

## Six-minute walk distance is not related to quality of life in patients with non-cystic fibrosis bronchiectasis\*

Distância percorrida no teste de caminhada de seis minutos não se relaciona com qualidade de vida em pacientes com bronquiectasias não fibrocísticas

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### Abstract

**Objective:** To evaluate physical performance on the six-minute walk test (6MWT) in patients with non-cystic fibrosis bronchiectasis and to investigate its relationship with quality of life (QoL). To identify predictors of exercise performance, we also investigated whether six-minute walk distance (6MWD) is associated with clinical and spirometric findings. **Methods:** This was a cross-sectional study involving patients with non-cystic fibrosis bronchiectasis (age,  $\geq 18$  years), with at least one respiratory symptom for  $\geq 2$  years and an  $FEV_1 \leq 70\%$  of predicted. Patients underwent clinical evaluation, pulmonary function tests, the 6MWT, and QoL assessment with the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36). **Results:** We included 70 patients (48 females). Mean age was  $54.5 \pm 17.7$  years, and mean  $FEV_1$  was  $44.9 \pm 14.5\%$  of predicted. The patients were divided into two groups: 6MWD-low (6MWD below the predicted lower limit;  $n = 23$ ); and 6MWD-norm (normal 6MWD;  $n = 47$ ). The following variables were significantly lower in the 6MWD-low group than in the 6MWD-norm group: age; age at diagnosis of bronchiectasis; proportion of former smokers; body mass index (BMI);  $FEV_1$  % of predicted; and MEP% of predicted. There were no significant differences in the SF-36 scores between the groups. In the logistic regression model, lower age and lower BMI were significantly associated with lower 6MWD. **Conclusions:** In this sample, there was a high proportion of patients who had a lower than expected 6MWD. Although 6MWD was not related to QoL, it was associated with age and BMI.

**Keywords:** Bronchiectasis; Quality of life; Respiratory function tests; Exercise tolerance.

### Resumo

**Objetivo:** Avaliar o desempenho físico de pacientes com bronquiectasias não fibrocísticas no teste de caminhada de seis minutos (TC6) e investigar sua associação com a qualidade de vida (QV). Secundariamente, analisar a associação entre a distância percorrida no TC6 (DTC6) com achados clínicos e espirométricos para se identificar preditores para esse desempenho. **Métodos:** Estudo transversal envolvendo pacientes com bronquiectasias não fibrocísticas, com idade  $\geq 18$  anos, pelo menos um sintoma respiratório por  $\geq 2$  anos e  $VEF_1 \leq 70\%$  do previsto. Os pacientes foram submetidos a avaliação clínica, teste de função pulmonar, TC6 e avaliação da QV por *Medical Outcomes Study 36-item Short-Form Health Survey* (SF-36). **Resultados:** Foram incluídos 70 pacientes (48 mulheres; média de idade =  $54,5 \pm 17,7$  anos; média de  $VEF_1 = 44,9 \pm 14,5\%$  do previsto. Os pacientes foram divididos em dois grupos: DTC6-menor, com desempenho menor que o limite inferior previsto ( $n = 23$ ); e DTC6-norm, com desempenho normal ( $n = 47$ ). Em comparação ao grupo DTC6-norm, o grupo DTC6-menor apresentou menor idade, menor idade ao diagnóstico das bronquiectasias, menor proporção de ex-fumantes, menor índice de massa corpórea (IMC), menor  $VEF_1$  em % do previsto e menor  $PE_{máx}$  em % do previsto. Não houve diferenças significativas nos escores do SF-36 entre os grupos. No modelo de regressão logística, menor idade e menor IMC se associaram significativamente com menor DTC6. **Conclusões:** Nesta amostra, uma elevada proporção de pacientes apresentou uma DTC6 menor que o esperado. A DTC6 não se relacionou com a QV. Idade e IMC se associaram a DTC6.

**Descritores:** Bronquiectasia; Qualidade de vida; Testes de função respiratória; Tolerância ao exercício.

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Financial support: This study received financial support from the *Fundo de Incentivo à Pesquisa do Hospital de Clínicas de Porto Alegre* (FIPE-HCPA, Research Incentive Fund of the Porto Alegre *Hospital de Clínicas*). Patrícia Santos Jacques is the recipient of a grant from the *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (CAPES, Office for the Advancement of Higher Education).

Submitted: 30 January 2012. Accepted, after review: 8 March 2012.

