Quality of life and its determinants in patients with noncystic fibrosis bronchiectasis

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Background: Promoting quality of life (QoL) in patients with bronchiectasis, as a chronic disease, is a part of therapeutic principles. This study aimed to investigate QoL and its determinants in patients with noncystic fibrosis (CF) bronchiectasis. **Materials and Methods:** This cross-sectional study was conducted on 62 patients (38.7% male, mean age: 44) with non-CF bronchiectasis and involvement of ≥2 lobes in Qazvin, Iran. QoL was evaluated using the St. George's Respiratory Questionnaire (SGRQ). The relationships of QoL subscales with clinical (cough, dyspnea, and sputum volume) and paraclinical (spirometry, computerized tomography scan, sputum microbiology, and 6-min walk test [6-MWT]) were assessed using Pearson's correlation coefficient and multiple linear regression analyses. **Results:** The mean SGRQ total score was 53.1 (standard deviation 19.8) out of 100. The level of dyspnea ($r = 0.543$, $P < 0.001$), cough ($r = -0.594$, $P < 0.001$), 6-MWT ($r = -0.520$, $P < 0.001$), sputum volume ($r = 0.423$, $P = 0.002$), and number of exacerbations ($r = 0.446$, $P = 0.009$) had significant correlation with SGRQ total score. In multiple regression analysis, forced expiratory volume in 1 s was an independent predictor of the symptom ($\beta = -0.22$, $P = 0.048$) and activity ($\beta = -0.43$, $P = 0.03$) subscales, whereas cough was an independent predictor of the symptom subscale ($\beta = -2.1$, $P = 0.002$). **Conclusion:** In patients with non-CF bronchiectasis, the extent of lung impairment has a lower effect on the QoL than clinical symptoms. It seems that the QoL can be improved through the proper treatment of clinical symptoms and rehabilitation for promoting 6-MWT.

Key words: Bronchiectasis, noncystic fibrosis, pulmonary function tests, quality of life

INTRODUCTION

Bronchiectasis is a chronic lung disease caused by frequent lung infections and bronchial degeneration. Wherein the individual is infected frequently because the body's immune system cannot remove the microbes from the bronchi. This infection and the subsequent inflammation result in the irreversible dilation of the respiratory tract.[1] Consequently, lung symptoms such as cough, sputum, hemoptysis, and dyspnea emerge cause restrictions in social relationships that lead to a frequent referral to the doctor. Prescribing drugs such as antibiotics and admission to the hospital decrease the quality of life (QoL). Many extrapulmonary involvements can also be observed.[2-4] Pulmonary and extrapulmonary involvement in bronchiectasis can reduce the QoL of the patient. Besides, it increases mortality.

Evaluating the QoL, finding the significant factors, and correcting those factors are among the most critical management issues in patients with chronic diseases. QoL of each individual is affected by various factors. In addition to socioeconomic conditions, health is the most vital factor affecting QoL of any individual. In chronic diseases, if controllable factors affecting QoL could be identified, QoL can be increased through programmed interventions.

Some patients with bronchiectasis have low QoL, although they have many clinical symptoms, a large

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extent of pulmonary involvement in computerized tomography (CT) scan, or high respiratory obstruction in spirometry. Besides, there are patients with poor QoL and minimum pulmonary involvement or low clinical symptoms. Few studies have focused on the factors affecting QoL of the patients with non-cystic fibrosis (CF) bronchiectasis,[5-7] particularly in developing countries. Therefore, we designed the present study to investigate the predictors of QoL and its determinants in patients with non-CF bronchiectasis.

