Evaluation of the Short-Form 36-Item Questionnaire to Measure Health-Related Quality of Life in Patients With Idiopathic Pulmonary Fibrosis*

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Objective: To validate the use of the 36-item short-form questionnaire (SF-36) for measuring health-related quality of life (HRQL) in patients with idiopathic pulmonary fibrosis (IPF).

Design: Observational data at a single point in time.

Setting: A specialized outpatient respiratory clinic.

Participants: Thirty-four patients (mean ± SE age, 58.29 ± 1.87 years) with IPF and no significant comorbidity. A matched control group for HRQL measurements was composed of 34 normal subjects (mean age, 58.00 ± 1.89 years).

Measurements and results: Dyspnea was measured by the baseline dyspnea index (BDI). Respiratory function evaluation included FVC, FEV₁, and resting arterial blood gases. IPF patients showed a mean BDI score of 5.21 ± 0.46. The mean FVC and FEV₁ values were 62.41 ± 2.96% and 66.41 ± 3.33%, respectively. The mean PaO₂ was 67 ± 2.51 mm Hg, and the mean PaCO₂ was 37 ± 1.05 mm Hg. Patients scored significantly worse than control subjects with respect to the SF-36 domains of physical functioning, physical role, general health perceptions, vitality, social functioning, emotional role, and mental health index. BDI scores were significantly correlated with five SF-36 components, and FVC and FEV₁ were significantly correlated with two SF-36 components. Significant negative correlations were found between arterial pH and four SF-36 domains.

Conclusions: Patients with IPF have a significant impairment of HRQL in both physical and psychological functioning. Dyspnea is the most important factor influencing the quality of life in these subjects. The SF-36 questionnaire is a valid instrument to evaluate HRQL in IPF patients.

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Key words: dyspnea; idiopathic pulmonary fibrosis; lung function; quality of life

Abbreviations: BDI = baseline dyspnea index; HRQL = health-related quality of life; IPF = idiopathic pulmonary fibrosis; SF-36 = 36-item short-form survey

Health-related quality of life (HRQL) is an important parameter for measuring the impact and progression of chronic diseases.¹ Over the past decades, HRQL has been studied for a considerable number of respiratory conditions, such as asthma, COPD, and sarcoidosis.²⁻⁷

Idiopathic pulmonary fibrosis (IPF) is a chronically progressive interstitial lung disease that results in severe disability and death in the majority of cases. Clinically, this disorder is characterized by dyspnea, reduced lung volumes, and abnormal gas exchange.⁸ IPF is the most common interstitial lung disease, with an incidence of about 15 cases/100,000/yr.⁹ Most important, the response to the available therapy is poor, and patients with IPF show an expected median survival of 3 to 5 years.¹⁰ Despite these facts, to our knowledge no studies dealing specifically with HRQL in IPF have been published.

HRQL instruments may be designed to assess
overall quality of life, or only those aspects directly related to a particular disease. In 1988, Stewart et al. described the Medical Outcomes Study 20-question short-form survey to quantify general health status. Later, this questionnaire was expanded to a 36-item short-form survey (SF-36), to incorporate additional concepts and improve the precision of the employed scales. The SF-36 is a brief generic instrument that has gained increasing applicability, both in daily care and in clinical research. Its validity and reliability have been established in many conditions, including COPD and asthma. The objective of the present study was to validate the use of the SF-36 questionnaire in patients with IPF and no comorbidity. We examined the relationships for dyspnea ratings and lung function with the scores of eight SF-36 components. In addition, we also compared the results of IPF patients with those of a matched, healthy control group.