## Introduction

Bronchiectasis is a term for an abnormal, irreversible dilatation of a given segment of the bronchial tree, caused by the destruction of the elastic and muscular components of the bronchial walls.<sup>(1,2)</sup>

Bronchiectasis represents the end stage of a variety of respiratory and systemic diseases.<sup>(3,4)</sup> In a study of patients with bronchiectasis,<sup>(5)</sup> extensive investigation led to the identification of the causative factor in 47% of cases. In Brazil, the leading causes of bronchiectasis are respiratory, viral, or bacterial infections in childhood, as well as tuberculosis.<sup>(6,7)</sup>

Patients with bronchiectasis commonly experience progressive exercise limitation and a reduction in their activities of daily living. The leading causes of exercise intolerance are associated with reduced lung capacity, reduced ventilatory reserve, loss of peripheral muscle mass, and changes in cardiovascular function.<sup>(8)</sup>

The six-minute walk test (6MWT) has been widely used in clinical practice in order to evaluate exercise limitation in chronic pulmonary disease. The 6MWT is a submaximal exercise test that evaluates exercise tolerance and exercise-related cardiorespiratory changes. The 6MWT is safe, simple, and easy to perform because patients can determine the intensity of the exertion. The 6MWT reflects the ability of individuals to perform activities of daily living.<sup>(9)</sup>

Another clinical aspect to be considered in individuals with bronchiectasis is the degree of quality of life impairment related to the morbidity of the disease.<sup>(10-12)</sup>

Data on exercise performance in patients with non-cystic fibrosis bronchiectasis and its relationship with quality of life and pulmonary function are scarce in the literature.<sup>(13,14)</sup> An investigation of the subject could contribute to improving the understanding of the pathophysiological mechanisms of the disease and to determining the need for therapeutic intervention through a pulmonary rehabilitation program.

The primary objective of the present study was to evaluate physical performance on the 6MWT in patients with non-cystic fibrosis bronchiectasis and to investigate its relationship with health-related quality of life. In addition, to identify predictors of exercise performance, we investigated

whether six-minute walk distance (6MWD) is associated with clinical and spirometric findings.

## Methods

This was a cross-sectional study of prospectively collected data. We sequentially studied all patients routinely treated at the outpatient clinics of the Department of Pulmonology of the *Hospital de Clínicas de Porto Alegre* (HCPA, Porto Alegre *Hospital de Clínicas*), located in the city of Porto Alegre, Brazil.

The study protocol was approved by the HCPA Research Ethics Committee (Process no. 08096). All patients gave written informed consent.

The study population consisted of patients treated at the outpatient clinics of the HCPA Department of Pulmonology. We included individuals aged  $\geq 18$  years and diagnosed with non-cystic fibrosis bronchiectasis on the basis of clinical criteria and radiological or CT criteria.<sup>(15)</sup> The diagnosis was confirmed by a physician who was a member of the research team. The inclusion criteria were as follows: having had at least one chronic or recurrent respiratory symptom (cough, expectoration, dyspnea, hemoptysis, or recurrent respiratory infection) for two years or more; having an  $FEV_1 \leq 70\%$  of predicted; and being clinically stable, clinical stability being defined as no hospitalization for at least 30 days and absence of clinical changes requiring changes in the maintenance treatment of the disease.

Patients with a confirmed or presumptive diagnosis of cystic fibrosis were excluded, as were those who, for any clinical reason, could not perform the procedures proposed by the study, those who were pregnant, and those who declined to participate in the study or who did not give written informed consent.

All volunteers were interviewed by the same research team member, who used a data collection form that addressed the following variables: age; gender; marital status; ethnicity; level of education; family income; smoking history; body mass index (BMI); causes of bronchiectasis; age at diagnosis of bronchiectasis; and degree of dyspnea, as measured by the Modified Medical Research Council scale.<sup>(16)</sup>

We reviewed the last three bacteriological tests on sputum, collected every 3–6 months in routine clinical practice, in the last 12 months. The material was collected by spontaneous expectoration. Processing of the sputum samples

included culture on blood agar, MacConkey agar, azide blood agar, and chocolate agar plates, followed by incubation of the plates at 35°C and examination of the plates after 24 h of incubation; if there was no growth, the plates were incubated for another 24 h; if there was growth, bacterial identification and susceptibility testing were performed.

Spirometry was performed with a MasterScreen spirometer (v4.31; Jaeger, Würzburg, Germany), in accordance with the technical acceptability criteria recommended in the Brazilian Thoracic Association guidelines for pulmonary function testing.<sup>(17)</sup> All tests were performed in the HCPA Department of Pulmonology. The following parameters were measured: FVC; FEV<sub>1</sub>; and the FEV<sub>1</sub>/FVC ratio. The participants had to perform three acceptable maneuvers, and the maneuver yielding the highest values was selected. All parameters are expressed as the percentage of the predicted value for age, gender, and height.<sup>(18)</sup>

Respiratory muscle strength was measured with a digital manometer (model MVD -500/+500, version 1.0; Microhard, Porto Alegre, Brazil). The MIP was measured at RV, whereas the MEP was measured at TLC. The technique was carried out in accordance with the aforementioned guidelines.<sup>(17)</sup> The maneuvers were performed five times, and at least three acceptable measurements were obtained.<sup>(19)</sup> The results are expressed as percentage of predicted.<sup>(20)</sup>

