Characterization of the severity of dyspnea in patients with bronchiectasis: correlation with clinical, functional, and tomographic aspects

Maria Cecília Nieves Maiorano de Nucci[1] [ID] ,
Frederico Leon Arrabal Fernandes[1] [ID] , João Marcos Salge[1] [ID] ,
Rafael Stelmach[1] [ID] , Alberto Cukier[1] [ID] , Rodrigo Athanazio[1] [ID]

1. Instituto do Coração, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, São Paulo (SP) Brasil.

ABSTRACT

Objective: To characterize a population of patients with bronchiectasis, correlating clinical, radiological, and functional aspects with the severity of dyspnea. **Methods:** This was a cross-sectional study involving adult patients with HRCT-confirmed bronchiectasis, categorized according to the severity of dyspnea (as being mildly or severely symptomatic, on the basis of the modified Medical Research Council scale). We correlated the severity of dyspnea with clinical parameters, functional parameters (spirometry values, lung volumes, and DLCO), and CT parameters. **Results:** We evaluated 114 patients, 47 (41%) of whom were men. The median age (interquartile range) was 42 years (30-55 years). The most common form was idiopathic bronchiectasis. Of the 114 patients, 20 (17.5%) were colonized with *Pseudomonas aeruginosa* and 59 (51.8%) were under continuous treatment with macrolides. When we applied the Exacerbation in the previous year, FEV_1, Age, Colonization, Extension, and Dyspnea score, the severity of dyspnea was categorized as moderate in 54 patients (47.4%), whereas it was categorized as mild in 50 (43.9%) when we applied the Bronchiectasis Severity Index. The most common lung function pattern was one of obstruction, seen in 95 patients (83.3%), and air trapping was seen in 77 patients (68.7%). The prevalence of an obstructive pattern on spirometry was higher among the patients with dyspnea that was more severe, and most functional parameters showed reasonable accuracy in discriminating between levels of dyspnea severity. **Conclusions:** Patients with bronchiectasis and dyspnea that was more severe had greater functional impairment. The measurement of lung volumes complemented the spirometry data. Because bronchiectasis is a complex, heterogeneous condition, a single variable does not seem to be sufficient to provide an overall characterization of the clinical condition.

Keywords: Bronchiectasis; Dyspnea; Respiratory function tests; Multidetector computed tomography; Plethysmography.

INTRODUCTION

Bronchiectasis is characterized by abnormal, irreversible dilatation of the airways and can have various causes, including congenital disorders, mechanical bronchial obstruction, respiratory infections, and immunodeficiency.[1-3] It is a chronic, heterogeneous condition of varying severity. It is usually progressive, and the presentation ranges from asymptomatic disease with no functional consequences to advanced disease, such as chronic respiratory failure.[1,2,4]

The interest in and amount of research on bronchiectasis have been increasing in the last decade, leading to advances in the treatment of patients with this disease.[5] In 2008, the Spanish Society of Pulmonology published their first guidelines for the diagnosis and treatment of bronchiectasis.[6] Subsequently, various societies worldwide published their own guidelines; however, recommendations differed considerably across guidelines and different local practices for managing this disease were highlighted.[7-9] More recently, the Brazilian Thoracic Association issued a consensus statement on non-cystic fibrosis bronchiectasis in Brazil.[10] At least some of the differences across guidelines can be explained by the wide variability in the clinical characteristics of the populations studied in different countries. In a recent study conducted in Latin America,[11] the long-term clinical outcomes were similar to those reported in studies conducted in Europe and in the United States.[12-15] However, the authors noted considerable differences between their study population and those evaluated in the latter studies, in terms of age, the etiology of bronchiectasis, the type of bronchial colonization, and the severity of functional impairment.

Because of the great variability in the presentation of bronchiectasis, it is essential that patients with the disease undergo a careful clinical and prognostic assessment.[16]

Multidimensional scores have been developed to assess disease severity in patients with a diagnosis of non-cystic fibrosis bronchiectasis. Examples of such scores include the **E**xacerbation in the previous year, **F**EV$_1$, **A**ge, **C**olonization, **E**xtension, and **D**yspnea (E-FACED) score[17] and the Bronchiectasis Severity Index (BSI),[13] both of which use a combination of clinical, functional, radiological, and microbiological aspects, with predictive value for mortality, hospital admissions, exacerbations, and quality of life.

There is as yet no single index that can accurately predict disease progression in patients with bronchiectasis. Currently, various phenotypes are recognized as being related to bronchiectasis on the basis of the underlying pathophysiological mechanism of this disease.[18] In addition, there have been improvements in the radiological characterization of patients with bronchiectasis, especially of morphological changes in the (large and small) airways and in the lung parenchyma (consolidation and atelectasis). Such findings can predict clinical outcomes, such as exacerbation, and correlate with the severity of lung involvement, although they do not define the complex, varied clinical presentation of this disease.[19] Therefore, ancillary methods may play an important role in improving the understanding of the heterogeneity of the clinical presentation in patients with bronchiectasis. In patients with bronchiectasis, the use of advanced methods of assessing lung function, such as plethysmography, shows great promise. By identifying specific patterns of air trapping, hyperinflation, and restriction, one can correlate different pathophysiological mechanisms with important characteristics in the management of such patients, such as the fact that dyspnea is closely related to the quality of life of such individuals.[20]

Although some studies have evaluated the use of plethysmography in patients with bronchiectasis,[21] little is known about the role of plethysmography in discriminating between levels of disease severity in such individuals. In addition, those studies are commonly based on European cohorts classically experiencing bronchiectasis that is less severe than that found in Latin American populations.[10,12,22] In the present study, we describe an in-depth assessment of lung function in a sample of individuals diagnosed with bronchiectasis in Brazil. The objective of the present study was to correlate clinical, functional, and radiological parameters with the severity of dyspnea in these individuals in order to determine which ones are most strongly associated with it. Other objectives were to assess lung volumes in relation to spirometry-classified functional patterns and to assess the correlation between functional parameters and a CT score.

