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The Assessment of Health-Related Quality of Life in Scleroderma-Interstitial Lung Disease

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ABSTRACT

Introduction: Pulmonary involvement is the most common cause of mortality and disability in patients with systemic sclerosis and it significantly affects the quality of life in these patients. Therefore, early diagnosis and treatment of pulmonary involvement seems necessary in patients with SSc. In this study, we aimed to assess the health-related quality of life (HRQoL) in patients with Scleroderma-Interstitial Lung Disease (SSc-ILD) and its relationship with pulmonary function parameters.

Materials and Methods: Considering the inclusion and exclusion criteria, 25 patients with SSc-ILD were enrolled in this cross-sectional study from April 2012 to June 2013. Full tests of lung function, including body plethysmography and diffusing capacity of the lungs for carbon monoxide (DLCO), 6-minute walk distance (6MWD), and pulse oximetry were performed. The HRQoL was assessed using St. George's and CAT questionnaires; also, dyspnea was evaluated for all the patients, using modified medical research council (MMRC) scale. Afterwards, the relationship between the total scores of HRQoL questionnaires and the severity of lung disease was analyzed, based on the recorded variables.

Results: The mean age of the patients was 40.36±9.50 years and the mean duration of the disease was 7.16±4.50 years. A statistically significant inverse correlation was observed between 6MWD (r=-0.50, *P*=0.01), DLCO (r=-0.67, *P*<0.001), and CAT total score. In addition, there was a statistically significant negative association between CAT score and total lung capacity (r=-0.46, *P*=0.01). Finally, a significant direct relationship was observed between the total scores of CAT and St. George's questionnaires (r=0.75, *P*<0.001).

Conclusion: The results of this study showed that CAT questionnaire is a suitable tool for assessing the quality of life in SSc patients; moreover, it is significantly related to the factors associated with pulmonary function. Therefore, the CAT questionnaire may be used to track pulmonary function in SSc patients.

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Introduction

Systemic sclerosis (SSc) is a connective tissue disease of unknown etiology. It is characterized by progressive tissue fibrosis and vascular damage, and is manifested as either diffuse or limited SSc (1). SSc, similar to other connective tissue diseases, is more common among women, particularly at reproductive age (2, 3). Diffuse SSc (dSSc) is characterized by the thickening of the

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skin and the apparent involvement of several internal organs, particularly the lungs, gastrointestinal tract, heart, and kidneys.

Interstitial lung disease (ILD) has been observed in many patients with dSSc and is now a major cause of morbidity and mortality (3). Pulmonary involvement may remain asymptomatic until the advanced stages of the disease. The most common presenting symptoms of pulmonary involvement are dyspnea, fatigue, and reduced exercise capacity. Pulmonary function disorder in these patients is characterized by a progressive decline in daily activities, the patient's emotional status, and Health Related Quality of Life (HRQoL) (4).

Given the importance of HRQoL in the daily function of patients with lung disease, several questionnaires have been designed to for its assessment, and St. George's questionnaire is one of the most widely used (5). This questionnaire has been previously used for patients with idiopathic pulmonary fibrosis, ILD, and SSc; it also has a close association with pulmonary function and daily activity level (4, 6). The main problem of this questionnaire is that it is too long and therefore time-consuming, which limits its application in clinical practice.

Another questionnaire has been recently designed, named COPD Assessment Test (CAT), which includes patients with pulmonary disease. This questionnaire is quite short and has a high potential for the assessment of HRQoL (7, 8). The CAT questionnaire is also used for ILD patients, and is associated with pulmonary function parameters in patients (9).

Given the importance of HRQoL in patients with scleroderma, and lack of similar studies in this field, the current study was designed with the aim to assess HRQoL, using CAT questionnaire in SSC-ILD patients. In addition, we evaluated the relationship between CAT scores and pulmonary function parameters in SSc patients.

