Follow-up of a cohort of patients with noncystic fibrosis bronchiectasis for 1 year

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SUMMARY

OBJECTIVE: The objective of this study was to evaluate the quality of life of patients with noncystic fibrosis bronchiectasis during a 1-year follow-up by using the EuroQol – 5 Dimensions – 3 Levels (EQ-5D-3L) questionnaire.

METHODS: A cohort study was conducted with 100 patients with noncystic fibrosis bronchiectasis and followed up with face-to-face visits or by telephone contact every 3 months for 1 year. All patients were recruited from a single referral center for bronchiectasis. At the time of recruiting and at the end of 1 year, the EQ-5D-3L questionnaire was applied to evaluate the patients' quality of life. Variables, such as exacerbation, emergency care, comorbidities, hemoptysis, colonization, and hospitalization, were assessed.

RESULTS: Of the 100 patients, 99 completed the study and 72% were women. There were no marked limitations in the mobility and self-care domains during the follow-up. At the end of the follow-up, 32 patients were extremely anxious or depressed. The quality of life assessed by using EQ-5D-3L had an initial mean score of 0.545 and of 0.589 after 1 year, which was statistically significant (p=0.011).

CONCLUSION: Patients with noncystic fibrosis bronchiectasis have a poor quality of life, and the EQ-5D-3L questionnaire may be a tool for monitoring patients with bronchiectasis.

KEYWORDS: Bronchiectasis. Quality of life. EQ-5D-3L. Exacerbation. Hospitalization.

INTRODUCTION

Noncystic fibrosis bronchiectasis (NCFB) is an irreversible disease, characterized by bronchial dilatation^{1,2} resulting from the destruction of the elastic and muscular components of its walls³. In general, symptoms include a chronic cough, sputum with or without hemoptysis, dyspnea, intermittent respiratory infections⁴, and fatigue⁵. Exacerbations are frequently observed in most bronchiectasis patients and have been associated with progressive loss of lung function, worsening of quality of life^{3,4}, and increased mortality^{2,5}. These disorders lead to changes in a patient's daily life and may restrict their usual activities. The worldwide epidemiological situation is unknown and varies according to the demographic area. The prevalence of NCFB in the American population is estimated at 139 cases per 100,000 individuals, with an annual incidence of 29 cases per 100,000 Americans⁶. In Germany, the estimated proportion is 67 per 100,000 inhabitants⁴. It is estimated that the prevalence and incidence of bronchiectasis in Brazilian individuals are high because they are mainly related to pulmonary tuberculosis (TB) that is highly prevalent in Brazil (coefficient of incidence of 33.5 cases per 100,000 inhabitants in 2017)7 and results in bronchiectasis sequelae in many patients8. NCFB is also associated with inadequate control of respiratory infections during childhood, difficulty in accessing health resources, and low socioeconomic status^{9,10}. There are several instruments that can be used to evaluate the health-related quality of life (HRQoL) in patients affected by numerous diseases. Among them is the EuroQol-5 Dimensions - 3 Levels (EQ-5D-3L)¹¹, a simple, easy-to-understand, widely used instrument, available in multiple languages and with various modes of administration. The EQ-5D-3L questionnaire addresses five important dimensions or domains related to patient health. Measuring the quality of life can help guide individualized treatment and contribute to better care. Bronchiectasis is a disease characterized by a high morbidity and mortality^{12,13}, and studies are needed to better understand the evolution of the disease and improve patient care. The objective of this study was to evaluate the quality of life of patients with bronchiectasis during a 1-year follow-up by using the EQ-5D-3L questionnaire.

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METHODS

Subject and study design

A cohort study was carried out in a university hospital in the State of Rio de Janeiro, from January 2017 to May 2018. Patients older than 18 years were recruited from an outpatient clinic specialized in pulmonology. All patients underwent high-resolution computed tomography (HRCT), which is considered the gold standard for the diagnosis of bronchiectasis. The Research Ethics Committee of the University Hospital Pedro Ernesto, Brazil, approved the research (no. 1,823,665). The patients were individually interviewed, a structured questionnaire with demographic and clinical data was administered. Then, the Quality-of-Life Questionnaire (EQ-5D-3L) and the pulmonary function test were scheduled. During the 12-month follow-up, the interviews were conducted by telephone or face-to-face contact before or after medical appointments, with an interval of 3 months. At the end of 1 year, the patients underwent a new spirometric test and responded to the EQ-5D-3L and Modified Medical Research Council (mMRC) questionnaires.