The 6MWT was performed in a 40-m corridor, following a standardized protocol, in accordance with the guidelines published by the American Thoracic Society.<sup>(9)</sup> The following parameters were recorded before and after the test: HR; RR; SpO<sub>2</sub>; systemic blood pressure; and dyspnea and leg fatigue scores (Borg scale).<sup>(21)</sup> At the end of the test, the 6MWD was recorded. The 6MWT was repeated after a 1-h rest period. The 6MWT yielding the highest 6MWD was considered for the study. The values (in percentage of predicted) and the predicted lower limit for 6MWD for each individual were calculated by an equation developed by Enright & Sherril.<sup>(22)</sup>

Quality of life was assessed with the Brazilian Portuguese-language version of the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36), previously validated for use in Brazil.<sup>(23)</sup> The instrument consists of 36 items grouped into eight domains: physical functioning; role-physical; bodily pain; general health; vitality;

social functioning; role-emotional; and mental health. The maximum score that can be obtained on the SF-36 is 100 points, indicating better quality of life.

All data collected were processed and analyzed with the Statistical Package for the Social Sciences, version 18.0 (SPSS Inc., Chicago, IL, USA).

In the descriptive analysis, quantitative data are expressed as mean  $\pm$  SD or as median (interquartile range). Qualitative data are expressed as n (%).

The t-test for paired samples was used for comparing the 6MWD values between the first and second tests.

For statistical analysis, the patients were divided into two groups: 6MWD-low (6MWD below the predicted lower limit); and 6MWD-norm (6MWD equal to or greater than the predicted lower limit).<sup>(22)</sup>

In order to compare the two groups, we used the Student's t-test for continuous variables with normal distribution, the Mann-Whitney U test for ordinal variables or continuous variables without normal distribution, and the chi-square test for categorical variables, Yates' correction or Fisher's exact test having been used when necessary.

Binary logistic regression analysis was performed with the enter method in order to identify predictors of lower 6MWD. Variables were selected on the basis of univariate analysis, those with a p value < 0.1 and no collinearity (adjusted for gender and age) having been entered into the model.

The level of significance was set at 0.05, and all tests were two-tailed.

The sample size calculation was based on the variable "quality of life" (SF-36). In order to find a 5-point difference between the groups for any of the SF-36 domains, with a standard deviation of 5 points, a power of 90%, and a level of significance of 0.05, 23 patients were required in each group. We estimated that, with a total of 70 patients with bronchiectasis, the target number for each group would be reached.

## Results

Between May of 2008 and August of 2010, 79 patients with bronchiectasis were evaluated. Nine patients were excluded from the study for the following reasons: 5 had an FEV<sub>1</sub> > 70% of predicted; 2 were unable to perform the 6MWT because they had orthopedic disorders; and 2 were

unable to attend their scheduled visits to perform the activities proposed in the study. Therefore, 70 patients were included in the study, and all of them completed the evaluations recommended in the study protocol.

Table 1 shows the general characteristics of the patients, of whom 48 (68.6%) were female. Most (88.6%) were White. The mean age was 54.5 years (range, 18–77 years).

On average, the distance covered in the first test was  $429.9 \pm 80.0$  m, and the distance covered in the second test was  $402.1 \pm 12.9$  m ( $p = 0.001$ ).

Table 2 compares the characteristics of the individuals with a 6MWD below the predicted lower limit (6MWD-low group) and those of those with a normal 6MWD (6MWD-norm group). The 6MWD-low group comprised 23 patients, and the 6MWD-norm group comprised 47 patients. There were no significant differences between the groups in terms of gender ( $p = 0.34$ ) or ethnicity ( $p = 1.00$ ). The mean age of the patients was significantly lower in the 6MWD-low group than in the 6MWD-norm group ( $40.9 \pm 18.5$  years vs.  $61.2 \pm 12.8$  years;  $p < 0.001$ ), as was the median age at diagnosis of bronchiectasis (18 years vs. 40 years;  $p = 0.006$ ). There was a significant difference in smoking history between the groups, the proportion of former smokers being lower in the 6MWD-low group than in the 6MWD-norm group (17.4% vs. 40.4%). There were no significant differences between the groups in terms of family income ( $p = 1.00$ ), level of education ( $p = 0.119$ ), causes of bronchiectasis ( $p = 0.65$ ), or results of sputum bacteriology ( $p > 0.05$ ). The mean BMI was significantly lower in the patients in the 6MWD-low group than in those in the 6MWD-norm group ( $22.8 \pm 5.8$  kg/m<sup>2</sup> vs.  $26.9 \pm 5.0$  kg/m<sup>2</sup>;  $p = 0.003$ ). The mean FEV<sub>1</sub>% of predicted was significantly lower in the 6MWD-low group than in the 6MWD-norm group ( $39.8 \pm 14.3\%$  vs.  $47.3 \pm 14.0\%$ ;  $p = 0.041$ ). There were no significant differences between the groups in terms of FVC% of predicted, FEV<sub>1</sub>/FVC% of predicted, or 6MWD (in m). However, there was a significant difference between the groups in terms of the 6MWD in percentage of predicted ( $66.4 \pm 10.9\%$  vs.  $91.1 \pm 14.1\%$ ;  $p < 0.001$ ). The groups did not differ regarding resting SpO<sub>2</sub> or post-6MWT SpO<sub>2</sub> ( $p = 0.137$  and  $p = 0.566$ , respectively). Post-6MWT HR, resting systolic blood pressure, and post-6MWT systolic blood pressure were significantly higher in the