MATERIALS AND METHODS

Study design and participants
This cross-sectional study was conducted on all patients with non-CF bronchiectasis referred to pulmonary diseases clinic in Qazvin, Iran, from May 2014 to September 2016. All eligible patients (by census method) entered into the study. The inclusion criteria were: the age of above 18 years old, non-CF bronchiectasis, disseminated bronchiectasis, the involvement of ≥2 lobes, and no exacerbation in the recent month. The patients with bronchiectasis caused by tuberculosis or those having any other chronic diseases (chronic obstructive pulmonary disease [COPD], congestive heart failure, malignancy, chronic kidney disease, pulmonary fibrosis, and cirrhosis) at the same time were excluded. This study is financially suppoted by Qazvin University of Medical Sciences.

Data collection
A trained team investigated the patients who referred to the hospital in the fasting state in the morning. They were asked not to use any bronchodilator drugs at least 12 h ago. Patients first filled out the primary questionnaire containing demographic information and then, the Persian St. George's Respiratory Questionnaire (SGRQ).

Quality of life
This SGRQ is one of the most reliable questionnaires for investigating QoL in lung patients, which was initially designed for assessing patients with COPD.[8] However, in numerous subsequent studies, the validity and reliability of this questionnaire have been approved in other lung diseases such as bronchiectasis.[9] SGRQ has already been translated into Persian, and its validity and reliability have been verified.[10] The questionnaire consists of 50 items and two sections (symptom and the patient's current condition).[8] The symptom subscale includes the patient's clinical symptoms (dyspnea, cough, sputum, wheezing, etc.) in terms of sequence and severity in the past month. The patient's current condition includes two subscales (activity and impact). The activity subscale assesses the effect of the disease on daily activity. The impact subscale assesses the impact of the disease on the overall health of the individual.

Since the SGRQ is a supervised self-administered questionnaire, all the patients filled out the questionnaire in the center under the supervision of a trained nurse. The principles of completing the questionnaire were based on the relevant guideline. The scores for total QoL and each subscale were computed by summing over the related items and then normalized into 0–100 range by the following formulae:

Normalized score = (raw score-min)/(max − min) × 100.

In each subscale and QoL score, 0 represents excellent health, and a higher score shows the lower QoL.[8]

Clinical signs and symptoms
Clinical signs and symptoms (dyspnea, cough, and sputum volume), number of exacerbations, 6-mi walk test (6-MWT), and lung parameters (spirometry, microbiology, and CT scan) were evaluated for every patient. Height was measured with an accuracy of 0.5 cm, and weight was measured to the nearest 100 g. Body mass index (BMI) was calculated as weight in kg divided by the height (m) squared. BMI <18.5 kg/m^2 was considered as malnutrition.[11]

Pulmonary function test
Lung function was evaluated by a spirometer (Jaeger Ltd Hochberg, Germany) per American Thoracic Society standards.[12] Spirometry was performed in two steps before and after receiving 200 μg of salbutamol spray. Forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and FEV1/FVC values were defined based on absolute number as well as percentage. FEV1/FVC ratio of <70% was considered as airway obstruction.[13] Based on FEV1, the patients were categorized into four groups (≤30%, 30%–50%, 50%–80%, and ≥80%). Although this classification is initially designed for COPD, it has also been used for bronchiectasis in numerous studies.[14] Reversibility in FEV1 was utilized to categorize the patients into two groups: Nonreversible and reversible (R). The reversibility standard was defined as an increase of above 12% and 200 ccs in FEV1.[12]

The six-minute walk test
The 6-MWT was performed in a 30-meter hall, and the distance walked per 6 min, the arterial oxygen saturation (satao2), and oxygen variations were recorded according to the standards.[15] The level of dyspnea was calculated based on the Medical Research Council's Dyspnea Scale (MRC). This five-level scale evaluates the level of dyspnea on the daily activities of the individual.[16] Level 5 is the worst severity of dyspnea, and Level 1 represents the lowest severity of dyspnea. For evaluating the severity of the cough, Leicester Cough Questionnaire (LCQ) was employed.[17] A 19-item questionnaire that consists of three subscales (physical, psychological, and social) evaluating

the effect of cough on the QoL. The score range for each subscale is 1–7, and the total score range is 3–21. A higher score represents the lower effect of cough on QoL.