METHODS

This was a cross-sectional study for which data were collected between May of 2014 and October of 2017. We evaluated patients treated at the Bronchiectasis Outpatient Clinic of the University of São Paulo School of Medicine *Hospital das Clínicas*, located in the city of São Paulo, Brazil. The study was approved by the local research ethics committee (Ruling no. SDC 4245/15/072), and all participating patients gave written informed consent.

Patients were sequentially recruited on the basis of the following inclusion criteria: being ≥ 18 years of age; having an HRCT-confirmed diagnosis of bronchiectasis; and having a clinical history of chronic cough with expectoration or recurrent infectious pulmonary exacerbations. Patients who had been diagnosed with cystic fibrosis, asthma, allergic bronchopulmonary aspergillosis, COPD, or active mycobacterial infection were excluded, as were those who had been treated for an infectious exacerbation with oral corticosteroids or antibiotics within the last 30 days, those who had previously undergone lung resection, those with a ≥ 10 pack-year smoking history, those on long-term home oxygen therapy, those with severe, uncontrolled systemic comorbidities, and those who were cognitively unable to perform pulmonary function tests, as well as those who were pregnant.

Clinical data were collected by using an interviewer-administered structured questionnaire designed to obtain information on demographics, severity of dyspnea measured by the modified Medical Research Council (mMRC) scale, frequency of exacerbations in the last 12 months, usual medications, and time since symptom onset. All patients were evaluated for the most common etiologies of bronchiectasis in accordance with our institutional protocol and international guidelines.[23] Data on chronic airway infection were based on sputum examination results in the last 12 months.[24]

Bronchiectasis severity was assessed by the E-FACED score and the BSI,[11,16] both of which are multivariate prognostic scores. The E-FACED score includes six variables (hospitalization in the last year, FEV$_1$, age, colonization with *Pseudomonas aeruginosa*, the radiological extent of bronchiectasis, and the severity of dyspnea, as measured by the mMRC scale), has a maximum score of 9 points, and categorizes disease severity as mild (0-3 points), moderate (4-6 points), or severe (7-9 points).[17] The BSI comprises eight factors: age; body mass index; FEV$_1$; hospital admissions in the last 2 years; exacerbations in the last year; the severity of dyspnea, as measured by the mMRC scale; colonization; and the extent of radiological involvement. The BSI has a maximum score of 25 and also classifies disease severity as mild (0-4 points), moderate (5-8 points), or severe (≥ 9 points).[13]

Participants underwent complete pulmonary function testing (spirometry, plethysmography, and measurement of DLCO). All tests were performed in accordance with the recommendations of the Brazilian Thoracic Association.[25] The reference values for spirometry and plethysmography were those established by Pereira et al.[26] and Neder et al.,[27] respectively. The radiological evaluation consisted of unenhanced HRCT of the chest. Images were acquired in a multislice CT scanner with

160 detector rows (Aquilion Prime; Toshiba Medical Systems Corporation, Otawara, Japan). All scans were assessed by a radiologist specializing in thoracic radiology. The extent and severity of bronchiectasis were classified by the modified Reiff score,[28] the use of which has been previously established in patients with bronchiectasis. The modified Reiff score assesses the number of lobes involved and the degree of the dilatation, with a maximum score of 18 points.[29] Data collection and all procedures were performed on a single day. Study participants, all of whom had previously been diagnosed with bronchiectasis and had been receiving outpatient follow-up care for varying periods, underwent the aforementioned tests in a systematic way and specifically for the purpose of the study.

Patients were divided into two groups on the basis of symptom intensity: those who were mildly symptomatic (mMRC scale score of 0 or 1); and those who were severely symptomatic (mMRC scale score ≥ 2). On spirometry, lung function patterns were classified as obstructive (FEV_1/FVC < 0.7 and FEV_1 < 80% of predicted) or nonspecific (FEV_1/FVC ≥ 0.7 plus FEV_1 and FVC < 80% of predicted). On the basis of the Lung volumes, patients were classified as having air trapping (RV/TLC > 40), hyperinflation (TLC > 120% of predicted), or a restrictive lung function pattern (TLC < 80% of predicted).

Our statistical analysis compared clinical, functional, and radiological characteristics between mildly and severely symptomatic patients. The Student's t-test was used for variables with normal distribution, the chi-square test was used for the comparison of proportions, and the Mann-Whitney test was used for variables with non-normal distribution. Spearman's correlation coefficient was calculated to determine the relationship between functional variables and the CT (modified Reiff) score.[28] A ROC curve analysis was performed to determine the accuracy of functional and CT variables to predict the severity of symptoms in patients with bronchiectasis (mildly vs. severely symptomatic patients). Differences were considered statistically significant at $p < 0.05$. The IBM SPSS Statistics software package, version 22.0 (IBM Corporation, Armonk, NY, USA) was used for the statistical analysis.

RESULTS

We evaluated 208 patients, 94 of whom were excluded, for the following reasons: being on long-term home oxygen therapy (n = 38); having undergone lung resection (n = 18); having a > 10 pack-year smoking history (n = 16); having uncontrolled systemic comorbidities (n = 9); having been diagnosed with asthma (n = 6); being unable to perform pulmonary function tests (n = 6); and having active mycobacterial infection (n = 1). Therefore, the final sample comprised 114 patients.

