Comparison of two questionnaires which measure the health-related quality of life of idiopathic pulmonary fibrosis patients

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Abstract

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The objective of the present study was to determine if there is a health-related quality of life (HRQL) instrument, generic or specific, that better represents functional capacity dysfunction in idiopathic pulmonary fibrosis (IPF) patients. HRQL was evaluated in 20 IPF patients using generic and specific questionnaires (Medical Outcomes Short Form 36 (SF-36) and Saint George's Respiratory Questionnaire (SGRQ), respectively). Functional status was evaluated by pulmonary function tests, 6-min walking distance test (6MWDT) and dyspnea indexes (baseline dyspnea index) at rest and after exercise (modified Borg scale). There was a restrictive pattern with impairment of diffusion capacity (total lung capacity, TLC = 71.5 ± 15.6%, forced vital capacity = 70.4 ± 19.4%, and carbon monoxide diffusing capacity = 41.5 ± 16.2% of predicted value), a reduction in exercise capacity (6MWDT = 435.6 ± 95.5 m) and an increase of perceived dyspnea score at rest and during exercise (6 ± 2.5 and 7.1 ± 1.3, respectively). Both questionnaires presented correlation with some functional parameters (TLC, forced expiratory volume in 1 s and carbon monoxide diffusing capacity) and the best correlation was with TLC. Almost all of the SGRQ domains presented a strong correlation with functional status, while in SF-36 only physical function and vitality presented a good correlation with functional status. Dyspnea index at rest and 6MWDT also presented a good correlation with HRQL. Our results suggest that a specific instead of a generic questionnaire is a more appropriate instrument for HRQL evaluation in IPF patients and that TLC is the functional parameter showing best correlation with HRQL.

Introduction

Idiopathic pulmonary fibrosis (IPF) is a distinctive type of chronic fibrosing interstitial pneumonia of unknown cause associated with a surgical lung biopsy showing a histological pattern of usual interstitial pneumonia (1). Usually, the age at onset is more than 50 years and IPF is slightly more common in males. Clinically, it is characterized by dyspnea, nonproductive cough, reduced lung volumes, and abnormal gas exchange. Constitutional symptoms such as weight loss, malaise, and fatigue may also be present (2, 3). Since treatment remains unsatisfactory, IPF patients present a progressive course that results in severe disability and death in the majority of cases. Clinical deterioration is the most frequent result of disease progression, with almost half the deaths being due to progressive respiratory failure (3-5). Thus, prognosis is poor with a median length of survival from time of diagnosis of less than four years (1,3-6). During the clinical course of the disease, patients invariably become severely limited in their activities and dependent on supplemental oxygen (3).

An international consensus for the diagnosis of IPF (1) has been recently published, but controversy persists in terms of treatment and factors affecting prognosis (7-9). It seems that pulmonary function tests continue to be the best parameter to assess response to therapy, prognosis and survival in IPF patients (1,10). Erbes and associates (11) also showed that total lung capacity (TLC) alone or in combination with vital capacity holds greater prognostic value than diffusing capacity at rest or during exercise.

Probably, more important than how long the patient survives or even the results of pulmonary function tests, is the health status or quality of life of these patients. Health-related quality of life (HRQL) assesses the influence of disease on physical, emotional, and social functioning and is an important parameter for measuring the impact and pro-gression of chronic diseases. During the last 25 years, HRQL questionnaires have been applied to quantify average changes in health and the effects on patient daily life in several types of chronic lung diseases (12-14).

There are few studies evaluating HRQL in IPF patients (3) and even those have not established which sort of questionnaire should be used, and its relationship with functional measurements. Two kinds of questionnaires have been used: generic and disease specific. Generic instruments have the advantage of having been thoroughly tested in several clinical settings and populations. There is evidence suggesting that disease-specific respiratory questionnaires are unnecessary for measuring HRQL in IPF patients (15,16). In contrast, Chang and associates (17) suggest that nonspecific as well as specific disease questionnaires are sensitive and can be applied to IPF patients.

The main goal of the present study was to determine if there is an HRQL instrument, generic or specific, that better represents functional capacity dysfunction in IPF patients.