6MWD-low group than in the 6MWD-norm group ( $p = 0.026$ ;  $p = 0.004$ ; and  $p < 0.001$ , respectively).

Although MIP% of predicted did not differ significantly between the groups ( $p = 0.336$ ), MEP% of predicted was significantly lower in the 6MWD-low group than in the 6MWD-norm group ( $63.3 \pm 24.2\%$  vs.  $75.9 \pm 19.0\%$ ;  $p = 0.021$ ). There were no significant differences between the groups in terms of the SF-36 domains: physical functioning ( $p = 0.905$ ); role-physical ( $p = 0.716$ ); bodily pain ( $p = 0.429$ ); general health ( $p = 0.980$ ); vitality ( $p = 0.575$ ); social functioning ( $p = 0.193$ ); role-emotional ( $p = 0.275$ ); and mental health ( $p = 0.220$ ). There was also no difference between the groups in terms of the dyspnea scale scores ( $p = 0.579$ ).

Binary logistic regression analysis (Table 3) identified two variables that were independently associated with lower 6MWD: age ( $\beta = -0.09$ ; OR = 0.92;  $p = 0.002$ ) and BMI ( $\beta = -0.15$ ; OR = 0.86;  $p = 0.034$ ).

## Discussion

This cross-sectional study evaluated patients with non-cystic fibrosis bronchiectasis treated at a tertiary care center. Our study demonstrated that a significant proportion of patients (33%) had impaired exercise performance, as evaluated by the 6MWT. Two independent factors were identified to be associated with lower 6MWD, namely age and BMI. Although the sample as a whole had reduced quality of life on all of the SF-36 domains, especially on the vitality and general health domains, no significant associations were found between the different domains and exercise capacity.

Other studies have also demonstrated that a significant proportion of patients with non-cystic fibrosis bronchiectasis have reduced exercise capacity.<sup>(13,14)</sup> One group of authors<sup>(13)</sup> evaluated 15 adult patients with bronchiectasis by using maximum incremental exercise testing on a cycle ergometer. Exercise performance was reduced in 7 of the 15 patients. The authors concluded that bronchiectasis patients with abnormal lung mechanics and higher chronic dyspnea scores had reduced exercise capacity. In another study,<sup>(14)</sup> 6 patients with bronchiectasis were evaluated for exercise tolerance by means of the 6MWT, and 4 of the participants had a lower than expected 6MWD. The authors concluded that bronchiectasis

**Table 1** – General characteristics of the individuals with non-cystic fibrosis bronchiectasis.<sup>a</sup>

Variables	Patients (n = 70)
Gender	
Male	22 (31.4)
Female	48 (68.6)
Ethnicity	
White	62 (88.6)
Non-White	8 (11.4)
Age, years <sup>b</sup>	54.5 ± 17.7
Age at diagnosis of bronchiectasis, years <sup>c</sup>	32 (34)
Smoking history	
Never-smoker	43 (61.4)
Active smoker	4 (5.7)
Former smoker	23 (32.9)
Family income, number of times the national minimum wage	
< 3	53 (74.6)
≥ 3	17 (23.9)
Level of education	
9 years of schooling	24 (33.8)
High school	44 (62.0)
College	2 (2.8)
Causes of bronchiectasis	
Idiopathic	32 (45.7)
Tuberculosis	23 (32.9)
Post-infection causes other than tuberculosis	10 (14.2)
Collagen diseases	3 (4.3)
Ciliary dyskinesia	2 (2.9)
Sputum bacteriology	
<i>Pseudomonas aeruginosa</i>	20 (28.6)
<i>Haemophilus influenza</i>	20 (28.6)
<i>Streptococcus pneumoniae</i>	10 (14.3)
<i>Staphylococcus aureus</i>	7 (10.0)
<i>Moraxella catarrhalis</i>	3 (4.3)
<i>Enterobacter</i> sp.	1 (1.4)
No bacterial identification	25 (35.7)
FEV <sub>1</sub> , % of predicted <sup>b</sup>	44.9 ± 14.5
FVC, % of predicted <sup>b</sup>	59.5 ± 15.3
FEV <sub>1</sub> /FVC, % of predicted <sup>b</sup>	75.9 ± 19.0
6MWD, m <sup>b</sup>	440.4 ± 81.8
6MWD, % of predicted <sup>b</sup>	83.0 ± 18.0
SF-36 domains, % <sup>c</sup>	
Physical functioning	52.5 (40)
Role-physical	50.0 (25)
Bodily pain	62.0 (31)
General health	40.0 (25)
Vitality	35.0 (25)
Social functioning	75.0 (37)
Role-emotional	66.0 (33)
Mental health	56.0 (21)
Degree of dyspnea	
No dispnea	3 (4.2)
Mild	26 (36.6)
Moderate	27 (38.0)
Moderately severe	12 (16.9)
Severe	2 (2.8)
Very severe	0 (0.0)