Materials and Methods

Study Population

A group of 34 patients with IPF who attended the outpatient clinic at our university hospital were studied. There were 20 men and 14 women, with a mean ± SD age of 58.29 ± 1.87 years. None of the participating subjects had a significant comorbidity or a medical history that might have influenced quality of life. The diagnosis of IPF was confirmed by an open lung biopsy in 27 patients, and was based only on typical clinical and high-resolution CT findings in seven other cases. Histopathologic criteria for the diagnosis of IPF included the presence of a patchy infiltrative process demonstrating varying degrees of interstitial fibrosis associated with inflammatory infiltrates and areas of honeycombing. No evidence of a specific cause of pulmonary fibrosis such as connective tissue disease or fibrogenic drug therapy, nor significant occupational or environmental exposure was present in any patient. At the time of the interview, all patients were receiving oral prednisone, 10 to 60 mg/d; 12 patients (35%) also received oral cyclophosphamide, 100 mg to 200 mg/d. Although seven patients had indication for continuous oxygen therapy, only one patient was receiving it, since at that time the Brazilian health system would not pay for it.

A group of 34 subjects matched for sex and age (58.00 ± 1.89 years), comprising people with no significant comorbidity, were selected among employees of our medical school and members of a local community center as control subjects for HRQL measurements. They all answered a standard questionnaire, denying respiratory symptoms and the use of any cardiovascular or respiratory medications. All study participants provided signed written consents, and the protocol was approved by the Institutional Ethics Committee.

Data Collection

All patients were evaluated during a clinically stable period at the outpatient clinic. Dyspnea and HRQL scores were obtained by an interview that was performed by one of two trained researchers (TYM, SMG). Dyspnea, HRQL scores, pulmonary function, and arterial blood gas values of the patients were determined within a short period of time.

HRQL was assessed with a version of the SF-36 validated for the Portuguese language spoken in Brazil. The questionnaire consists of 36 questions that cover nine health concepts: physical functioning, physical role, pain index, general health perceptions, vitality, social functioning, emotional role, mental health index, and health transition. In the present study, we did not evaluate the health transition component, which deals with changes in health status during the previous 12 months. Measures of the remaining eight health components were transformed linearly to scores in scales of 0 (the worst possible condition) to 100 (the best possible condition). Dyspnea was graded using the baseline dyspnea index (BDI). The scores in this index depend on ratings for three different categories: functional impairment, magnitude of task, and magnitude of effort. Dyspnea is graded from 0 (severe) to 4 (unimpaired) for each category. The ratings for the three categories are added to form the baseline score, ranging from 0 to 12.

Pulmonary function tests were measured using Medgraphics PF-DX (St. Paul, MN) equipment. Predicted normal values of FVC and FEV₁ for the Brazilian population were taken from Pereira et al. Arterial blood gas values were obtained at rest and were measured with an ABL 330 (Beckman Instruments; Carlsbad, CA) system.

Results are presented as mean ± SD unless otherwise stated. Spearman coefficients (r) were calculated to evaluate the degree of correlation among components of the SF-36 and the BDI scores, lung function, and blood gases measurements. The Wilcoxon test was used for comparisons of the SF-36 results between patients and healthy control subjects. Statistical analyses were performed using an IBM personal computer with the SigmaStat software (Jandel Scientific; San Rafael, CA). A p value < 0.05 was considered significant.

Results

Patients with IPF showed percent predicted FVC values ranging from 114 to 33%. Percent predicted FEV₁ values ranged from 118 to 37%. Mean FVC and FEV₁ for the IPF group were 62.41 ± 2.96% and 66.41 ± 3.33%, respectively. All IPF patients showed normal percent predicted FEV₁/FVC ratios, with a mean for the group of 106.12 ± 1.67%. According to one criterion for assessing the severity of pulmonary function abnormalities, restriction was classified as mild in two patients, moderate in eight, moderately severe in nine, severe in eight, and very severe in one. Six patients showed normal results of spirometric tests. The diagnosis of IPF was confirmed by an open lung biopsy in five of these six patients, and was based on typical clinical and high-resolution CT findings in the other patient. The group as a whole may be classified as having a moderate degree of restriction.