Material and Methods

Patients

All patients with documented IPF, identified through clinical records, who attended the Interstitial Lung Diseases Group as outpatients at Hospital das Clínicas, University of São Paulo (São Paulo, SP, Brazil) over a period of 6 months, were invited to participate in the study. Twenty-four eligible patients were identified and 22 participated after providing written informed consent. Two of them presented significant clinical deterioration before finishing the protocol and were excluded. A group of 20 patients completed all the tests. There were 12 men and 8 women, with a mean (± SD) age of 61.4 ± 10.5 years, and 3.1 ± 1.8 years of presence of the disease since the diagnosis

of IPF. None of them presented interstitial lung disease associated with connective tissue disease, significant occupational or environmental exposure, active coronary artery disease or other illnesses precluding performance of the 6-min walking distance test (6MWDT). IPF diagnosis was based on clinical, functional and radiological findings (1). An open-chest lung biopsy was performed in 18 patients and bronchoscopic evaluation (bronchoalveolar lavage and transbronchial biopsy) in 1, and evaluation based on typical clinical and high-resolution CT findings was performed in another one (1). The following criteria were considered for the diagnosis of IPF: abnormal pulmonary function studies showing evidence of pulmonary restriction (reduced TLC/forced vital capacity (FVC) with a normal or increased forced expiratory volume in 1 s, FEV_1/FVC ratio) and/or impaired gas exchange, increased alveolar-arterial O_2 gradient with rest or exercise, or decreased diffusing lung capacity for carbon monoxide (DL_{CO}) (1).

When the protocol started, 11 patients were taking intravenous steroids (pulse therapy with 1 g methyl-prednisolone per week) and the others were taking only 1 mg colchicine per day. Five patients were under oxygen supplementation 24 h/day.

Study design

The study was conducted on two nonconsecutive days no longer than 15 days apart. On the first day, patients answered two HRQL questionnaires, a generic one (Medical Outcomes Short Form 36 (SF-36)) (18) and a respiratory disease-specific instrument (Saint George's Respiratory Questionnaire, SGRQ) (19), and the baseline dyspnea index (BDI) (20). Next, a 6MWDT was performed and a modified Borg scale was applied (21). On the second day, another 6MWDT followed by the modified Borg scale was performed. A complete lung func-

tion test including DL_{CO} was performed within 2 months of answering the questionnaires.

Health-related quality of life

Medical Outcomes Short Form 36. The SF-36 is a generic HRQL instrument which has been used to assess quality of life in a variety of chronic respiratory conditions including chronic obstructive pulmonary disease, asthma and IPF (16,18,22). The SF-36 version validated for the Portuguese language was used (23). The questionnaire covers nine concepts: physical functioning, physical role, pain index, general health perceptions, vitality, social functioning, emotional role, mental health index, and health transition. We did not evaluate the health transition component, which deals with changes in the health status during the previous 12 months. Each dimension is scored separately on a 0 to 100 scale, in which higher scores correspond to a better quality of life.

Saint George's Respiratory Questionnaire. The SGRQ is a respiratory-specific HRQL instrument developed for patients with chronic obstructive pulmonary disease. Its validity, reproducibility, and response to change over time have been demonstrated in patients with asthma, bronchiectasis and IPF (17,10,24). The questionnaire has three components: symptoms, which measures respiratory symptoms, activities, which measures impairment of mobility or physical activity, and impact, which measures the psychosocial impact of disease. Scores for these components and the summary score are on a 100-point scale, which is opposite in direction to the SF-36. Higher scores correspond to worse health-related quality of life.

Dyspnea analysis

Baseline dyspnea index. The BDI comprises three subscales which are used to

assess the severity of breathlessness: 1) the magnitude of effort needed to produce dyspnea, 2) the magnitude of the task needed to produce dyspnea, and 3) the degree of functional impairment due to dyspnea (20). Dyspnea is graded from zero to 4, and the lower the number the greater the severity of the dyspnea. Each subscale score is summed to provide a total score of 0 to 12.

Six-minute walking distance test

The test was performed in a 36-m long corridor. This test has been shown to be a reliable, valid and safe method of assessing functional status in both patients with chronic obstructive pulmonary disease and congestive heart failure (25,26). Patients remained sitting for at least 10 min before the test. Before and after the test, heart rate, oxygen saturation, blood pressure, and modified Borg scale were measured. During the test, we did not use any encouragement phrases. Patients were allowed to stop and restart during the 6 min of the test, if necessary, and were allowed to use supplemental oxygen at the same inspired concentration normally used for their daily activities. The test was performed on two non-consecutive days to account for a learning effect and the best result was considered (27). After completing the walk, patients rated the amount of dyspnea experienced during the test on a modified Borg scale (21).