Outcome data

There are several factors that favor the development of bronchiectasis^{1,9,10}. In this study, we considered the following groups: idiopathic, postinfectious by pulmonary TB, postinfection non-TB, primary immunodeficiency (common variable immunodeficiency), Kartagener's syndrome, and "undetermined." The cases in which the etiology was under investigation or was incomplete were classified as "undetermined" etiology.

Exacerbation was defined as the care of the patient in an outpatient unit when not previously scheduled or in an emergency unit, with or without the need for antibiotic therapy intervention, with the at least three of the following four clinical data: increased dyspnea intensity, increased daily volume of sputum, altered secretion color, or fever [4,14] (>37.5°C). According to the study by Murray et al., sputum was defined as mucoid (clear), mucopurulent (pale yellow/pale green), and purulent (dark yellow/dark green)¹⁵.

Patients who had a daily cough with a mucoid, mucopurulent, or purulent sputum for at least 3 consecutive months in the 12-month period were considered as having "wet" bronchiectasis.

Functional indices such as the pre- and post-bronchodilator forced expiratory volume in 1 s (FEV₁), forced vital capacity (FVC), and FEV₁/FVC ratio were evaluated at the initial consultation and after 12 months. Ventilatory disorders were defined according to the criteria published by the American Thoracic Society (ATS)/European Respiratory Society (ERS) as normal, obstructive, restrictive, and mixed¹⁶.

Baseline and follow-up questionnaire

The baseline questionnaire contained the following data for collection: age, body mass index (BMI), the number of exacerbations, emergency visits, hospitalizations, the presence of fever (>37.5°C), increased dyspnea and sputum, change in sputum color and appearance, hemoptysis, the degree of dyspnea, the mMRC, therapeutic intervention with antibiotics, smoking (active, passive, ex-smokers, and nonsmokers), spirometry, etiology, "wet bronchiectasis," the number of affected lobes (the lingula was considered a separate lobe), daily approximate volume of sputum, comorbidities, vaccines (e.g., influenza and pneumococcal), respiratory physical therapy, colonization with Pseudomonas aeruginosa (PA), Aspergillus, and infections caused by nontuberculous mycobacteria (NTM). Items monitored at follow-up included the number of exacerbations, emergency visits, hospitalizations, the presence of fever (>37.5°C), increased dyspnea and sputum, change in sputum color and appearance, hemoptysis, and antibiotic therapy.

The quality-of-life questionnaire is an instrument composed of the EQ-5D-3L questionnaire and the Visual Analogue Scale (VAS)¹¹. The EQ-5D-3L jointly addresses physical functions (i.e., mobility, self-care, and pain/discomfort domains), social functions (i.e., habitual activities domain), and mental functions (i.e., anxiety/depression domain). Each domain/dimension is related to three levels of severity (i.e., no problems, some problems, and extreme problems)¹¹. The VAS consists of a ruler numbered from zero (worst health state imaginable) to 100 (best health state imaginable)¹¹, and the patient records the value that best represents his or her health state at the time. The survey was registered in the EuroQol Research Foundation website, and an authorization to apply the self-complete version of the EQ-5D-3L questionnaire and the face-to-face version of the EQ-5D-3L for patients with reading or writing difficulties was obtained. A validated version of the questionnaire in Portuguese was used in the study¹¹.

For the sample calculation, a standard deviation of 0.5 was considered, requiring 50 patients to detect a 7% difference in the quality of life with 95% confidence and 80% power. Numerical data were presented using mean and standard deviation or median and interquartile range, and categorical data were presented using percentage and absolute values. The Student's t, Mann–Whitney U, Kruskal–Wallis, ANOVA, chi-square, and Fisher's exact tests were used. For the elaboration of the graphs, the plotly package was used.

RESULTS

Of the 122 patients recruited, 1 patient withdrew the consent form, 21 were excluded because they did not meet all the eligible criteria, and 1 patient was lost to follow-up. Finally, only 100 patients were included in the analysis (Figure 1).