Table 1 presents data on the demographic and clinical characteristics of the study sample. Most of the patients were female and young (mean age, 42.5 years). The bronchiectasis was idiopathic in most cases, although there were also cases in which it was attributed to ciliary dyskinesia or (to a lesser degree) a previous infection. In general, mildly and severely symptomatic patients were comparable in terms of age, gender, time since diagnosis, etiology, and extent of radiological involvement. However, severely symptomatic patients used respiratory medications more frequently, had a higher number of exacerbations, and had worse lung function, as determined by spirometry, by measurement of lung volumes, and by determination of the DLCO.

More than 80% of the patients had an obstructive pattern on spirometry. The most common finding resulting from the measurement of lung volumes by plethysmography was air trapping, seen in 77 patients (67.5%). Of those 77 patients, 24 (31.1%) also had hyperinflation. In addition, among the patients with a confirmed diagnosis of bronchiectasis, the spirometry and plethysmography results were normal in approximately 5% and 7%, respectively. The prevalence of an obstructive pattern on spirometry was higher in the severely symptomatic group than in the mildly symptomatic group (Table 2).

Figure 1 presents the results of the ROC curve analysis of the accuracy of various functional and CT parameters in discriminating between mildly and severely symptomatic patients with bronchiectasis. Spirometric and plethysmographic parameters showed reasonable accuracy in the symptomatic classification of these patients. The most accurate spirometric parameters (Figure 1A) were FEV_1—area under the curve (AUC) = 0.684—and $FEF_{25-75\%}$ (AUC = 0.677), whereas the most accurate plethysmographic parameters (Figure 1B) were RV/TLC (AUC = 0.682) and RV (AUC = 0.625). Similarly to the spirometric and plethysmographic parameters, DLCO was able to identify patients who were more severely symptomatic (AUC = 0.684), unlike the CT score,[28] which showed no discriminatory power (AUC = 0.421; Figure 1C).

Patients with bronchiectasis were divided into three groups on the basis of the lung function patterns seen on spirometry, and, subsequently, the patients in each group were classified on the basis of the patterns obtained by measurement of lung volumes by plethysmography. There was a considerable degree of disagreement between spirometry and plethysmography findings, as shown in Table 3. Of the patients who had normal spirometry, 67% had plethysmographic abnormalities. A nonspecific lung function pattern on spirometry was seen in 12 patients (11.4%); however, in only one of those patients was a reduction in TLC confirmed by plethysmography. In addition, patients with an obstructive pattern predominantly had air trapping or hyperinflation on plethysmography.

Table 4 presents the data on correlations between the modified Reiff score and the functional variables assessed in the patients with bronchiectasis. Various spirometric and plethysmographic parameters showed

Table 1. Demographic data and clinical characteristics of the patients with bronchiectasis.[a]

Variable	Total (N = 114)	Mildly symptomatic (n = 63)	Severely symptomatic (n = 51)	p
Male gender	47 (41)	29 (46)	18 (35)	0.247*
Age, years	42 (30-55)	41 (27-53)	47 (34-57)	0.167[†]
BMI, kg/m^2	24.4 ± 4.8	23.4 ± 4.3	25.7 ± 5.1	0.009[§]
Time since diagnosis, years	11 (4-16.3)	8 (4-16)	7 (3-17)	0.526[†]
Exacerbation	1 (0-2)	0 (0-1)	1 (0-2)	0.005[†]
Colonization				
Pseudomonas aeruginosa	20 (17.5)	9 (14.2)	11 (21.5)	0.346*
Other	8 (7.0)	6 (9.6)	2 (3.9)	
None	86 (75.5)	48 (76.2)	38 (74.6)	
Medications being used				
Macrolides	59 (51.8)	29 (46.0)	30 (58.8)	
Inhaled corticosteroid	24 (21.1)	14 (22.2)	10 (19.6)	
Long-acting β$_2$ agonist	7 (6.1)	2 (3.1)	5 (9.8)	0.037*
Inhaled antibiotic	4 (3.5)	1 (1.5)	3 (5.8)	
Hypertonic saline	4 (3.5)	3 (4.7)	1 (1.9)	
Etiology				
Idiopathic	39 (34.2)	18 (28.5)	21 (41.1)	
Ciliary dyskinesia	21 (18.4)	14 (22.2)	7 (13.7)	
Post-infectious	19 (16.7)	11 (17.4)	8 (15.6)	
Bronchiolitis	14 (12.3)	8 (12.6)	6 (11.7)	0.785*
CTD	6 (5.3)	3 (4.7)	3 (5.8)	
Immunodeficiency	4 (3.5)	3 (4.7)	1 (1.9)	
Other	11 (9.6)	6 (9.5)	5 (9.8)	
Lung function				
FEV$_1$, % predicted	48.7 ± 19.81	54.66 ± 21.68	41.54 ± 14.37	< 0.001[§]
FVC, % predicted	70 ± 17.17	74.55 ± 17.80	64.9 ± 14.84	0.002[§]
FEV$_1$/FVC	0.57 ± 0.14	0.6 ± 0.15	0.52 ± 0.11	0.003[§]
FEF$_{25-75\%}$, % predicted	27 (11-36)	25 (13-49)	14 (9-27.4)	0.001[†]
TLC, % predicted	107.0 ± 17.1	106.1 ± 16.4	108.0 ± 18.0	0.573[§]
RV, % predicted	201.0 ± 58.0	190.7 ± 57.5	214.1 ± 56.6	0.034[§]
RV/TLC	53.0 ± 10.3	49.9 ± 10.7	56.5 ± 8.6	< 0.001[§]
DLCO, % predicted	70.0 ± 26.4	77.6 ± 26.9	60.5 ± 22.5	0.001[§]
Modified Reiff score	7 (7-11)	7 (4-11)	8 (6-11)	0.131[†]
Prognostic scores				
E-FACED				
Mild disease	52 (45.6)	49 (77.8)	3 (5.9)	
Moderate disease	54 (47.4)	14 (22.2)	40 (78.4)	< 0.001
Severe disease	8 (7.0)	0 (0)	8 (15.7)	
BSI				
Mild disease	50 (43,9)	37 (58,7)	13 (25,5)	
Moderate disease	42 (36,8)	19 (30,2)	23 (45,1)	0.001
Severe disease	22 (19,3)	7 (11,1)	15 (29,4)	