Pulmonary function tests

All pulmonary function tests were performed using Collins GS II equipment (Louisville, CO, USA), including a constant volume body plethysmograph. Static lung volumes and their subdivisions, vital capacity, TLC, residual volume were measured, and the results were reported as percentage of predicted values calculated according to gender, height, and age using Goldman reference equations of normality (28). FEV_1, dynamic lung volumes and maximal expiratory flows were measured with a volume displacement spirometer according to ATS technical recommendations (29), based on acceptability and reproducibility criteria. The results are reported as the best curve obtained in three maneuvers and presented as percentage of the value predicted by Knudson and co-workers (30). DL_{CO} was measured by the single-breath method (29). Values are reported as percentage of the value predicted by Gaensler and Smith (31).

Statistical analysis

Correlation between quality of life scores and pulmonary function tests, 6MWDT, and BDI was evaluated by Pearson's coefficient. The Sigma Stat version 2.03 software package (San Jose, CA, USA) was used for statistical analysis, with the level of significance set at $P < 0.05$.

Results

The demographic and functional characteristics of the patients are summarized in Table 1. Twenty patients performed all evaluations and presented, on average, a moderate reduction in lung volumes (in percentage of predicted value): TLC: 71.5 ± 15.6%, FVC: 70.4 ± 19.4%, and FEV_1: 77.3 ± 21.3%. Two patients presented a percent predicted residual volume over 100%; however, all other pulmonary function parameters suggested a restrictive pattern. Reduction in DL_{CO} was the main alteration in the pulmonary function tests (41.5 ± 16.2% of predicted). Patients presented on average impairment of exercise capacity (6MWDT - average of 435.6 m) and results ranged from no limitation (648 m) to severe limitation (272 m; Table 1). The values of the resting dyspnea index determined by the BDI scale were compatible with some limitation (6 ± 2.5) and the total score obtained was equally distributed among functional impairment (2.1

± 1.1), magnitude of task (2.1 ± 1) and magnitude of effort (1.7 ± 0.75; Tables 1 and 2). Exertion dyspnea (modified Borg scale) also presented values compatible with limitation (7.1 ± 1.3; Table 1).

Table 2 shows the HRQL scores determined by specific (SGRQ) and generic (SF-36) questionnaires. Both instruments revealed a reduction in HRQL (SGRQ = 48.4 ± 17.9 and SF-36 = 55.7 ± 28.4). The most affected domain in the SGRQ was activity (higher value, 62.4 ± 19; Table 2). In the SF-36, the mental health domain was the least affected (higher value) while physical function, vitality and emotional aspect were the most affected (lower values, 46 ± 18.3, 49.2 ± 24.3, and 46.6 ± 39.5, respectively; Table 2).

Total SGRQ domains presented a good correlation (r > 0.5) with TLC (0.66), FEV_1 (0.57), and DL_{CO} (0.47) as well as 6MWDT (0.72) and rest dyspnea index (0.72; Table 3). Good correlations were also observed between lung function, exercise capacity and rest dyspnea index and all SGRQ domains, except the symptom domain that showed correlation only with residual volume. When HRQL was evaluated by the SF-36, only the physical function and vitality domains presented a good correlation with FEV_1 (0.50 and 0.48, respectively) and TLC (0.61 and 0.51, respectively), and only vitality correlated with DL_{CO} (0.54; Table 3). The physical function and vitality domains also presented a good correlation with 6MWDT (0.69 and 0.50, respectively) and the physical function, vitality and social function domains correlated with BDI (0.73, 0.58, and 0.47, respectively). Interestingly, 6MWDT presented a good correlation with FEV_1 (0.56), TLC (0.65) and DL_{CO} (0.54), whereas dyspnea correlated only with FEV_1 (0.51) and DL_{CO} (0.45).

Discussion

The present results showed that generic (SF-36) and specific (SGRQ) questionnaires

revealed a similar decrease in HRQL aspects of IPF patients. However, the SGRQ seems to evaluate HRQL more appropriately in our population since almost all of its domains

Table 1. Clinical and physiological features of idiopathic pulmonary fibrosis patients.