The general characteristics of the study population are expressed in Table 1. The patients were predominantly female (72%) and nonsmokers (81%), with a mean age of 56.94±15.32 years and a mean BMI of 24.42±5.13 kg/m². Women were older and had a higher BMI than men. In the tomographic findings, 79 (79%) individuals had bronchiectasis in more than one pulmonary lobe. The etiological predominance was related to the sequelae of pulmonary TB in 53% of the cases. Of the 79 (79%) patients with an associated comorbidity, 29 (29%) had at least one aggravation and 50 (50%) had two or more associated aggravations. Based on the history of recurrent respiratory disease, 55 (55%) patients had rhinosinusitis and 53 (53%) had a previous pneumonia at least once. The most commonly reported comorbidities in descending order were as

follows: systemic arterial hypertension (SAH, 27.9%), chronic obstructive pulmonary disease (COPD, 25.3%), diabetes mellitus (DM, 21.5%), and osteoarticular diseases (16.5%).

In the course of 1 year, 21 (21%) patients were colonized by PA and 2 (2%) were colonized by NTM. Also, 3 (3%) patients were previously colonized by fungi (Aspergillus). In the beginning of the study, 21 (21%) subjects presented grade 3 dyspnea according to the mMRC scale, and after 12 months of follow-up, this categorization increased by 53% (32 subjects). In addition, 22 (22%) patients had an exacerbation, 27 (27%) had two or more exacerbations, and 50 (50%) experienced no exacerbations. Of the 49 (49%) individuals who experienced exacerbations, 5 required hospitalization and 1 patient required two hospitalizations. A total of 20 (20%) patients sought the emergency unit or went to the clinic without prior appointment at least once, while 34 (34%) sought care two or more times (Table 2). There were no deaths during the study. Therapeutic intervention with antibiotics was not necessary in more than 50% of the patients.



Figure 1. Flowchart of the population in the study.

Table 1. Demographics and clinical characteristics of patients with noncystic fibrosis bronchiectasis.

Data	n=100	Male n=28	Female n=72	p-value*			
Age, years	56.94±15.32	55±15.31	57.69±15.36	0.435			
Body mass index, kg/m ²	24.42±5.13	22.75±3.44	25.07±5.54	0.042			
Smoking status							
Current smoker	4 (4.0)	1 (3.6)	3 (4.2)				
Former smoker	12 (12.0)	6 (21.4)	6 (8.3)	0.2498			
Passive smoker	3 (3.0)	0	3 (4.2)				
Nonsmoker	81 (81.0)	21 (75.0)	60 (83.3)				
Etiology							
Idiopathic	15 (15.0)	4 (14.2)	11 (15.3)				
Postinfection tuberculosis	53 (53.0)	16 (57.2)	37 (51.4)				
Postinfection nontuberculosis	23 (23.0)	7 (25.0)	16 (22.2)	0.6403			
Kartagener's syndrome	2 (2.0)	1 (3.6)	1 (1.4)				
Primary immunodeficiency	1 (1.0)	0	1 (1.4)				
Undetermined*	6 (6.0)	0	6 (8.3)				
Moist bronchiectasis	44 (44.0)	13 (46.4)	31 (43.1)	0.8243			
Number of affected lobes, n=92		·		0.5000			
1 lobe	13(14.1)	2 (8.0)	11 (16.4)	0.5023			
≥2 lobes	79 (85.9)	23 (92.0)	56 (83.6)				
Approximate daily sputum volume							
<100 ml	47 (47.0)	16 (57.2)	31 (43.1)	0.4080			
100-200 ml	23 (23.0)	6 (21.4)	17 (23.6)				
No sputum	30 (30.0)	6 (21.4)	24 (33.3)				
Number of comorbidities							
No comorbidities	21 (21.0)	7 (25.0)	14 (19.5)	0.8020			
1 comorbidity	29 (29.0)	8 (28.6)	21 (29.2)				
≥2 comorbidities	50 (50.0)	13 (46.4)	37 (51.4)				
Previous respiratory disease							
Rhinosinusitis	55 (55.0)	16 (57.1)	39 (54.2)	0.8262			
Tuberculosis	55 (55.0)	18 (64.9)	37 (51.9)	0.2710			
Pneumonia	53 (53.0)	12 (42.9)	41 (56.9)	0.2656			
Comorbidities	n=79	n=21	n=58				
Systemic arterial hypertension	45 (57.0)	8 (38.1)	37 (63.8)	0.0704			
Diabetes mellitus	17 (21.5)	5 (23.8)	12 (20.7)	0.7637			
GERD	7 (8.9)	1 (4.8)	6 (10.3)	0.6680			
Osteoarticular disease	13 (16.5)	1 (4.8)	12 (20.7)	0.1666			
Neoplastic disease	8 (10.1)	3 (14.3)	5 (8.6)	0.4322			
Cardiovascular disease	6 (7.6)	2 (9.5)	4 (6.9)	0.6538			
HIV	2 (2.5)	1 (4.8)	1 (1.7)	0.4635			
COPD	20 (25.3)	7 (33.3)	13 (22.4)	0.3836			
Asthma*	22 (27.9)	7 (33.3)	15 (25.9)	0.5744			
Pneumonectomy	3 (3.8)	0	3 (5.2)	0.5610			
Lobectomy	5 (6.3)	3 (14.3)	2 (3.4)	0.1139			
Depressive disorder	7 (8.9)	1 (4.8)	6 (10.3)	0.6696			
Hypothyroidism	4 (5.1)	0	4 (6.9)	0.5687			
Other comorbidities*	21 (26.6)	6 (28.6)	15 (25.9)	0.7816			

