura inspiratória e qualidade de vida de portadores de doença pulmonar obstrutiva crônica. *J Bras Pneumol* 2005;31(2):118-24.
16. Amorim PB, Stelmach R, Carvalho CRF, et al. Barreiras associadas à menor atividade física em portadores de DPOC. *J Bras Pneumol* 2014;40(5):504-12.