	Mean ± SD	Range
Age (years)	61.46 ± 10.52	
Lung function values		
FVC (% of predicted)	70.4 ± 19.4	40-113
FEV_1 (% of predicted)	77.3 ± 21.3	42-125
TLC (% of predicted)	71.5 ± 15.6	45-102
VC (% of predicted)	69.8 ± 20.2	37-110
DL_{CO} (% of predicted)	41.5 ± 16.2	10-74
Functional scores		
6MWDT (m)	435.6 ± 95.5	272-648
SaO_2 (%)	95.5 ± 2.6	89-98
Dyspnea		
BDI	6 ± 2.5	2-11
Borg scale	7.1 ± 1.3	3-10

Data are reported as means ± SD and range for 12 male and 8 female patients. FVC = forced vital capacity, FEV_1 = forced expiratory volume in 1 s; TLC = total lung capacity; VC = vital capacity, DL_{CO} = CO diffusing capacity; 6MWDT = 6-min walking distance test; SaO_2 = oxygen saturation of hemoglobin; BDI = baseline dyspnea index.

Table 2. Health-related quality of life scores.

SGRQ	
Symptom	46.4 ± 20.3
Activity	62.4 ± 19
Impact	43.6 ± 20.9
Total score	48.4 ± 17.9
SF-36	
Physical function	46 ± 18.3
Body pain	60.6 ± 31.9
Physical role	57.5 ± 39.8
General health	53.7 ± 24.1
Vitality	49.2 ± 24.3
Social function	56.9 ± 32.2
Emotional aspects	46.6 ± 39.5
Mental health	66.8 ± 17
BDI	
Functional impairment	2.1 ± 1.1
Magnitude of task	2.1 ± 1
Magnitude of effort	1.7 ± 0.75
Total score	6 ± 2.5

Data are reported as means ± SD. SGRQ = Saint George's Respiratory Questionnaire; SF-36 = Medical Outcomes Short Form 36 questionnaire; BDI = baseline dyspnea index.

presented a good relationship with lung function, exercise capacity and dyspnea. Besides, TLC presented a strong relationship with both HRQL instruments and seems to be the functional parameter that best represents HRQL aspects.

IPF is a disease causing progressive breathlessness and commonly resulting in respiratory failure and death (3,32). IPF treatment has been focused on avoiding disease progression and improving survival. However, improving quality of life is extremely important for many patients and should perhaps be a more realistic goal (26). Over the last few years, some studies have examined HRQL in patients with IPF (15-17) and, independent of subject inclusion criteria and instrument used, all studies observed significant impairment in IPF patients' HRQL and quality of life relative to the general population.

Two types of HRQL questionnaires are widely available: generic and disease-specific instruments. Disease-specific instruments are tailored to patients with a certain disease or condition and are likely to be more sensitive to changes in a patient's status than generic instruments (33). SGRQ and the Chronic Respiratory Questionnaire (CRQ) were developed specifically for patients with chronic airflow obstruction and contain three domains: impact, activities and symptoms (24,34). SF-36 is a general HRQL instrument but has already been extensively validated for respiratory and non-respiratory conditions (18). Few studies have evaluated HRQL in patients with IPF and five different instruments have been used, two disease-specific ones developed for patients with obstructive lung disease (CRQ and SGRQ) (16,17,34), two generic HRQL instruments (SF-36 and Quality of Well Being) (16,17,34,35), and a generic quality of life instrument (WHOQOOL-100) (15,36). Despite these studies, there are still some concerns about the availability of a better instrument to evaluate patients' HRQL (33).

In general, validation of these instruments is based on testing an *a priori* hypothesis that a worse quality of life score should

Table 3. Correlations between health-related quality of life scores and functional status.

	TLC (% predicted)	FEV$_1$ (% predicted)	VC (% predicted)	DL$_{CO}$ (% predicted)	6MWDT (m)	BDI
SGRQ						
Symptoms	0.37	0.08	0.14	0.41	0.41	0.62*
Activities	0.65*	0.57*	0.54*	0.32	0.72*	0.75*
Impact	0.58*	0.52*	0.61*	0.39	0.63*	0.63*
Total	0.66*	0.57*	0.56*	0.47*	0.72*	0.72*
SF-36						
Physical function	0.61*	0.50*	0.54*	0.47	0.69*	0.73+
Body pain	0.27	0.28	0.28	0.00	0.28	0.20
Physical role	0.43*	0.20	0.34	0.13	0.37	0.30
General health	0.68*	0.10	0.13	0.17	0.27	0.52*
Vitality	0.51*	0.48*	0.57*	0.54*	0.50*	0.58*
Social function	0.47	0.23	0.27	0.36	0.34	0.47*
Emotional aspects	0.32	0.22	0.28	0.25	0.31	0.24
Mental health	0.13	0.04	0.04	0.16	0.00	0.06
BDI	0.51*	0.51*	0.36	0.45*	0.72*	–
6MWDT	0.65*	0.56*	0.53*	0.54*	–	0.72*