Materials and Methods

The present cross-sectional study was performed from April 2012 to June 2013, in COPD Research Center, Mashhad University of Medical Sciences, Mashhad, Iran. All patients with dSSc, who had referred to the Rheumatology Research Center of Mashhad University of Medical Sciences, and were willing to participate, were included in the study. The patients were selected after the confirmation of dSSc by a rheumatologist, [according to the diagnostic criteria of American Rheumatism Association (ARA)] (10) and the presence of a lung restrictive pattern in the spirometry (FVC<80%).

The exclusion criteria were as follows: 1) secondary pulmonary fibrosis due to factors such as idiopathic pulmonary fibrosis, occupational diseases, radiation, and medication use, 2) previous history of pulmonary diseases (restrictive/obstructive pulmonary diseases) due to the reasons other than scleroderma, 3) movement disorders such as joint problems or severe skin stiffness of lower extremities, 4) previous history of smoking, 5) psychiatric and mood disorders, and 6) pulmonary arterial hypertension (PAP> 60).

All patients were referred to the COPD Research Center to perform complete pulmonary function tests (PFTs) under the supervision of two pulmonologists. Body plethysmography (ZAN 500 Plethysmograph, nSpire Health, Inc., Longmont, Co, US) was performed for all patients and forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC, and diffusion of lung for carbon monoxide (DLCO) were recorded. All patients performed the 6-minute walk distance (6MWD) test on a 30-meter flat corridor, based on the American Thoracic Society guideline (11).

The percent of oxygen saturation (SpO2) was determined by pulse oximetry before and after 6MWD (PC60C, Devon Medical, King of Prussia, PA, USA). The severity of dyspnea in patients was recorded based on the patients' response to the grading system of Modified Medical Research Council scale (MMRC). The grading was as follows:

grade 0: no dyspnea; grade 1: dyspnea when walking fast on a flat surface or climbing the stairs; grade 2: walking slower than Individuals of the same age on a flat surface or dyspnea while walking on a flat surface; grade 3: subject stops walking when walking normally on a flat surface or for a 100-meter distance, grade 4: unable to leave the house due to dyspnea, or dyspnea while getting dressed (12).

The CAT questionnaire was used to assess HRQoL (8). This questionnaire composed of eight questions regarding coughing, sputum, chest tightness, dyspnea during physical activity, restriction of movement at home, the ability to leave the house, sleeping, and energy. Each question was allocated a score between 0 to 5, based on the patient's response; therefore, the maximum score was 40. It should be noted that in this study, the validated Farsi version of the questionnaire was used (13).

In addition, the patient's HRQoL was evaluated through the validated Farsi version of St. George's questionnaire (14). In general, this questionnaire is considered a standard tool for assessing the quality of life in patients. It is composed of 76 questions in three parts of symptoms, activity, and the effect of disease on the patient's life. The scores range from 0 to 100

Table 1. Mean values of pulmonary function parameters and CAT score in patients with scleroderma

Parameters	Value (mean ±SD)
FEV1(%)	18.50±69.15
FVC(%)	11.50±64
FEV1/FVC(%)	96.80±13.75
TLC(%)	12.38±78.80
DLco(%)	21.75±68
Spo2(%)	3.26±94.50
6MWD(m)	355.85±80
Total CAT score	5.9±14.44

CAT: COPD assessment test, DLco: diffusion of lung for carbon monoxide, FEV1: forced expiratory volume in one second, FVC: forced vital capacity, Spo2: oxygen Saturation, TLC: total lung capacity, 6MWD: 6 minute walk distance

for all the questions (5).

The more impaired the patient's HRQOL is, the higher the St. George's overall score will be. It should be noted that the validity and reliability of the mentioned questionnaires were already approved in patients with ILD (4, 9). Afterwards, the association between the total scores of the questionnaires and the severity of pulmonary disease was examined, based on the recorded variables.

This study was approved by the ethics committee of Mashhad University of Medical Sciences (project number: 910022). The informed consents were obtained from all the participants in the study.