Date are presented as number (%) or mean±standard deviation (SD). BMI: body mass index; GERD: gastroesophageal reflux disease; COPD: chronic obstructive pulmonary disease; HIV: human immunodeficiency virus. *Other comorbidities such as psoriasis, chronic renal failure, alpha-1 anti-trypsin deficiency, cor pulmonale, glaucoma, Sjögren syndrome, and malnutrition.

The presence of limitations in relation to domains is detailed in Table 3. It was observed that no patient was confined in bed (mobility domain, level 3) or was unable to maintain their personal care (self-care domain, level 3) between the onset and after 12 months of follow-up. The habitual activities and pain/discomfort domains were statistically significant (p=0.0078 and p=0.0097, respectively). An increase of 18.5% in the incidence of extreme anxiety/depression was observed. During the study, no patient presented extreme limitations in all the domains. The quality-of-life assessment had an average score of 0.545±0.187 and 0.589±0.208, respectively (Table 3), between the onset and after the 1-year follow-up. There was statistical significance in the evaluation of HRQoL determined by EQ-5D-3L (p=0.011) and VAS (p=0.0018) (Table 3). After 1 year, 3 patients were unable to undergo a new spirometric test due to the associated diseases. Pulmonary function assessments showed a predominance of an obstructive ventilatory disorder (OVD) at baseline (67%) and after 12 months (72.9%).

Table 3 presents the mean value of the quality of life stratified by groups: with exacerbation and without exacerbation, with emergency unit care and those who did not require emergency care, with comorbidities and without comorbidities, and with hemoptysis and without hemoptysis. There was a statistically significant difference at the beginning and after 1 year of follow-up between the group with and without exacerbation (p=0.002 and p=0.001, respectively) and between the group with and without emergency unit care (p=0.006 and p=0.011, respectively).

DISCUSSION

Bronchiectasis is a complex and heterogeneous disease with clinical, radiological, microbiological, and prognostic variability, as seen in this study. The identification of risk factors related to worsening health can help in the development of

Table 2. EQ-5D-3L and spirometry at baseline and after 1-year follow-up.