TLC = total lung capacity; FEV$_1$ = forced expiratory volume in 1 s; VC = vital capacity; DL$_{CO}$ = CO diffusing capacity; 6MWDT = 6-min walking distance test; BDI = baseline dyspnea index; SGRQ = Saint George's Respiratory Questionnaire; SF-36 = Medical Outcomes Short Form 36 questionnaire.
*P < 0.05; +P < 0.001 for linear correlation coefficient of each parameter evaluated.

correlate with more severe physiologic impairment in clinical and exercise tests. Since there is no reference "gold standard" for the psychological construct HRQL, clinical parameters must be used as reference. Chang et al. (17) first evaluated HRQL in patients with interstitial lung diseases (IPF, sarcoidosis, hypersensitivity pneumonitis, and asbestosis) using four distinct questionnaires and only the SF-36 and SGRQ tools presented a relationship (from weak to moderate) with pulmonary function, 6MWDT and dyspnea score. In addition, SGRQ presented a better (moderate) relationship with all functional parameters than SF-36. Martinez et al. (16) evaluated quality of life specifically in IPF patients using only SF-36 and showed that only some aspects of the questionnaire (physical and social functioning, general health and vitality) presented a good relationship with dyspnea score. de Vries et al. (36) observed that WHOQOOL-100 presented a weak relationship with pulmonary function in IPF patients.

Taken together, these studies show that generic and specific questionnaires can evaluate HRQL in patients with IPF; however, their validity remains poorly known since many questionnaires have been used and few studies have tested their associations with clinical and functional parameters (33). Our study is the first to evaluate specific (SGRQ) and generic (SF-36) questionnaires regarding pulmonary function, exercise capacity and dyspnea specifically in IPF patients. Our results show that some domains of SF-36 (physical functioning, physical role and vitality) presented a moderate to good relationship with clinical parameters, whereas all SGRQ domains presented a good relationship with clinical parameters.

In contrast to previous results, we observed a good relationship between clinical and HRQL parameters. It is possible that the age of our patients and their advanced disease stage (with some of them receiving oxygen supplementation) could explain the better relationship observed between clinical aspects and HRQL. If this is true, it supports the fact that a specific questionnaire could be more adequate to assess patient HRQL and their clinical evaluation.

Static lung volumes are typically reduced in patients with IPF, whose prognosis has been mostly related to pulmonary function (37,38). On this basis, pulmonary volumes should be the most important parameters used in HRQL validation. However, at present there are only three studies in which correlations between lung functions and HRQL were calculated (13-15). In general, the results of lung function testing correlate with HRQL scores in patients with interstitial pulmonary fibrosis, but many of these correlations are weak and not statistically significant. Besides, only two studies specifically evaluated IPF patients (15,16) and each study reported the results of only some pulmonary function parameters, impairing comparison between their results and ours.

In contrast to previous results, our study showed a moderate to good relationship between HRQL and TLC, FEV_1, and DL_{CO}. Interestingly, some studies have shown that prognosis is poorer in IPF patients with a reduction in TLC (8,11,39). Erbes et al. (11) observed a decreased survival rate in IPF patients with a pre-therapy TLC of less than 78% of the predicted value. Besides, a combined reduction in vital capaciy and TLC was associated with a 46% reduction in 5-year survival rates (7). These results agreed with previous data reported by Schwartz et al. (9) who observed an association between higher FVC and TLC and improved survival rates. Another study reported that IPF patients with a TLC lower than 60% of the predicted value are less responsive to new medication (prednisone and cyclophosphamide) than patients with TLC >80% (8). These results suggest that TLC can be a lung function parameter that better represents the impact of the disease on IPF patients and might support our findings.

In a very recent investigation, Nishiyama et al. (40) studied 41 IPF patients and showed that BDI and TLC were significantly correlated with total SGRQ score. However, the BDI score was the only factor significantly contributing to the total SGRQ score. Although these results appear to differ from those obtained in our study, they should be evaluated with caution since SGRQ was related to TLC in liters instead of percent predicted as shown in the present study. In our study, TLC measured in liters was not related to SGRQ. It is possible that lung volumes measured in liters do not represent the real effect of the disease on each patient. Besides, in our study dyspnea also presented a good relationship with SGRQ.

In conclusion, our results show that a specific (SGRQ) rather than a generic (SF-36) questionnaire is a more appropriated instrument to evaluate HRQL in IPF patients. Our data also suggest that TLC presented a strong relationship with HRQL in the studied population.

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