Computerized tomography scan
The extent of pulmonary involvement was evaluated by an expert radiologist using high-resolution computed tomography and based on the Bhalla score.[18] Lingula and middle lobe were considered as independent lobes. Each lung lobe was scored as 0 (no bronchiectasis), (1) (cylindrical bronchiectasis in a single lung segment), (2) (cylindrical bronchiectasis in more than one lung segment), or (3) (cystic bronchiectasis). The maximum score was 18 points.

Bacteriologic evaluation
For bacteriological studies, the morning sputum was collected after oral washing and transferred to the laboratory. In addition to smear, the culture was performed in a typical environment. The presence of <10 epithelial cells and more than 25 PMN cells per microscopic field was considered an acceptable sputum sample. According to the bacteria isolated from the smear and sputum cultures, the patients were categorized into three groups of *Pseudomonas aeruginosa*, nonpseudomonas aeruginosa, and negative culture. On the other hand, a 50-cc scaled container was given to the patient to determine the sputum volume, the patient was asked to collect the sputum for 24 h, and its volume was recorded. Exacerbation frequencies leading to the hospitalization of patients in the past year were recorded based on the reports of the patient.

Ethical considerations
Ethics Committee approved the research protocol of Qazvin University of Medical Sciences. All the patients signed the informed consent form.

Statistical analysis
Data were described as mean standard deviation (SD) and frequency (percent) for numeric and categorical variables, respectively. The normality of the numeric variables was assessed and confirmed by the Kolmogorov–Smirnov test, Shapiro–Wilk test, and q-q plot. For missing data, the mean replacement was used. Pearson's correlation coefficients assessed the relationships between QoL and the subscales' scores with other variables. Homojesity of varicances was also assessed by Leven test, which was satistified. The relationships between QoL and the subscales' scores and bacteriologic categories were evaluated by the Analysis of Variance followed by Tukey *post hoc* tests. To assess the simultaneous relationships and to control confounders, multiple linear regression analyses (Stepwise method) were carried out for QoL and the subscales' scores, separately. The independent variables were the variables significantly correlated to the total and subscales' scores in the correlation

analysis. Squared of a simple correlation coefficient of determination coefficient ($R2$) was used to determine the contribution of identified variables in predicting each subscale and total score. All analyses were conducted using the SPSS software version 22 (IBM Corp., Armonk, NY, USA) at the alpha = 0.05 significance level.

RESULTS

Seventy-three participants were eligible for the study and 11 patients were excluded as they didn't meet the criteria for various reasons. Five patients had tuberculosis, three patients had comorbidities at the same time (COPD and heart failure), and three patients did not complete the study. A total of 62 patients were entered the study. The mean age was 44 (SD15.8) years old. Twenty-four patients (38.7%) were male. The clinical and paraclinical characteristics of the study patients are presented in Table 1. The mean SGRQ total score was 53.1 (SD 19.8). The highest SGRQ score was in symptom and activity subscales. Forty-three patients (68%) had airway obstruction, and only 14 (20.2%) were reversible in FEV1. Eleven patients (17.7%) had malnutrition, and 19 patients (30%) were infected with Pseudomonas. In the 6-MWT, the average walked distance was 449 (SD 94) m, and 14 patients (22%) had a drop of above 4% in O2 saturation.

The correlations between QoL and the subscales scores' with other variables are shown in Table 2. The level of dyspnea, cough rate, and walked distance in 6-MWT had the highest correlation with the QoL score ($P < 0.001$). The sputum volume and number of admissions due to exacerbation had a strong correlation with the QoL score ($P < 0.05$). The sputum volume and cough rate were associated with all the QoL subscales. The respiratory obstruction rate based on the FEV1/FVC ratio, as well as the extent of pulmonary involvement based on a CT scan, was not associated with any of the QoL subscales.