6MWD: six-minute walk distance; and SF-36: Medical Outcomes Study 36-item Short-form Health Survey. <sup>a</sup>Values expressed as n (%), except where otherwise indicated. <sup>b</sup>Values expressed as mean ± SD. <sup>c</sup>Values expressed as median (interquartile range).

**Table 2** – Comparison between the patients with a six-minute walk distance (6MWD) below the predicted lower limit (6MWD-low group) and those with a normal 6MWD (6MWD-norm group) in terms of their characteristics.<sup>a</sup>

Variables	6MWD	6MWD	p
	low group (n = 23)	norm group (n = 47)	
Gender			
Male	5 (21.7)	17 (36.2)	0.343
Female	18 (78.3)	30 (63.8)	
Ethnicity			
White	20 (87.0)	42 (89.4)	1.000
Non-White	3 (13.0)	5 (10.6)	
Age, years <sup>b</sup>	40.9 ± 18.5	61.2 ± 12.8	<0.001
Age at diagnosis of bronchiectasis, years <sup>c</sup>	18 (33)	40 (30)	0.006
Smoking history			
Never-smoker	16 (69.6)	27 (57.4)	0.048
Active smoker	3 (13.0)	1 (2.1)	
Former smoker	4 (17.4)*	19 (40.4)*	
Family income, number of times the national minimum wage			
< 3	17 (73.9)	36 (76.6)	1.000
≥ 3	6 (26.1)	11 (23.4)	
Level of education			
9 years of schooling	7 (30.4)	17 (36.2)	0.119
High school	14 (60.9)	30 (63.8)	
College	2 (8.7)	0 (0.0)	
Causes of bronchiectasis			
Idiopathic	13 (56.5)	19 (40.4)	0.65
Tuberculosis	5 (21.7)	18 (38.3)	
Post-infection causes other than tuberculosis	3 (13.0)	7 (14.9)	
Collagen diseases	1 (4.3)	2 (4.3)	
Ciliary dyskinesia	1 (4.3)	1 (2.1)	
No bacterial identification	10 (43.5)	15 (31.9)	
Sputum bacteriology			
<i>Pseudomonas aeruginosa</i>	6 (26.1)	14 (29.8)	0.968
<i>Haemophilus influenzae</i>	7 (30.4)	13 (27.7)	
<i>Streptococcus pneumoniae</i>	4 (17.4)	6 (12.8)	
<i>Staphylococcus aureus</i>	2 (8.7)	5 (10.6)	
<i>Moraxella catarrhalis</i>	0 (0.0)	3 (6.4)	
No bacterial identification	10 (43.5)	15 (31.9)	
No bacterial identification	10 (43.5)	15 (31.9)	
BMI, <sup>b</sup> kg/m <sup>2</sup>	22.8 ± 5.8	26.9 ± 5.0	0.003
FEV <sub>1</sub> , % of predicted <sup>b</sup>	39.8 ± 14.3	47.3 ± 14.0	0.041
FVC, % of predicted <sup>b</sup>	55.3 ± 15.7	61.5 ± 14.8	0.116
FEV <sub>1</sub> /FVC, % of predicted <sup>b</sup>	73.0 ± 21.1	77.2 ± 17.8	0.388
6MWD, m <sup>b</sup>	417.7 ± 86.7	451.5 ± 77.8	0.104
6MWD, % of predicted <sup>b</sup>	66.4 ± 10.9	91.1 ± 14.1	<0.001
Resting SpO <sub>2</sub> , % <sup>b</sup>	96.3 ± 2.2	95.4 ± 2.2	0.137
Post-6MWT SpO <sub>2</sub> , % <sup>b</sup>	93.7 ± 4.9	93.0 ± 4.7	0.566
Resting HR, bpm <sup>b</sup>	90.7 ± 12.6	87.6 ± 14.1	0.381

BMI: body mass index; 6MWD: six-minute walk distance; 6MWT: six-minute walk test; and SF-36: Medical Outcomes Study 36-item Short-form Health Survey. aValues expressed as n (%), except where otherwise indicated. bValues expressed as mean ± SD. cValues expressed as median (interquartile range). The independent sample t-test was used for variables with normal distribution; the Mann-Whitney U test was used for ordinal variables or variables without normal distribution; and the chi-square test was used for categorical variables. \*Statistically significant adjusted standardized residuals (< -1.96 or > 1.96).