Resting arterial blood gases could not be obtained at the time of interview for one patient. The remaining 33 patients showed a mean PaO₂ value of 67 ± 2.51 mm Hg (range, 33 to 91 mm Hg), and a mean PaCO₂ of 37 ± 1.05 mm Hg (range, 25 to 52 mm Hg). Mean arterial pH was 7.41 ± 0.005 (range, 7.33 to 7.48). The group as a whole may be classified as normocapnic and having mild hypoxemia. The
BDI scores for the IPF group ranged from 2 to 12, with a mean value of 5.21 ± 0.46. These overall results represent a spectrum of patients with different degrees of respiratory impairment and HRQL levels.

Patients with IPF scored significantly worse than control subjects with respect to the SF-36 components of physical functioning, physical role, general health perceptions, vitality, social functioning, emotional role, and mental health index. IPF patients and control subjects had similar scores only for the pain index component (Fig 1 and Table 1).

The BDI score was significantly correlated with five of the eight components: physical functioning, general health perceptions, vitality, social functioning, and mental health index. With respect to pulmonary function parameters, FVC and FEV₁ as percent of predicted were significantly correlated with physical functioning and general health perceptions. Significant negative correlations were found between arterial pH and physical functioning, vitality, social functioning, and emotional role. An unexpected significant inverse correlation was found between PaO₂ and the pain index. We also investigated the Spearman coefficients between BDI scores and pulmonary function data. The BDI showed significant correlations with FVC, FEV₁, pH, and PaO₂ (Table 2).

**Discussion**

Although the expression *quality of life* has always enjoyed colloquial use in several human fields, its application as a scientific concept is relatively new. Nevertheless, over the past 2 decades, increasing attention has been paid to studies of HRQL in several respiratory and nonrespiratory conditions.¹ According to Jones,²⁰ the measurement of HRQL may be defined as “quantification of the impact of disease on a patient’s life and perceived well being in a formal and standardized manner.” In recent years, these measurements have been recognized as important features and outcomes in the care of chronic disabling illnesses.¹

HRQL instruments can be designed to assess the overall quality of life, including facets such as emotional functioning, social role functioning, and activities of daily living, or only domains directly related to a particular disease.¹,²¹ For instance, specific chronic respiratory instruments can assess aspects such as dyspnea, cough, sputum production, exercise tolerance, and mood. Although disease-specific questionnaires are likely to be more sensitive to particular symptoms and to small responses to therapeutic interventions, the generic instruments have the advantage of being thoroughly tested in several clinical settings and populations. In addition, generic tools enable comparisons among widely disparate conditions, like chronic respiratory failure and rheumatic diseases. Whichever instrument is chosen, it is necessary to determine its validity before it is introduced for practical usage. Among several available generic instruments, the SF-36 questionnaire has been widely employed by researchers, and has been adopted by a number of health-care organizations.
Its validity has been well described in different conditions, including COPD and asthma.\textsuperscript{2,5,13,14} In the present study, a group of patients with IPF followed up at a specialized clinic of a teaching hospital showed significant decreases of seven SF-36 components in comparison to healthy people matched for gender and age (Fig 1 and Table 1). Scores were reduced in different components described for patients with COPD, but with a more pronounced impairment of mental features.\textsuperscript{2} The HRQL scores obtained in this study were very close to values observed in patients with severe heart failure.\textsuperscript{25} Based on such findings, we believe that among the pulmonary diseases, IPF and probably other fibrotic conditions may produce the most striking deleterious effects on HRQL.

The present results also provide support for the validity of the SF-36 tool to assess HRQL in patients with IPF. There are no “gold standards” to measure instruments of HRQL against; consequently, correlations with biological indicators of disease should be employed. A useful instrument should correlate in the theoretically expected direction with markers of disease severity. The correlation coefficients reported in Table 2 demonstrate statistically significant relationships between BDI scores and physical functioning, general health perceptions, vitality, social functioning, and mental health index. The magnitude of these correlations was moderate to weak. The number and degree of statistically significant correlations between parameters of lung function and SF-36 components were fewer and lower than those observed with the BDI scores. In fact, very high correlations would not be anticipated, since when evaluating HRQL, the intention is not to duplicate other measures.