The mean score of the activity subscale was 76.40 (SD 22.56), 54.19 (SD 25.69), and 52.94 (SD 24.11) in patients with *Pseudomonas aeruginosa*, nonpseudomonas aeruginosa, and negative culture, respectively ($P = 0.025$). The activity score in patients with *Pseudomonas aeruginosa* was significantly higher than patients with negative culture ($P = 0.041$). The activity score in patients with *Pseudomonas aeruginosa* was significantly different from the patients with nonpseudomonas aeruginosa with borderline significance ($P = 0.056$).

The results of the multiple regression analysis of the predictors of QoL are presented in Table 3. MRC, sputum volume, 6-MWD, exacerbation, LCQ, and BMI explained 62.2% of the variances in the total score. Among the subscales, the factors evaluated in this study could predict the highest (61.8%) and lowest (47.7%) variances in the

activity subscale and symptom subscale, respectively. FEV1 was an independent predictor of the symptom and activity subscales, while cough was an independent predictor of the symptom subscale. None of the studied factors was an independent predictor of QoL.

Table 1: Demographic profile of the patients (*n*=62)

Parameter	Mean/n (SD/%)	Minimum-maximum
Age (year)	44.0 (15.8)	18.0-72.0
Male	24 (38.7)	
BMI	25.3 (6.6)	13.5-40.4
MRC	2.4 (1.2)	1.0-5.0
FEV1 (%) $_{pre}$	57.8 (23.3)	22.3-131.6
FVC (%) $_{pre}$	70.1 (20.2)	35.1-128.6
FEV1/FVC (%) $_{pre}$	66.8 (12)	42.5-90.0
Reversibility	14 (20.21)	
CT score	3.3 (1.4)	2.0-18.0
6-MWT		
$\quad$ Sat$_a$O$_2$ at rest	90.8 (5.1)	74.0-99.0
$\quad$ Distance	446 (94)	162-636
$\quad$ >4% decrease in Sat$_a$O$_2$	14 (22)	
Cough scale LCQ	10.5 (4.3)	5.0-21.0
Admit for exacerbation (N/y)	0.64 (0.25)	0.0-7.0
Sputum volume (cc)	35 (31)	10-150
Bacteria		
$\quad$ *Pseudomonas aeruginosa*	19 (30.6)	
$\quad$ Nonpseudomonas	19 (30.6)	
$\quad$ Negative culture	24 (38.7)	
QoL and the subscales' scores		
$\quad$ Symptom	59.4 (19.6)	11.7-100.0
$\quad$ Activity	59.7 (24.3)	13.7-100.0
$\quad$ Impact	47.0 (23.0)	6.7-86.0
$\quad$ Total	53.1 (19.8)	15.7-88.5

BMI=Body mass index; MRC=Medical Research Council's Dyspnea Scale; FEV1=Forced expiratory volume in 1 s; FVC=Forced vital capacity; CT=Computerized tomography; 6-MWT=The 6 min walk test; LCQ=Leicester cough questionnaire; QoL=Quality of life; SD=Standard deviation

DISCUSSION

This study was designed to evaluate the predictors of QoL among non-CF bronchiectasis patients. In this study, it was found that evaluating clinical symptoms based on objective criteria (dyspnea [MRC], cough [LCQ], and sputum volume) were related to QoL subscales. The maximum correlation belonged to dyspnea. In the regression analysis that was performed separately for each subscale, the independent relationship was found in the FEV1 level before bronchodilators on the activity subscale, in cough rate, and FEV1 on the symptom subscale, and dyspnea level on the impact subscale. However, none of the evaluated predictors were independently predicted the QoL score. However, the dyspnea level, cough rate, and sputum volume were the most related predictors for the QoL score. The extent of pulmonary involvement in CT scans had no significant relation with the QoL of patients. Although the severity of respiratory obstruction in the spirometry was not related to QoL in the primary analysis, it was found as an independent predictor in multiple regression analysis.