**Tabela 2** – Continued...

Variables	6MWD		p
	low group (n = 23)	norm group (n = 47)	
Post-6MWT HR, bpm <sup>b</sup>	108.6 ± 14.3	119.1 ± 19.7	0.026
Resting RR, breaths/min <sup>b</sup>	19.0 ± 3.4	19.9 ± 4.6	0.373
Post-6MWT RR, breaths/min <sup>b</sup>	24.1 ± 4.7	26.9 ± 5.9	0.054
Borg scale score <sup>c</sup>			
Resting dyspnea	0 (0)	0 (0)	0.256
Post-6MWT dyspnea	1 (3)	2 (4)	0.166
Leg fatigue at rest	0 (0)	0 (0)	0.943
Post-6MWT leg fatigue	0 (3)	1 (3)	0.915
Resting systolic blood pressure, mmHg <sup>b</sup>	114.4 ± 8.8	128.3 ± 18.2	0.004
Post-6MWT systolic blood pressure, mmHg <sup>b</sup>	119.2 ± 20.2	141.3 ± 24.6	<0.001
Resting diastolic blood pressure, mmHg <sup>b</sup>	74.4 ± 12.0	77.2 ± 11.9	0.346
Post-6MWT diastolic blood pressure, mmHg <sup>b</sup>	74.8 ± 12.0	79.0 ± 14.2	0.222
MIP, % of predicted <sup>b</sup>	61.5 ± 30.0	67.2 ± 18.5	0.336
MEP, % of predicted <sup>b</sup>	63.3 ± 24.2	75.9 ± 19.0	0.021
SF-36 domains, % <sup>c</sup>			
Physical functioning	50.0 (30)	55.0 (45)	0.905
Role-physical	25.0 (50)	50.0 (25)	0.716
Bodily pain	62.0 (44)	52.0 (31)	0.429
General health	37.0 (27)	40.0 (22)	0.980
Vitality	35.0 (30)	35.0 (20)	0.575
Social functioning	75.0 (25)	75.0 (37)	0.193
Role-emotional	66.0 (33)	66.0 (33)	0.275
Mental health	60.0 (16)	56.0 (20)	0.220
Degree of dyspnea			
No dyspnea	1 (4.3)	2 (4.3)	0.579
Mild	11 (47.8)	15 (31.9)	
Moderate	8 (34.8)	19 (40.4)	
Moderately severe	2 (8.7)	10 (21.3)	
Severe	1 (4.3)	1 (2.1)	
Very severe	0 (0)	0 (0)	

BMI: body mass index; 6MWD: six-minute walk distance; 6MWT: six-minute walk test; and SF-36: Medical Outcomes Study 36-item Short-form Health Survey. <sup>a</sup>Values expressed as n (%), except where otherwise indicated. <sup>b</sup>Values expressed as mean ± SD. <sup>c</sup>Values expressed as median (interquartile range). The independent sample t-test was used for variables with normal distribution; the Mann-Whitney U test was used for ordinal variables or variables without normal distribution; and the chi-square test was used for categorical variables. \*Statistically significant adjusted standardized residuals (< -1.96 or > 1.96).

can lead to reduced exercise tolerance, as evaluated by the 6MWT.

In the present study, age was negatively associated with 6MWD, i.e., younger patients had a lower 6MWD. This can be attributed to the fact that pulmonary disease was more severe and had been diagnosed earlier in the younger patients included in the study than in the older patients. Because this was a cross-sectional study, there might have been a survival bias, meaning that the patients who were older would be those

with milder disease diagnosed later. In contrast to the findings of the present study, Lee et al.<sup>(10)</sup> evaluating 27 patients with bronchiectasis and mild pulmonary disease, found no significant correlation between 6MWD and age.

The BMI is a global nutritional index that can identify patients who are malnourished and have reduced muscle mass. We found a negative association between BMI and 6MWD, meaning that patients with a lower BMI had a lower 6MWD. In contrast to this finding, Lee et al.<sup>(10)</sup> and

**Table 3** – Binary logistic regression for lower than expected six-minute walk distance.

Variable	B	Wald	Significance	OR	95% CI
Age	-0.09	9.3	0.002	0.92	0.86-0.97
Male gender	-1.23	2.1	0.146	0.29	0.56-1.53
Age at diagnosis	0.02	0.4	0.522	1.01	0.97-1.08
BMI	-0.15	4.5	0.034	0.86	0.75-0.99
FEV <sub>1</sub> , % of predicted	-0.02	0.72	0.398	0.98	0.93-1.03
MEP, % of predicted	0.004	0.05	0.819	1.00	0.97-1.04
Smoking <sup>a</sup>	-0.17	0.06	0.813	0.84	0.21-3.50
Constant	8.45	11.2	0.001	4.672.63	

BMI: body mass index. <sup>a</sup>Smoking includes former smokers and active smokers.