BMI: body mass index; CTD: connective tissue disease; E-FACED: Exacerbation in the previous year, FEV$_1$, Age, Colonization, Extension, and Dyspnea; and BSI: Bronchiectasis Severity Index. [a]Values expressed as n (%), as mean ± SD, or as median (interquartile range). *Chi-square test. [†]Mann-Whitney U test. [§]Student's t-test.

a correlation with the modified Reiff score,[(28)] RV/TLC being the most strongly correlated.

DISCUSSION

In the present study, we present an extensive characterization of clinical, functional, and radiological parameters in 114 patients with bronchiectasis and report the impact of those parameters on the severity of dyspnea. Patients who were more severely symptomatic had experienced a higher number of exacerbations in the previous year, used respiratory medications more frequently, and had worse lung function. An obstructive lung function pattern was the most common finding in this population, being more prevalent among severely symptomatic patients. Various functional parameters
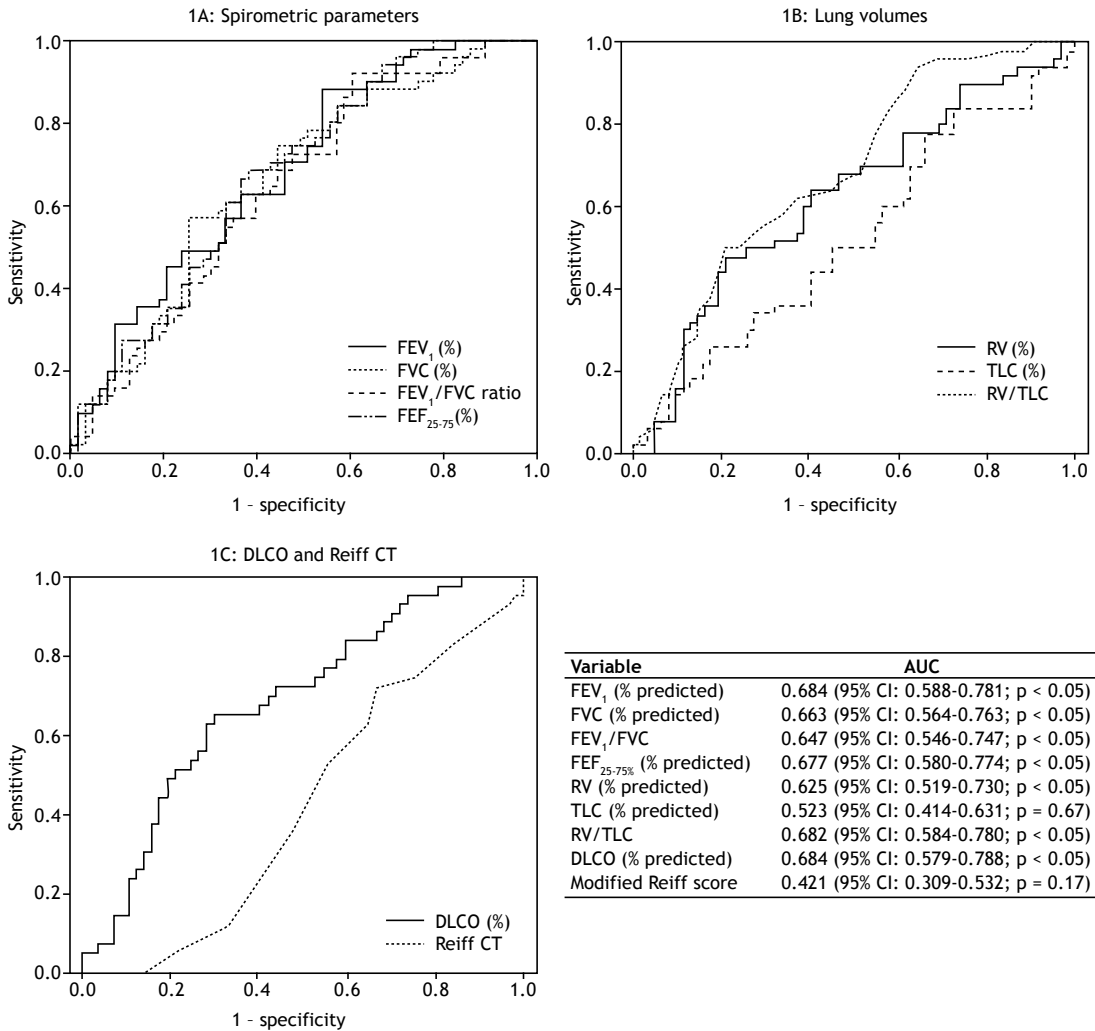
1A: Spirometric parameters — FEV$_1$ (%), FVC (%), FEV$_1$/FVC ratio, FEF$_{25-75}$(%)