In previous works, different relations of the predictors were found with QoL. According to Martinz *et al*., the sputum volume, dyspnea level, and FEV1 level were the most related predictor in the QoL of the patients with bronchiectasis.[7] However, according to Wilson *et al*., the frequency of exacerbation in the past year was the most related predictor of QoL.[9] In most studies, the sputum volume was a predictor of the QoL of the patients with non-CF bronchiectasis.[7,19,20] The dyspnea level in the patients with bronchiectasis was one of the predictors of QoL.[9,21] In this study, the dyspnea level predicted other subscales, except the symptom subscale.

Table 2: Pearson correlation coefficient (*r*) between the study variables with subscale and quality of life and the subscales' scores

	Age (year)	BMI	FEV1 pre	FVC pre	FEV1/ FVC	MRC	Sputum V.	6-MWT	O$_2$ rest	Exacerba	CT	Reversi	Microb	LCQ
Symptoms														
r	0.101	0.186	−0.257	−0.168	−0.244	0.181	**0.416**	−0.245	−0.210	0.222	0.086	−0.167	0.202	**−0.503**
P	0.456	0.173	0.058	0.221	0.073	0.185	**0.002**	0.074	0.127	0.193	0.596	0.257	0.205	**<0.001**
Activity														
r	0.185	0.318	**−0.300**	−0.245	−0.210	**0.577**	0.345	**−0.607**	**−0.328**	**0.466**	0.220	−0.028	**−0.361**	**−0.296**
P	0.172	0.019	**0.028**	0.074	0.127	**<0.001**	0.012	**0.000**	**0.016**	**0.005**	0.172	0.848	**0.022**	**0.037**
Impacts														
r	0.183	0.230	−0.086	−0.098	0.019	**0.505**	**0.411**	**−0.440**	−0.255	**0.373**	0.091	−0.038	0.003	**−0.640**
P	0.185	0.101	0.547	0.489	0.894	**<0.001**	**0.003**	**0.001**	0.070	**0.033**	0.585	0.799	0.988	**<0.001**
QoL														
r	0.184	0.276	−0.192	−0.171	−0.084	**0.543**	**0.423**	**−0.520**	**−0.338**	0.446	0.154	−0.058	−0.063	**−0.594**
P	0.186	0.050	0.176	0.230	0.558	**<0.001**	**0.002**	**<0.001**	**0.016**	0.009	0.362	0.702	0.706	**<0.001**

Pearson correlations and *P* values for significant relationships are shown in bold. BMI=Body mass index; MRC=Medical Research Council's Dyspnea Scale; FEV1=Forced expiratory volume in 1 s; FVC=Forced vital capacity; CT=Computerized tomography; 6-MWT=The 6-min walk test; LCQ=Leicester cough questionnaire; QoL=Quality of life

Table 3: Results of the multivariate regression examining the contributions of the studied variables to the quality of life and subscales' scores

Variable	R	R2 (%)	β	P
Symptom	0.48	47.7		
Sputum volume			0.07	0.345
Sum-LCQ			−2.05	**0.002**
FEV1 pre			−0.22	**0.048**
Activity	0.86	85.6		
BMI			1.28	0.137
FEV1 pre			−0.34	**0.035**
Sputum volume			0.22	0.308
Microbe			−15.88	0.055
6-MWT			−0.01	0.911
Exacerbation			−1.81	0.541
Sum LCQ			−0.83	0.599
Impact	0.62	61.8		
MRC			7.90	**0.034**
Sputum volume			0.02	0.904
6-MWD			0.04	0.568
Exacerbation			0.62	0.845
Sum LCQ			−1.30	0.176
Total	0.62	62.2		
MRC			5.44	0.091
Sputum volume			0.04	0.788
6-MWD			−0.03	0.651
Exacerbation			1.26	0.652
Sum-LCQ			−1.30	0.130
BMI			5.90	0.337