Kosmas et al.<sup>(13)</sup> found no significant association between BMI and exercise performance in patients with bronchiectasis. However, a study of patients with chronic obstructive pulmonary disease<sup>(24)</sup> demonstrated a significant correlation of BMI and fat-free mass with 12-min walk distance, suggesting that exercise impairment occurs only when fat-free mass decreases to low values. In addition, a selective loss of leg muscle mass and strength, regardless of respiratory muscle function impairment, might explain the impaired exercise performance in those patients.<sup>(25)</sup>

In the univariate analysis, MEP% of predicted was significantly lower in the 6MWD-low group than in the 6MWD-norm group. This could be attributed to more severe pulmonary disease, worse nutritional status, and lower respiratory muscle strength. However, in the logistic regression analysis, the difference did not reach statistical significance.

In our study, the cut-off point to differentiate between lower than expected 6MWD and normal 6MWD was based on the lower limit of normality reported in a study by Enright & Sherrill,<sup>(22)</sup> who demonstrated that anthropometric factors, such as age, weight, and height, were independently associated with 6MWD. Those authors developed reference equations for 6MWD in normal individuals, as well as for the lower limit of normality.

Few studies have evaluated the impact of bronchiectasis on patient self-reported quality of life.<sup>(10-12)</sup> Martínez-García *et al.*<sup>(11)</sup> studied 86 patients with non-cystic fibrosis bronchiectasis, having assessed quality of life with the Saint George's Respiratory Questionnaire (SGRQ), in which zero is the best possible score and 100 is the worst possible score. The mean scores were as follows: symptoms domain, 45.4; activity domain, 53.5; psychosocial impact domain, 39.7;

and total score, 45.5. The authors concluded that the factors that were associated with the total quality of life score were degree of dyspnea, post-bronchodilator FEV<sub>1</sub>, and daily sputum production. However, that study did not assess exercise performance. O'Leary et al.<sup>(12)</sup> studied 111 patients with bronchiectasis in order to evaluate mood disorders, having assessed quality of life (using the SGRQ), pulmonary function, and exercise capacity (using the shuttle walk test). The mean scores for the symptoms, activity, and impact domains were 71, 49, and 34, respectively, whereas the mean total score was 44. The anxiety and depression scores correlated significantly with the quality of life scores. The depression scores were inversely correlated with shuttle walk test distance. Correlations between quality of life and walk test were not analyzed in that study. In another study,<sup>(10)</sup> quality of life was also assessed with the SGRQ and the SF-36. The mean total SGRQ score was 41.5. The mean scores for the SF-36 role-physical and mental health domains were 38.5 and 48.3, respectively. The 6MWD correlated positively with the SF-36 role-physical domain and negatively with the SGRQ domains. In our study, we observed moderately reduced scores for nearly all of the SF-36 domains. Although the patients in our study were functionally more impaired than were those in the study by Lee et al.<sup>(10)</sup> (mean FEV<sub>1</sub> = 44.9% of predicted vs. mean FEV<sub>1</sub> = 73.9% of predicted), the mean scores for the SF-36 role-physical and mental health domains were higher (50.0 and 56.0, respectively). However, in the present study, there were no significant associations between 6MWD and the SF-36 domains.

The present study has some limitations. First, the major limitation of our study is its cross-sectional design, which does not allow us to examine temporal relationships between



6MWD and the remaining variables, especially the SF-36 domains. Second, it should be borne in mind that the present study was conducted in a tertiary public hospital and that it included only patients with respiratory symptoms and an  $FEV_1 < 70\%$  of predicted, which translated to a sample of patients of lower socioeconomic status and with greater disease severity. This limits the generalization of results. Third, the predicted 6MWD values on which the cut-off point to form the groups were based were unrelated to those for the Brazilian population.

We conclude that, in this sample of patients with non-cystic fibrosis bronchiectasis, a significant proportion had a low 6MWD. Exercise performance was not associated with quality of life. Age and BMI were independently associated with lower 6MWD.