1B: Lung volumes — RV (%), TLC (%), RV/TLC

1C: DLCO and Reiff CT — DLCO (%), Reiff CT

Variable	AUC
FEV$_1$ (% predicted)	0.684 (95% CI: 0.588-0.781; p < 0.05)
FVC (% predicted)	0.663 (95% CI: 0.564-0.763; p < 0.05)
FEV$_1$/FVC	0.647 (95% CI: 0.546-0.747; p < 0.05)
FEF$_{25-75\%}$ (% predicted)	0.677 (95% CI: 0.580-0.774; p < 0.05)
RV (% predicted)	0.625 (95% CI: 0.519-0.730; p < 0.05)
TLC (% predicted)	0.523 (95% CI: 0.414-0.631; p = 0.67)
RV/TLC	0.682 (95% CI: 0.584-0.780; p < 0.05)
DLCO (% predicted)	0.684 (95% CI: 0.579-0.788; p < 0.05)
Modified Reiff score	0.421 (95% CI: 0.309-0.532; p = 0.17)

Figure 1. Accuracy of functional parameters and a CT score in discriminating between patients who were severely symptomatic and those who were mildly symptomatic with dyspnea. AUC: area under the ROC curve; and Reiff CT: modified Reiff score.

were related to the severity of dyspnea. On the basis of our results, we can also state that spirometry alone often fails to provide important information, information that can be complemented by data from complete pulmonary function testing.

We observed that most functional measures (spirometric and lung volume parameters) were associated with the severity of dyspnea, especially variables such as FEV$_1$, RV/TLC, and DLCO, all of which showed better discriminatory power than did other variables. However, those variables showed varying levels of correlation, which suggests that no single functional parameter is sufficiently robust to characterize the intensity of dyspnea in patients with bronchiectasis. The measurement of dyspnea in patients with chronic airway disease is an important prognostic predictor, as has been demonstrated in previous studies involving patients with bronchiectasis[12,13] and patients with COPD.[28] In a large study characterizing a population of patients with a diagnosis of bronchiectasis, the authors did not assess the correlation between the severity of dyspnea and functional parameters.[30] The characterization of dyspnea is a complex process and may be related to various factors in patients with bronchiectasis, as we have recently demonstrated during the validation of a symptom score in this population.[31] Therefore, various factors should be taken into consideration for a careful assessment of the determinants affecting the characterization of dyspnea in patients with bronchiectasis.

In our sample, most patients had an obstructive pattern on spirometry and signs of air trapping on plethysmography. However, previous studies differ regarding this prevalence. Habesoglu et al.[32] performed spirometry in 304 patients with bronchiectasis and demonstrated that only 47.4% of the patients had an obstructive lung function pattern, whereas 20.8% had normal spirometry results. Recently, two studies confirmed the high prevalence of air trapping among patients with bronchiectasis.[33,34] Radovanovic et

Table 2. Functional patterns in patients with bronchiectasis, as determined through analysis of spirometry and lung volume data.[a]

Variable	Total	Mildly symptomatic	Severely symptomatic	p
Spirometry				
Obstruction	95 (83.3)	48 (76.2)	47 (92.2)	
Nonspecific	13 (10.5)	9 (14.3)	4 (7.8)	0.03
Normal	6 (5.2)	6 (9.5)	0 (0.0)	
Plethysmography*				
Air trapping (A)	76 (67.8)	40 (63.4)	36 (70.6)	
Hyperinflation (H)	1 (0.9)	1 (1.6)	0 (0.0)	
A + H	25 (22.32)	12 (19.0)	14 (27.4)	
Normal	8 (7.1)	7 (11.1)	1 (2.0)	0.23
Restriction	1 (0.9)	1 (2.6)	0 (0.0)	
Mixed obstruction and restriction	1 (0.9)	1 (2.6)	0 (0.0)	

[a]Values expressed as n (%). *Two patients (1.8%) had no data because of technical problems during the procedure.

Table 3. Information provided by measurement of lung volumes in relation to spirometry-classified functional patterns (n = 112).[a]

Spirometry	Lung volumes
Normal (n = 6)	Air trapping, n = 1 (17%) Hyperinflation, n = 1 (17%) Air trapping + hyperinflation, n = 2 (33%) Normal, n = 2 (33%)
Obstruction (n = 94)	Air trapping, n = 65 (69%) Air trapping + hyperinflation, n = 22 (24%) Restriction, n = 1 (1%) Normal, n = 6 (6%)
Nonspecific (n = 12)	Air trapping, n = 11 (92%) Restriction, n = 1 (8%)

[a]One patient in the obstruction group and one patient in the nonspecific group had no data on lung volumes because of technical problems during the procedure.

Table 4. Correlation between functional parameters and the modified Reiff score.

Variable	Modified Reiff score*
FEV_1, % predicted	−0.343[†]
FVC, % predicted	−0.348[†]
FEV_1/FVC	−0.232[‡]
$FEF_{25-75\%}$, % predicted	−0.303[†]
RV, % predicted	0.247[†]
TLC, % predicted	0.012
RV/TLC	0.356[†]

*Spearman's correlation coefficient. [†]$p < 0.05$. [‡]$p < 0.01$.

al.[33] demonstrated the presence of air trapping in 70.2% of their sample, whereas an obstructive pattern was present in only 41.1%. This variability in the identification of patterns on pulmonary function testing can be explained by the different characteristics of the populations studied. Our study sample was characterized by a significant number of patients who were more severely symptomatic and had worse lung function. In populations with milder disease, methods for assessing lung homogeneity (lung clearance index) and the small airways (oscillometry) may even be more sensitive than are traditional methods.[34,35]

The various methods of assessing lung function collect complementary information and can discriminate between different pathophysiological processes in the same patient. When we performed a complete functional assessment, many of the patients classified as normal or as having a nonspecific lung function pattern on spirometry could actually be identified as having air trapping or hyperinflation on plethysmography. The disagreement between spirometric and lung volume parameters is a relevant issue, because, as shown by Martínez-García et al.,[36] obstruction in bronchiectasis is a factor clearly distinct from lung hyperinflation.