P values for significant relationships are shown in bold. BMI=Body mass index; MRC=Medical Research Council's Dyspnea Scale; FEV1=Forced expiratory volume in 1 s; FVC=Forced vital capacity; CT=Computerized tomography; 6-MWT=The 6 min walk test; LCQ=Leicester cough questionnaire; QoL=Quality of life

The findings of spirometry, microbial colonization, as well as the extent of pulmonary involvement in CT scans were the most related lung parameters of the patients with bronchiectasis. It seems that these parameters should have a significant effect on the QoL of patients with bronchiectasis. In the present study, the presence of *Pseudomonas aeruginosa* was related to lower QoL in the activity subscale. FVC, FEV1/FVC, and reversibility level of respiratory after salbutamol inhalation were not related to QoL. On the other hand, although FEV1 was an independent predictor of the activity subscale before bronchodilator consumption, it was not related to other subscales. No relationship was observed between the extent of pulmonary involvement in CT scan and QoL of the patients with bronchiectasis. Few studies have found such a correlation,[14] but in different studies such as this one, no correlation was found between the extent of pulmonary involvement in CT scan and.[7,22-24] This indicates that the related factors for the daily life of the patients with bronchiectasis are beyond the extent of the lung tissue damage. The results were also different regarding the relationship of microbial colonization with the QoL of the patients with bronchiectasis. In some studies, the infection with Pseudomonas was negatively related to QoL;[9,25,26] in some other works, the correlation has not been found.[7] In this study, the infection with *Pseudomonas aeruginosa* only was related to the activity subscale, but not other subscales.

Bronchiectasis leads to weakness of the peripheral muscles, and the resulting decrease in exercise capacity, along with lung dysfunction, reduces the 6-MWD.[4] In such conditions, the QoL of the patient is expected to be reduced. According to our findings, the 6-MWD was directly related to activity and impact subscales. However, it was not related to the QoL score. Although the primary arterial oxygen saturation was related to QoL, the oxygen drop during activity was not related to QoL. In some studies, 6-MWD has been related to QoL.[27]

In this study, the primary analysis of several factors was related to QoL. However, in the multiple regression analysis, the independent relations were only observed for cough and FEV1 on the symptom, FEV1 level on activity, and dyspnea level (MRC) on the impact subscale. There was no independent predictor for QoL. Since bronchiectasis is a disease with many extrapulmonary effects, no factor independently predicted the QoL of patients. Moreover, since the socio-economic factors are also crucial in this regard, no independent predictor was found. However, the finding showed that the most important predictors of QoL were controllable factors. The clinical parameters with the most related predictors with the QoL of the patients with bronchiectasis. Some of the studies carried out on other chronic lung diseases such as COPD have also indicated that the clinical symptoms affected more considerably than the extent of pulmonary involvement in QoL.[28] Accordingly, regardless of pulmonary impairment, the QoL of patients can be improved by controlling the clinical symptoms.

Limitation
This study had some limitations. First, it's the cross-sectional design in which the cause and effect relationships could not be inferred. Cohort studies to pursue the change in QoL of the patients are suggested. Second, the small sample size that makes our study under power to detect the important relationships, especially in the multivariate analyses, more extensive or multicenter studies, to find and confirm the results are highly recommended. However, it should be noted that all patients in the only referral clinic in Qazvin were evaluated in this study.

CONCLUSION

In this study, it was found that the extent of pulmonary involvement in CT scan, spirometry, and microbial colonization of bronchi had the lowest effect on QoL, the predictors in which no intervention can be performed.

Therefore, it seems that via the proper treatment of dyspnea, management of malnutrition, rehabilitation for promoting 6-MWD, and supportive interventions for reducing the sputum production, QoL of the patients can be improved.

Conflicts of interest
There are no conflicts of interest.

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