Data		Baseline n=100	1 year n=99	p-value
EQ-5D-3L	-	0.545±0.187	0.589±0.208	0.011
Domain	Level response			
Mobility	No problems	38 (38.0)	47 (47.5)	0.1985
	Some problems	62 (62.0)	52 (52.5)	
	Extreme problems	O (O)	O (O)	
Self-care	No problems	61 (61.0)	69 (69.7)	0.2339
	Some problems	39 (39.0)	30 (30.3)	
	Extreme problems	O (O)	O (O)	
Usual activities	No problems	28 (28.0)	32 (32.3)	0.0078
	Some problems	71 (71.0)	57 (57.6)	
	Extreme problems	1 (1.0)	10 (10.1)	
Pain/discomfort	No problems	18 (18.0)	36 (36.4)	0.0097
	Some problems	63 (63.0)	52 (52.5)	
	Extreme problems	19 (19.0)	11 (11.1)	
Anxiety/depression	No problems	22 (22.0)	29 (29.3)	0.2014
	Some problems	51 (51.0)	38 (38.4)	
	Extreme problems	27 (27.0)	32 (32.3)	
FEV ₁ , L	Pre-BD	1.35±0.60	1.32±0.61	0.1099
	Post-BD	1.38±0.61	1.37±0.62	0.3555
FVC, L	Pre-BD	2.34±2.93	2.05±0.78	0.4013
	Post-BD	2.07±0.73	2.09±0.80	0.6854
FEV ₁ /FVC, %	Pre-BD	64.36±13.40	64.16±13.73	0.9310
	Post-BD	1.35±0.60	1.32±0.61	0.1099

Data are expressed as n (%) and mean \pm SD. VAS: Visual Analogue Scale; VEF₁: forced expiratory volume in 1 s; FVC: forced vital capacity; pre-BD: pre-bronchodilation; post-BD: post-bronchodilation.

Groups	EQ-5D-3L Baseline	p-value ^a	EQ-5D-3L 1 year	p-value ^b
Exacerbation ^c	0.487±0.139	0.000	0.521±0.190	0.001
Nonexacerbation	0.601±0.210	0.002	0.656±0.204	
Visit to emergency unit ^d	0.499±0.158	0.007	0.551±0.195	0.011
Number of visits to the emergency unit	0.599±0.204	0.006	0.651±0.200	
One comorbidity ^e	0.564±0.161		0.632±0.199	0.050
≥2 comorbidities	0.511±0.196	0.147	0.539±0.207	
No comorbidities	0.601±0.189		0.650±0.200	
Hemoptysis ^f	0.537±0.169	07/0	0.576±0.204	0.664
No hemoptysis	0.549±0.195	0.768	0.595±0.211	
Colonized ^g	0.463±0.155	0.175	0.508±0.181	0.112
Noncolonized	0.555±0.189	0.165	0.605±0.211	
Hospitalized due to respiratory problems ^h	0.387±0.182		0.405±0.165	0.461
Hospitalized due to other causes	-	0.181	0.396±0.111	
Not hospitalized	0.550±0.186		0.601±0.207	

Table 3. Quality of life stratified by groups at baseline and after 1-year follow-up.

Data are expressed as mean±SD. ^ap=baseline. ^bp=1-year follow-up; ^cExacerbation vs. nonexacerbation groups. ^dVisit to emergency unit vs. no visit to the emergency unit groups. ^e1 comorbidity vs. ≥2 comorbidities vs. non-comorbidities groups. ^fHemoptysis vs. nonhemoptysis groups. ^gColonized vs. noncolonized groups. ^hHospitalized due to respiratory problems vs. hospitalized due to other causes vs. not hospitalized groups.

individualized strategies to improve the quality of life. Choosing the EQ-5D-3L multiparameter instrument to monitor the quality of life of patients facilitates understanding, as it uses a scale with score ranging from 0 to 100%. The health status of each individual was determined through the EQ-5D-3L tool. Similar to the previous findings by Hill et al.¹, Aksamit et al.¹⁷, and Bogossian et al.⁹, we found a higher incidence of bronchiectasis in women (72%) than in men (28%). The results also showed that the main etiology of bronchiectasis was related to the sequelae of pulmonary TB (52%). This cause is common in countries with a high number of TB cases¹⁸. This prevalence is also evident in Brazil (Bogossian et al.⁹, 42.7%) and China (Xu et al.¹⁹, 31.1%), in contrast to the etiological findings of developed countries with about 40% of cases attributable to idiopathic bronchiectasis¹⁴. We noted a poor quality of life for these individuals, as assessed by the EQ-5D-3L questionnaire, which is used to measure and evaluate the health status of patients with bronchiectasis. The mobility and self-care domains were associated with a lesser effect on health status, whereas habitual activities and anxiety/ depression contributed to a poorer health status, thus reducing the quality of life. The study also reported that exacerbation, emergency care, comorbidities, colonization, and hospitalization had had a significant negative effect on health status. The results indicate that these variables contribute to the worsening of the quality of life of these individuals. Patients with