### Table 1—Mean $\pm$ SE (Median) Values for the SF-36 Components for IPF Patients and Control Subjects

<table>
<thead>
<tr>
<th>SF-36 Components</th>
<th>IPF Patients</th>
<th>Control Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical functioning</td>
<td>42.79 ± 4.40 (37.50)</td>
<td>86.18 ± 2.47 (90.00)</td>
<td>$&lt; 0.0001$</td>
</tr>
<tr>
<td>Physical role</td>
<td>44.12 ± 8.11 (25.00)</td>
<td>90.44 ± 4.35 (100.00)</td>
<td>$&lt; 0.0001$</td>
</tr>
<tr>
<td>Pain index</td>
<td>76.91 ± 4.16 (84.00)</td>
<td>76.74 ± 3.17 (84.00)</td>
<td>$&gt; 0.05$</td>
</tr>
<tr>
<td>General health perceptions</td>
<td>53.50 ± 3.90 (47.00)</td>
<td>76.35 ± 2.48 (77.00)</td>
<td>$&lt; 0.0001$</td>
</tr>
<tr>
<td>Vitality</td>
<td>50.44 ± 4.88 (50.00)</td>
<td>73.53 ± 2.39 (77.50)</td>
<td>$&lt; 0.0001$</td>
</tr>
<tr>
<td>Social functioning</td>
<td>60.29 ± 6.69 (68.80)</td>
<td>82.72 ± 3.84 (87.50)</td>
<td>0.0176</td>
</tr>
<tr>
<td>Emotional role</td>
<td>60.76 ± 8.26 (100.00)</td>
<td>91.18 ± 3.54 (100.00)</td>
<td>0.000645</td>
</tr>
<tr>
<td>Mental health index</td>
<td>57.53 ± 4.07 (60.00)</td>
<td>78.24 ± 2.35 (80.00)</td>
<td>$&lt; 0.0001$</td>
</tr>
</tbody>
</table>

### Table 2—Spearman Correlation Coefficients Calculated for the Group of Patients With IPF

<table>
<thead>
<tr>
<th>Variables</th>
<th>BDI</th>
<th>FVC, % Predicted</th>
<th>FEV$_1$, % Predicted</th>
<th>pH</th>
<th>PaO$_2$</th>
<th>PaCO$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36 components</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical functioning</td>
<td>0.780†</td>
<td>0.426*</td>
<td>0.394*</td>
<td>−0.540†</td>
<td>0.118</td>
<td>0.150</td>
</tr>
<tr>
<td>Physical role</td>
<td>0.170</td>
<td>−0.042</td>
<td>−0.111</td>
<td>−0.233</td>
<td>0.002</td>
<td>0.170</td>
</tr>
<tr>
<td>Pain index</td>
<td>−0.077</td>
<td>0.124</td>
<td>0.259</td>
<td>0.131</td>
<td>−0.407*</td>
<td>0.146</td>
</tr>
<tr>
<td>General health perceptions</td>
<td>0.495†</td>
<td>0.398*</td>
<td>0.452†</td>
<td>−0.150</td>
<td>0.052</td>
<td>0.211</td>
</tr>
<tr>
<td>Vitality</td>
<td>0.650†</td>
<td>0.274</td>
<td>0.234</td>
<td>−0.383*</td>
<td>0.216</td>
<td>0.211</td>
</tr>
<tr>
<td>Social functioning</td>
<td>0.486†</td>
<td>0.135</td>
<td>0.134</td>
<td>−0.419*</td>
<td>0.186</td>
<td>0.219</td>
</tr>
<tr>
<td>Emotional role</td>
<td>0.083</td>
<td>0.072</td>
<td>0.092</td>
<td>−0.359*</td>
<td>0.127</td>
<td>0.247</td>
</tr>
<tr>
<td>Mental health index</td>
<td>0.394*</td>
<td>0.212</td>
<td>0.309</td>
<td>−0.291</td>
<td>0.197</td>
<td>0.342</td>
</tr>
<tr>
<td>BDI</td>
<td></td>
<td>0.378*</td>
<td>0.344*</td>
<td>−0.437*</td>
<td>0.350*</td>
<td>−0.017</td>
</tr>
</tbody>
</table>

* $p < 0.05$.
† $p < 0.001$. 
Interpretation of spearman correlation coefficients.