Obstruction is mainly related to bronchial wall thickening and secretion in the large airways, as proposed by Roberts et al.,[37] whereas hyperinflation is more strongly related to small airways involvement. In addition, plethysmographic parameters such as air trapping, as well as reduced DLCO, are more strongly associated with a worse prognosis in bronchiectasis than are spirometric parameters.[33] Finally, these measures may also behave differently in terms of bronchodilator response, being tools that are more sensitive and characterizing a subgroup with a better clinical course or more favorably affected by specific therapeutic interventions.[33,34]

To our knowledge, ours is the first study to perform a complete functional characterization of a population sample of individuals diagnosed with non-cystic fibrosis bronchiectasis in Brazil and to assess the association of functional, clinical, and radiological variables with the presence of dyspnea. Some studies have characterized populations of patients with bronchiectasis in Brazil, although many of those studies were retrospective and assessed a limited number of parameters. In 1998, Bogossian et al.[38] studied 314 patients with bronchiectasis, comparing symptoms, lung function, and location of bronchiectasis between those with bronchiectasis due to tuberculosis sequelae and those with bronchiectasis of other etiologies. Patients with bronchiectasis due to tuberculosis sequelae were characterized as experiencing more significant functional limitation and having bronchiectasis that was

predominantly located in the upper lobes and on the right side. In 2003, Moreira et al.[39] studied the profile of a population of 170 patients with bronchiectasis, comparing those who received clinical treatment and those who received surgical treatment, in terms of symptoms, bronchial colonization, etiology, and spirometry data. Patients who underwent surgical resection were those with more well preserved lung function, indicating that baseline functional status can even have an impact on the choice of treatment. Subsequently, Faria et al.[40] characterized a broad sample of patients with bronchiectasis, reporting that an obstructive pattern was the most common finding in those individuals, albeit at a lower proportion than that found in our population (43.5% vs. > 80%). However, that study[40] did not consider lung volume measurements, radiological data, or prognostic scores. Finally, in 2015, Lopes et al.[41] primarily assessed the impact of various etiologies of bronchiectasis on clinical findings, lung function data, and CT findings. The authors concluded that etiology, CT score, and severity of dyspnea are independent predictors of FEV_1 and DLCO. They also established an association between FEV_1 and CT score.

We found that the extent of bronchiectasis seen on CT, as measured by the modified Reiff score,[28] showed weak correlations with functional parameters and with the severity of dyspnea. That finding is in line with those of previous studies. Lynch et al.[42] assessed and reported the relationships that FEV_1, FVC, and FEV_1/FVC have with the extent of bronchiectasis on CT, the type of bronchiectasis, bronchial wall thickening, air trapping, and mucoid impaction. Dimakou et al.[30] also found that the radiological extent of bronchiectasis correlated only weakly with spirometric parameters. Given the complex, heterogeneous nature of bronchiectasis, the extent to which bronchiectasis affects the respiratory tract should not be assessed by a single method. Chest CT is highly important as a gold standard for the diagnosis of bronchiectasis and provides useful information on potential etiologies. In addition, subjective radiological assessment or radiological assessment by scores, such as the modified Reiff score,[28] allows assessment of regional involvement by bronchiectasis, which is not possible via pulmonary function testing. However, CT scores that include images obtained during inspiration and expiration can be used in order to improve the characterization of small airways involvement and, consequently, of air trapping. By using this methodology, a greater correlation can be found between CT findings and pulmonary function test findings.[42]

Although we systematically characterized a significant sample of patients with a diagnosis of non-cystic fibrosis bronchiectasis, through a detailed description of clinical, functional, and radiological data, our study has some limitations. This was a cross-sectional study, and therefore assessment of causality was not possible; prospective studies are needed in order to determine whether the inclusion of lung volumes in the evaluation adds prognostic value or leads to changes to the follow-up of such patients. In addition, we used a simple CT score that was based solely on the expiratory phase. Therefore, we were unable to assess the correlation between air trapping detected by CT and the various functional parameters measured. Finally, caution should be exercised in extrapolating the results, because the study sample was based on a population with severe lung involvement at a tertiary care hospital and with a lower prevalence of post-infectious etiologies than that commonly found in the Brazilian population.

Patients with bronchiectasis who had more severe dyspnea showed greater functional impairment on spirometry and plethysmography. On spirometry, FEV_1, which is a parameter used in the two main prognostic scores in bronchiectasis,[13,17] is an important marker of severity in patients with bronchiectasis. However, spirometry alone is not sufficient to characterize such patients clinically, especially regarding the severity of dyspnea. The measurement of lung volumes by plethysmography can add relevant information because it provides information on small airways involvement and has proven to be a useful complement to the functional assessment in patients with bronchiectasis. Therefore, given the complex nature of bronchiectasis, a combination of clinical, functional, and radiological evaluations is essential for an adequate characterization of the disease, thus making appropriate clinical management and determination of the prognosis.

REFERENCES

1. Lasserson T, Holt K, Evans D, Greenstone M. Anticholinergic therapy for bronchiectasis. Cochrane Database Syst Rev. 2001;(4):CD002163. https://doi.org/10.1002/14651858.CD002163

2. Franco F, Sheikh A, Greenstone M. Short acting beta-2 agonists for bronchiectasis. Cochrane Database Syst Rev. 2003;(3):CD003572. https://doi.org/10.1002/14651858.CD003572

3. Martínez García MÁ, Máiz Carro L, Catalán Serra P. Treatment of non-cystic fibrosis bronchiectasis [Article in Spanish]. Arch Bronconeumol. 2011;47(12):599-609. https://doi.org/10.1016/j.arbr.2011.06.003

4. ten Hacken N, Kerstjens H, Postma D. Bronchiectasis. BMJ Clin Evid. 2008;2008:1507.