Statistical analysis

Data were analyzed using SPSS version 11.5. The graphs and statistical tables were used for data description and independent t-test, ANOVA, Pearson's correlation coefficient or Spearman test were used to analyze the data. P less than 0.05 was considered statistically significant.

Results

In total, 25 patients were included in the study, among whom 4% (n=1) and 96% (n=24) were man and women, respectively. The subjects' age ranged between 24-59 years, with the mean of 40.36±9.5 years. The mean duration of the disease was calculated as 7.16±4.5 years. Eighty percent (n=20) and 20% (n=5) of the subjects were married and single, respectively. The mean of each evaluated pulmonary variable is presented in Table 1. Patients were divided into 4 groups according to the predicted percentage of DLCO; the frequency distribution of the groups is indicated in Figure 1.

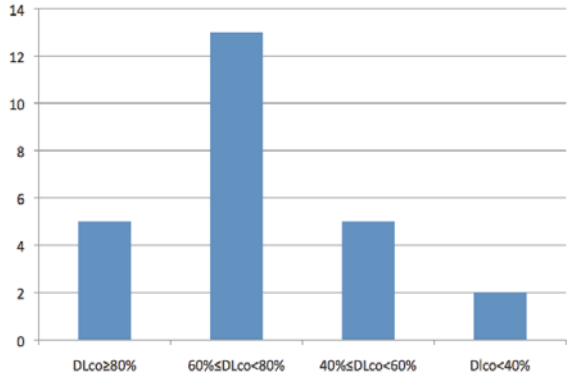

Figure 1. The distribution of different stages of SSc-ILD based on DLCO classification

Table 2. The relationship between total CAT score and pulmonary function parameters in studied patients with scleroderma

parameters	*P* value	Correlation Coefficient(r)
FEV1	0.001	-0.63
FVC	<0.001	-0.73
TLC	0.01	-0.46
DLco	<0.001	-0.67

CAT: COPD assessment test, DLco: diffusion of lung for carbon Monoxide, FEV1: forced expiratory volume in one second, FVC: forced vital capacity, TLC: total lung capacity

In the evaluation of the relationship between the total scores of CAT and St. George's questionnaires, a significant relationship was observed between the scores obtained in the mentioned questionnaires; the scores are indicated in Figure 2 (r=0.75, *P*<0.001).

As shown in Table 2, the total CAT score had a significant inverse relationship with all the parameters of body plethysmography. In addition, according to DLCO classification in Figure 1, there was a statistically significant difference in the mean CAT score among the study groups (*P*<0.001). In Figure 3, a significant inverse relationship was observed between DLCO and total CAT score.

In Figure 4, an inverse relationship was observed between the total CAT score and 6MWD (r=-0.50, *P*=0.01). In addition, a significant direct relationship was found between the total CAT score and MMRC (r=0.72, *P*<0.001). Moreover, a significant inverse association was observed between total CAT score and the percentage of arterial oxygen saturation (r=-0.40, *P*= 0.04).

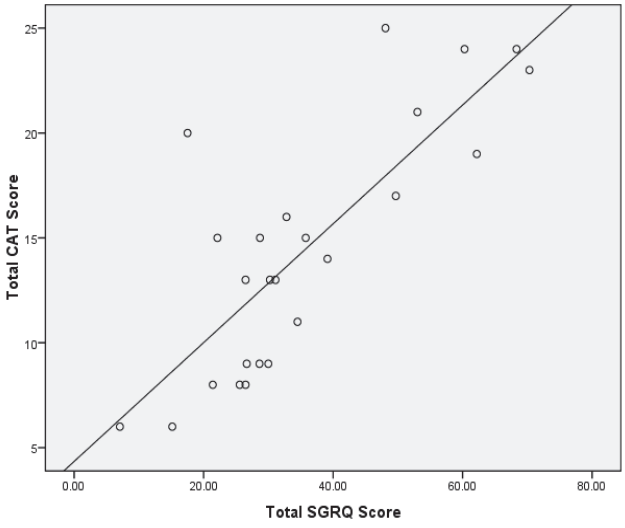

Figure 2. The significant relationship between the total CAT and St. George's questionnaires scores (r = 0.75, *P*<0.001)