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An unexpected number of significant inverse correlations were found between resting arterial pH and the components of physical functioning, vitality, social functioning, and emotional role. These findings could be explained by the occurrence of hyperventilation secondary to more severe breathlessness, emotional distress, hypoxemia, and/or restrictive abnormalities in patients with advanced disease. However, neither the resting PaCO₂ nor the PaO₂ showed expressive relationships with those components. Therefore, further studies, including exercise physiology measurements, are necessary to better explain such data. Finally, resting PaO₂ levels showed a significant negative correlation only with the pain index. Since IPF patients and control subjects showed similar scores for pain, we have not been able to obtain a convincing interpretation for this finding.

Although the present patients represent a spectrum of distinct respiratory impairment, a substantial number of subjects could be classified as having advanced disease. It is well known that IPF patients with FVC of around 60% predicted usually have a poor survival, and the mean FVC value for the group was 62.41%. In addition, according to published criteria and not considering their age, 19 of 34 patients (55.88%) could be classified as potential lung transplant candidates. Despite these facts, we believe that this group fairly reflects the population of IPF patients regularly seen at medical offices. Even though the clinical course of the disease may be variable, virtually every subject with IPF will develop breathlessness as the disease progresses. According to one study, 36% of the patients were severely disabled by shortness of breath, becoming dyspneic at rest or with minimal exertion. In the present study, the best correlations between HRQL domains and respiratory parameters were found with the BDI score. Therefore, these data clearly show that dyspnea is the most important limiting factor influencing the HRQL of patients with IPF. Similar findings have been described in patients with COPD.

Analysis of correlations between BDI scores and functional parameters gave virtually identical results, as the coefficients obtained for the SF-36 subscore of physical functioning. These results show that the BDI incorporates a substantial amount of information analogous to the physical components of the SF-36, suggesting that the physical components of HRQL questionnaires could be replaced with clinical dyspnea ratings in cross-sectional assessments of patients with fibrotic lung diseases. However, BDI does not give information about social, emotional, and psychological features, as SF-36 and other HRQL instruments do. Therefore, we believe that it still remains to be established if HRQL questionnaires could be replaced with a dyspnea scale like the BDI as a single measurement of health status in patients with chronic respiratory failure.

Clinicians treating patients with IPF have struggled for decades trying to find the best measures that correlate with histology, clinical status, and prognosis. The variables studied include demographics, symptoms, roentgenographic patterns, pulmonary function tests, exercise physiology, radioisotopic lung scans, and cellular and biochemical BAL profiles. An additional problem has been to decide whether the treatment is producing any effect. Available therapeutic modalities result in objective improvements only in 20 to 30% of patients, and the outcomes usually evaluated are physiologic or radiographic changes and survival. Glucocorticoids at high doses and cytotoxic agents are the drugs traditionally employed in the treatment of IPF. During prolonged periods of therapy, side effects and complications commonly occur. These are factors that certainly aggravate the impairment of HRQL in such patients. Therefore, we believe that HRQL instruments should be incorporated into the routine evaluations of IPF patients, since they measure dimensions not estimated by traditional methods of clinical assessment.

In summary, HRQL is an increasingly important item for measuring the impact of chronic disease, including IPF. Patients with IPF have a significant impairment of HRQL in terms of both physical and psychological functioning. The level of dyspnea seems to be the most important factor influencing the quality of life in these subjects. The SF-36 questionnaire, alone or associated with a disease-specific tool, is a valid instrument to evaluate HRQL in IPF patients. Additional studies are necessary to investigate how changes in health status over time correlate with variations in SF-36 scores in this population.

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