bronchiectasis tend to present with exacerbation frequently, resulting in the aggravation or appearance of clinical symptoms that may require hospitalization and inclusion of drug therapy involving antibiotics, corticosteroids, and bronchodilators. According to the study by Redondo et al.⁴, the increase in the frequency of exacerbations was associated with factors such as colonization, mainly by PA, air pollution, and comorbidities. Chang and Bilton²⁰ reported in their study that exacerbations result in lung function decline, a worsened quality of life, and hospital admissions. In our study, we found that exacerbations were frequent at the 1-year follow-up. Of the 49 patients who experienced exacerbations, 82% had comorbidities associated with bronchiectasis. Most exacerbations were marked by increased dyspnea and volume of sputum, sputum purulence, hemoptysis, and fever.

Currently, despite the technological advances and the elaboration of guidelines, there are still difficulties and a lack of consensus in some of the approaches related to bronchiectasis. Less is known about the real risk factors that could lead to hospitalization. Ringshausen et al.²¹ reported that the average annual hospitalizations in the United States was 16.5 admissions per 100,000 inhabitants, while in Germany this value was 9.4. In our study, there were 9 (9%) hospitalizations during the follow-up. Notably, 5 individuals required hospitalization due to bronchiectasis, and 1 patient required a new hospitalization.

Hemoptysis is another complication that can affect bronchiectasis patients and may require immediate medical assistance and the administration of large blood volumes. In their recent study, Bhalla et al.²² described the main etiologies of hemoptysis in patients who sought emergency care in India. Of the patients admitted, 65% had hemoptysis due to active pulmonary TB or its sequelae and 9.3% of cases were due to bronchiectasis. Lundgren et al.²³ who conducted their study in Brazil found that 38% of cases of hemoptysis were caused by bronchiectasis. In this study, of the 31 patients who reported small volumes of hemoptysis (<100 mL/24 h) or blood streaks, 17 previously had pulmonary TB.

Bronchiectasis individuals are commonly colonized by the pathogens PA and *Haemophilus influenzae*. In this study, 21 (21%) patients were colonized by PA. Colonization by PA may involve 25–58% of cases and tends to lead to a more rapid lung function decline, frequent exacerbations, and poorer quality of life²⁴.

We identified 79 patients with comorbidities concurrent with bronchiectasis, with half of the subjects presenting multiple comorbidities. The recent consensus stated that cardiovascular disorders, COPD, diabetes, gastroesophageal reflux disease (GERD), psychological diseases, and pulmonary hypertension are more likely to exist in conjunction with bronchiectasis and that such comorbidities contribute to morbidity and mortality, and worsening of the quality of life²⁵.

The main limitations of this study are related to sample size and the follow-up period, with long-term studies being required. Another limitation of the study was the recruitment

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of volunteers from a single-center specialized in bronchiectasis, representing a subgroup of patients who regularly attended medical appointments. However, one of the strengths of the article was its prospective design, with close monitoring and determining that quality of life needs to be incorporated as one of the indicators of therapeutic management.

CONCLUSION

Our population had a high frequency of exacerbations, multiple comorbidities, and airflow obstruction. Patients with NCFB presented with marked impairment in HRQoL with moderate-to-extreme limitations of their daily activities. The quality of life tended to worsen in the presence of exacerbations and in individuals who sought emergency care and had comorbidities, colonization, and hospitalization. The incorporation of a quality-of-life assessment in patients with bronchiectasis in the clinical practice is a necessary effort to be implemented, considering that this parameter may lead to an individualized treatment, thus improving the outcomes for these patients.

AUTHORS' CONTRIBUTIONS

SPM, BRT, RR: Conceptualization and writing – original draft. **SPM, CHC, AJL, CHC, BRT:** Data curation. **SPM, REBS, WC:** Investigation. **SPM, BRT, CHC, RR:** Methodology. **BRT:** Formal analysis. **SPM, RR:** Writing – review and editing, and project administration. **RR:** Supervision.

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