5. Martínez-García MÁ, de la Rosa-Carrillo D. Bronchiectasis: Rising from its own ashes. Arch Bronconeumol. 2018;54(2):59-60. https://doi.org/10.1016/j.arbr.2017.11.008

6. Vendrell M, de Gracia J, Olveira C, Martinez-Garcia MA, Girón R, Máiz L, et al. Diagnosis and treatment of bronchiectasis. Spanish Society of Pneumology and Thoracic Surgery [Article in Spanish]. Arch Bronconeumol. 2008;44(11):629–640. https://doi.org/10.1157/13128330

7. Hill AT, Sullivan AL, Chalmers JD, De Soyza AD, Elborn JS, Floto RA, et al. British Thoracic Society Guideline for bronchiectasis in adults. Thorax. 2019;74(Suppl 1):1-69. https://doi.org/10.1136/thoraxjnl-2018-212463

8. Martínez-García MÁ, Máiz L, Olveira C, Girón RM, Rosa D, Blanco M, et al. Spanish Guidelines on the Evaluation and Diagnosis of Bronchiectasis in Adults [published correction appears in Arch Bronconeumol. 2020 Apr;56(4):265]. Arch Bronconeumol. 2018;54(2):79-87. https://doi.org/10.1016/j.arbres.2017.07.015

9. Martínez-García MÁ, Máiz L, Olveira C, Girón RM, Rosa D, Blanco M, et al. Spanish Guidelines on Treatment of Bronchiectasis in Adults. Arch Bronconeumol. 2018;54(2):88-98. https://doi.org/10.1016/j.arbr.2017.07.014

10. Pereira MC, Athanazio RA, Dalcin PTR, Figueiredo MRF, Gomes M, Freitas CG, et al. Brazilian consensus on non-cystic fibrosis bronchiectasis. J Bras Pneumol. 2019;45(4):e20190122. https://doi.org/10.1590/1806-3713/e20190122

11. Athanazio R, Pereira MC, Gramblicka G, Cavalcanti-Lundgren F, de Figueiredo MF, Arancibia F, et al. Latin America validation of FACED score in patients with bronchiectasis: an analysis of six cohorts. BMC Pulm Med. 2017;17(1):73. https://doi.org/10.1186/s12890-017-0417-3

12. Martínez-García MÁ, de Gracia J, Vendrell Relat M, Girón RM, Carro LM, Carrillo DR, et al. Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score. Eur Respir J. 2014;43(5):1357-1367. https://doi.org/10.1183/09031936.00026313

13. Chalmers JD, Goeminne P, Aliberti S, McDonnell MJ, Lonni S, Davidson J, et al. The bronchiectasis severity index. An international derivation and validation study. Am J Respir Crit Care Med. 2014;189(5):576-585. https://doi.org/10.1164/rccm.201309-1575OC

14. Chalmers JD, Aliberti S, Polverino E, Vendrell M, Crichton M, Loebinger M, et al. The EMBARC European Bronchiectasis Registry: protocol for an international observational study. ERJ Open Res. 2016;2(1):00081-2015. https://doi.org/10.1183/23120541.00081-2015

15. Aksamit TR, O'Donnell AE, Barker A, Olivier KN, Winthrop KL, Daniels MLA, et al. Adult Patients With Bronchiectasis: A First Look at the US Bronchiectasis Research Registry. Chest. 2017;151(5):982-992. https://doi.org/10.1016/j.chest.2016.10.055

16. Martínez-García MÁ, Vendrell M, Girón R, Máiz-Carro L, Carrillo DR, Gracia J, et al. The Multiple Faces of Non-Cystic Fibrosis Bronchiectasis. A Cluster Analysis Approach. Ann Am Thorac Soc. 2016;13(9):1468-1475. https://doi.org/10.1513/AnnalsATS.201510-678OC

17. Martinez-Garcia MA, Athanazio RA, Girón R, Máiz-Carro L, Rosa D, Olveira C, et al. Predicting high risk of exacerbations in bronchiectasis: the E-FACED score. Int J Chron Obstruct Pulmon Dis. 2017;12:275-284. https://doi.org/10.2147/COPD.S121943

18. Flume PA, Chalmers JD, Olivier KN. Advances in bronchiectasis: endotyping, genetics, microbiome, and disease heterogeneity. Lancet. 2018;392(10150):880-890. https://doi.org/10.1016/S0140-6736(18)31767-7

19. Sheehan RE, Wells AU, Copley SJ, Desai SR, Howling SJ, Cole PJ, et al. A comparison of serial computed tomography and functional change in bronchiectasis. Eur Respir J. 2002;20(3):581-587. https://doi.org/10.1183/09031936.02.00284602

20. 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):739-745. https://doi.org/10.1378/chest.128.2.739

21. Loebinger MR, Wells AU, Hansell DM, Chinyanganya N, Devaraj A, Meister M, et al. Mortality in bronchiectasis: a long-term study assessing the factors influencing survival. Eur Respir J. 2009;34(4):843-849. https://doi.org/10.1183/09031936.00003709

22. McDonnell MJ, Aliberti S, Goeminne PC, Dimakou K, Zucchetti SC, Davidson J, et al. Multidimensional severity assessment in bronchiectasis: an analysis of seven European cohorts. Thorax. 2016;71(12):1110-1118. https://doi.org/10.1136/thoraxjnl-2016-208481

23. Polverino E, Goeminne PC, McDonnell MJ, Aliberti S, Marshall SE, Loebinger MR, et al. European Respiratory Society guidelines for the management of adult bronchiectasis. Eur Respir J. 2017;50(3):1700629. https://doi.org/10.1183/13993003.00629-2017

24. 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):1277-1284. https://doi.org/10.1164/ajrccm.162.4.9906120

25. Sociedade Brasileira de Pneumologia e Tisiologia. Diretrizes para Testes de Função Pulmonar. J Pneumol. 2002;28(Suppl 3):S1-S238.