## References

- Barker AF. Bronchiectasis. *N Engl J Med*. 2002;346(18):1383-93. PMID:11986413. <http://dx.doi.org/10.1056/NEJMra012519>
- Kim DN, Lazarus AA. Management of bronchiectasis. *Dis Mon*. 2008;54(8):540-6. PMID:18638622. <http://dx.doi.org/10.1016/j.disamonth.2008.05.003>
- Cohen M, Sahn SA. Bronchiectasis in systemic diseases. *Chest*. 1999;116(4):1063-74. PMID:10531174. <http://dx.doi.org/10.1378/chest.116.4.1063>
- O'Donnell AE. Bronchiectasis. *Chest*. 2008;134(4):815-23. PMID:18842914. <http://dx.doi.org/10.1378/chest.08-0776>
- Pasteur MC, Helliwell SM, Houghton SJ, Webb SC, Foweraker JE, Coulden RA, et al. An investigation into causative factors in patients with bronchiectasis. *Am J Respir Crit Care Med*. 2000;162(4 Pt 1):1277-84. PMID:11029331.
- Bogossian M, Santoro IL, Jamnik S, Romaldini H. Bronquiectasias: estudo de 314 casos tuberculose x não-tuberculose. *J Pneumol*. 1998;24(1):11-6.
- Moreira JJ, Felicetti JC, Cardoso PF, Moreira AL, Andrade CF. Bronquiectasias: aspectos diagnósticos e terapêuticos. Estudo de 170 pacientes. *J Pneumol*. 2003;29(5):258-63. <http://dx.doi.org/10.1590/S0102-35862003000500003>
- Swaminathan S, Kuppurao KV, Somu N, Vijayan VK. Reduced exercise capacity in non-cystic fibrosis bronchiectasis. *Indian J Pediatr*. 2003;70(7):553-6. <http://dx.doi.org/10.1007/BF02723157>
- ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. *Am J Respir Crit Care Med*. 2002;166(1):111-7. PMID:12091180.
- Lee AL, Button BM, Ellis S, Stirling R, Wilson JW, Holland AE, et al. Clinical determinants of the 6-Minute Walk Test in bronchiectasis. *Respir Med*. 2009;103(5):780-5. PMID:19070473. <http://dx.doi.org/10.1016/j.rmed.2008.11.005>
- Martínez-García MA, Perpiñá-Tordera M, Román-Sánchez P, Soler-Cataluña JJ. Quality-of-life determinants in patients with clinically stable bronchiectasis. *Chest*. 2005;128(2):739-45. PMID:16100162. <http://dx.doi.org/10.1378/chest.128.2.739>
- O'Leary CJ, Wilson CB, Hansell DM, Cole PJ, Wilson R, Jones PW. Relationship between psychological well-being and lung health status in patients with bronchiectasis. *Respir Med*. 2002;96(9):686-92. PMID:12243314. <http://dx.doi.org/10.1053/rmed.2002.1330>
- Kosmas EN, Milic-Emili J, Retsou S, Kontogiorgi M, Dimakou K, Roussos C, et al. Exercise testing and exercise-limiting factors in patients with bilateral bronchiectasis. *Pneumon*. 2009;22(4):306-14.
- Tomkinson JL, Bruton A. The 6-minute walk test for patients with bronchiectasis: comparison with normal predictive data. *ACPRC J*. 2009;41:16-21.
- Müller N, Fraser R, Colman N, Paré P. Doenças das vias respiratórias. In: Müller N, Fraser R, Colman N, Paré P, editors. *Diagnóstico Radiológico das Doenças do Tórax*. Rio de Janeiro: Editora Guanabara Koogan; 2003. p. 443-510.
- Mahler DA, Weinberg DH, Wells CK, Feinstein AR. The measurement of dyspnea. Contents, interobserver agreement, and physiologic correlates of two new clinical indexes. *Chest*. 1984;85(6):751-8. PMID:6723384. <http://dx.doi.org/10.1378/chest.85.6.751>
- Pereira CA. Espirometria. *J Pneumol*. 2002;28(Suppl 3):S1-S82.
- Pereira CA, Barreto SP, Simões JG, Pereira FW, Gerstler JG, Nakatani J. Valores de referência para espirometria em uma amostra da população brasileira adulta. *J Pneumol*. 1992;18(1):10-22.
- Souza RB. Pressões respiratórias estáticas máximas. *J Pneumol*. 2002;28(Suppl 3):S155-S165.
- Neder JA, Andreoni S, Lerario MC, Nery LE. Reference values for lung function tests. II. Maximal respiratory pressures and voluntary ventilation. *Braz J Med Biol Res*. 1999;32(6):719-27. <http://dx.doi.org/10.1590/S0100-879X1999000600007>
- Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*. 1982;14(5):377-81. <http://dx.doi.org/10.1249/00005768-198205000-00012>
- Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med*. 1998;158(5 Pt 1):1384-7. PMID:9817683.
- Ciconelli RM, Ferraz MB, Santos W, Meinão I, Quaresma MR. Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36). *Rev Bras Reumatol*. 1999;39(3):143-50.
- Schols AM, Mostert R, Soeters PB, Wouters EF. Body composition and exercise performance in patients with chronic obstructive pulmonary disease. *Thorax*. 1991;46(10):695-9. PMID:1750015 PMID:463385. <http://dx.doi.org/10.1136/thx.46.10.695>
- Drummond GB. Body composition and exercise performance in patients with chronic obstructive pulmonary disease (COPD). *Thorax*. 1992;47(1):66. PMID:1539152 PMID:463563. <http://dx.doi.org/10.1136/thx.47.1.66>

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