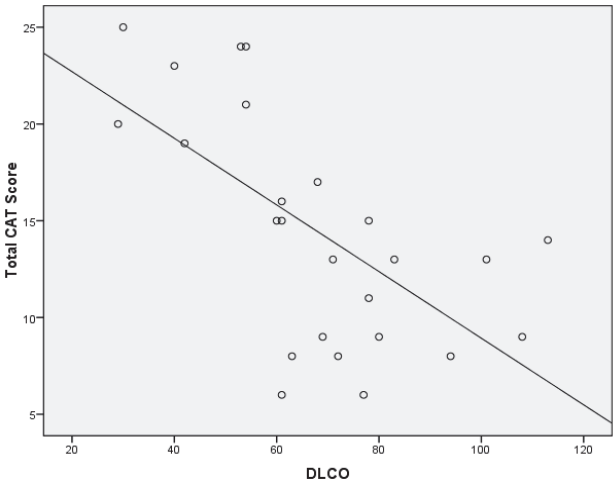

Figure 3. The significant association between total CAT score and DLCO (r = -0.67, *P* <0.001)

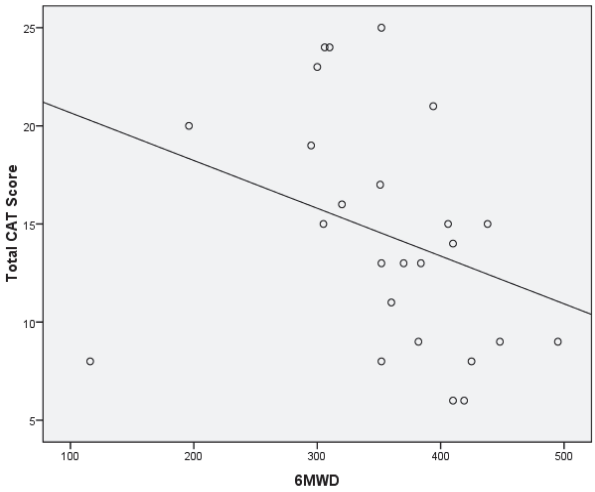

Figure 4. The significant association between total CAT score and 6MWD (r=-0.50, *P*=0.01)

Discussion

As research indicates, no study has been conducted on the evaluation of HRQoL in ILD patients with dSSc, based on the CAT questionnaire. This study showed that CAT questionnaire is a reliable tool for evaluating the HRQoL in ILD patients with scleroderma. There was a significant inverse relationship between total CAT score and lung volumes, the percentage of arterial oxygen saturation, and 6MWD. Additionally, a statistically significant association was observed between total CAT score and severity of dyspnea.

ILD is considered as one of the major causes of disability in patients with dSSc, and can significantly affect the survival rate of the patients (3). Pulmonary function tests are considered as sensitive methods for detecting pulmonary involvement in asymptomatic patients. The most common abnormalities in SSc are the reductions of FVC or DLCO. Pulmonary involvement, presented as pulmonary fibrosis and restrictive lung disease, is observed in most patients, and significantly affects the patients' daily activities and quality of life (15). HRQoL is an important issue for the patients and physicians, and has been recently considered in most diseases (9).

Several questionnaires have been designed to assess the quality of life in patients with pulmonary diseases. These questionnaires are mainly used for patients with chronic pulmonary diseases such as asthma or chronic obstructive pulmonary disease. For instance, in some previous studies, the efficacy of quality of life questionnaires such as St. George's and CAT has been evaluated and approved regarding chronic obstructive pulmonary disease and some interstitial lung diseases (9). Chang *et al,* after applying several quality of life questionnaires in ILD patients, showed that St. George's questionnaire is the best method for assessing HRQoL in these patients (9, 16).