26. Pereira CA, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. J Bras Pneumol. 2007;33(4):397-406. https://doi.org/10.1590/S1806-37132007000400008

27. Neder JA, Andreoni S, Castelo-Filho A, Nery LE. Reference values for lung function tests. I. Static volumes. Braz J Med Biol Res. 1999;32(6):703-717. https://doi.org/10.1590/S0100-879X1999000600006

28. Reiff DB, Wells AU, Carr DH, Cole PJ, Hansell DM. CT findings in bronchiectasis: limited value in distinguishing between idiopathic and specific types. AJR Am J Roentgenol. 1995;165(2):261-267. https://doi.org/10.2214/ajr.165.2.7618537

29. Global Initiative for Chronic Obstructive Lung Disease (GOLD) [homepage on the Internet]. Bethesda: GOLD [cited 2019 Jun 10]. Global Strategy for the Diagnosis, Management, and Prevention of COPD 2019 Report. [Adobe Acrobat document, 155p.]. Available from: https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-v1.7-FINAL-14Nov2018-WMS.pdf

30. Dimakou K, Triantafillidou C, Toumbis M, Tsikritsaki K, Malagari K, Bakakos P. Non CF-bronchiectasis: Aetiologic approach, clinical, radiological, microbiological and functional profile in 277 patients. Respir Med. 2016;116:1-7. https://doi.org/10.1016/j.rmed.2016.05.001

31. Lanza FC, Castro RAS, de Camargo AA, Zanatta DJM, Rached S, Athanazio R, et al. COPD Assessment Test (CAT) is a Valid and Simple Tool to Measure the Impact of Bronchiectasis on Affected Patients. COPD. 2018;15(5):512-519. https://doi.org/10.1080/15412555.2018.1540034

32. Habesoglu MA, Ugurlu AO, Eyuboglu FO. Clinical, radiologic, and functional evaluation of 304 patients with bronchiectasis. Ann Thorac Med. 2011;6(3):131-136. https://doi.org/10.4103/1817-1737.82443

33. Radovanovic D, Santus P, Blasi F, Sotgiu G, D'Arcangelo F, Simonetta E, et al. A comprehensive approach to lung function in bronchiectasis. Respir Med. 2018;145:120-129. https://doi.org/10.1016/j.rmed.2018.10.031

34. Guan WJ, Yuan JJ, Huang Y, Li HM, Chen RC, Zhong NS. Residual volume/total lung capacity ratio confers limited additive significance to lung clearance index for assessment of adults with bronchiectasis. PLoS One. 2017;12(9):e0183779. https://doi.org/10.1371/journal.pone.0183779

35. Guan WJ, Yuan JJ, Gao YH, Li HM, Zheng JP, Chen RC, et al. Impulse Oscillometry and Spirometry Small-Airway Parameters in Mild to Moderate Bronchiectasis. Respir Care. 2016;61(11):1513-1522. https://doi.org/10.4187/respcare.04710

36. Martínez-García MA, Perpiñá-Tordera M, Soler-Cataluña JJ, Román-Sánchez P, Lloris-Bayo A, González-Molina A. Dissociation of lung function, dyspnea ratings and pulmonary extension in bronchiectasis. Respir Med. 2007;101(11):2248-2253. https://doi.org/10.1016/j.rmed.2007.06.028

37. Roberts HR, Wells AU, Milne DG, Rubens MB, Kolbe J, Cole PJ, et al. Airflow obstruction in bronchiectasis: correlation between computed tomography features and pulmonary function tests. Thorax. 2000;55(3):198-204. https://doi.org/10.1136/thorax.55.3.198

38. Bogossian M, Santoro IL, Jamnik S, Romaldini H. Bronquiectasias: estudo de 314 casos tuberculose x não-tuberculose. J Pneumol. 1998;24(1):11-16.

39. Moreira JS, Porto NS, Camargo JJ, Felicetti JC, Cardoso PF, Moreira AL, et al. Bronchiectasis: diagnostic and therapeutic features: A study of 170 patients. J Pneumol. 2003;29(5):258-263. https://doi.org/10.1590/S0102-35862003000500003

40. Faria NS Jr, Bigatão AM, Santos SR, Leitão Filho FS, Jardim JR, Oliveira LV. Clinical significance in non-cystic fibrosis bronchiectasis followed in a real practice. Fisioter Mov. 2013;26(4):895-904. https://doi.org/10.1590/S0103-51502013000400018

41. Lopes AJ, Camilo GB, de Menezes SL, Guimarães FS. Impact of different etiologies of bronchiectasis on the pulmonary function tests. Clin Med Res. 2015;13(1):12-19. https://doi.org/10.3121/cmr.2014.1236

42. Lynch DA, Newell J, Hale V, Dyer D, Corkery K, Fox NL, et al. Correlation of CT findings with clinical evaluations in 261 patients with symptomatic bronchiectasis. AJR Am J Roentgenol. 1999;173(1):53-58. https://doi.org/10.2214/ajr.173.1.10397099