However, as already mentioned, the main problem of this questionnaire is that it is too long, which limits its application in outpatient clinical visits. On the other hand, the main advantage of CAT questionnaire is that it is short and reliable (previously examined in obstructive pulmonary diseases) (7, 8). In addition, the study of Tagata *et al* indicated that CAT and St George's questionnaires have a significant relationship in patients with ILDs (9).

The results of the aforementioned studies showed that CAT questionnaire provides a standard evaluation and a rating estimation of the disease's impact on the quality of life in patients, disregarding their language or race. This questionnaire, compared with other assessment methods such as St. George, is simpler and shorter. In a previous study performed by Berta *et al*, it was determined that St. George's questionnaire is valid for assessing HRQoL in ILD patients with scleroderma, and has a significant relationship with patient's exercise capacity (6MWD) and the severity of dyspnea (4).

In another study, Nagata *et al* assessed HRQoL in ILD patients with different etiologies (such as collagen-vascular diseases, vasculitis, and idiopathic pulmonary fibrosis) and CAT and St. George's questionnaires were used for this purpose. A significant relationship was observed between the mentioned questionnaires for ILD patients, and it was concluded that CAT questionnaire could be used as a valid tool for assessing HRQoL in ILD patients (9).

In the current study, a strong statistical association was observed between CAT and St. George's total scores, which is consistent with the results of Nagata in ILD patients (9). Considering the validity of St. George's questionnaire for HRQoL assessment in patients with scleroderma

(4), the validity of CAT and St George's questionnaires in ILD patients (9), and our findings; we can conclude that CAT questionnaire is suitable for ILD patients with scleroderma.

Moreover, 6MWD is a scientific and simple method for evaluating the exercise capacity of patients with scleroderma. Studies have shown that it may help predict patients' health-related outcomes (17). This test is safer for determining the patients' exercise capacity, compared with other methods (18). In this study, a significant inverse relationship was observed between CAT total score and 6MWD results. This finding was consistent with the results of the study by Berta *et al*; however, in the study by Berta *et al*, HRQoL was evaluated using St. George's questionnaire (4).It should be noted that one of the problems in performing 6MWD is related to patients who have severe skin firmness in lower extremities or advanced joint problems, which impair their walking ability; in the current study, we did not include such patients.

As previously noted, the diagnostic and predictive value of pulmonary function tests in scleroderma patients with ILD is quite evident. Among these tests, DLCO is the most sensitive method, which starts to decline earlier than other factors. In this study, a significant inverse association was observed between total CAT score and DLCO.

Moreover, a significant inverse association was seen between total (CAT) score and other important spirometric variables, particularly TLC and FVC. These findings were consistent with the results of the study by Nagata and colleagues (9). The decline in the percentage of arterial oxygen saturation during either resting or activity is a sign of the severity of pulmonary involvement in scleroderma patients, and affects the decrease in patient's exercise capacity and impaired HRQoL (15, 19). In our study, a significant inverse relationship was observed between total CAT score and percentage of oxygen saturation.

Dyspnea is a common complaint in scleroderma patients (prevalent among 50% of the patients) (20). It is in fact one of the most important factors affecting the performance and quality of life in patients with scleroderma. In our study, a significant association was found between total CAT score and the severity of dyspnea. These findings were consistent with the results of the study by Nagata and colleagues (9).

The present study had some limitations. Firstly, the assessment of the severity of pulmonary involvement by CT scan and its relationship with CAT score could more illuminate the significance of this questionnaire. Secondly, this study was cross-sectional, therefore, repeating the questionnaire evaluation would help with patients' visits and even their response to treatment.

Conclusion

This study was conducted with the aim to assess the status of CAT questionnaire in ILD patients with scleroderma. It was revealed that CAT has a strong relationship with St. George's questionnaire. In addition, total CAT score was associated with important parameters of pulmonary function. Therefore, this questionnaire can be used to assess patients' quality of life and estimate their pulmonary function.

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Conflict of Interest

The authors declare no conflict of interest.

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