Predictors of physical and mental health-related quality of life in patients with interstitial lung disease: a multifactorial analysis*, **

Fatores preditores da qualidade de vida relacionada à saúde física e mental em pacientes com doença pulmonar intersticial: uma análise multifatorial

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Abstract

Objective: To determine predictors of health-related quality of life (HRQoL) in patients with interstitial lung disease (ILD). **Methods:** A cross-sectional study comprising 63 patients, all of whom underwent lung function testing and the six-minute walk test. The following instruments were used: the Medical Outcomes Study 36-item Short-form Survey (SF-36), the Saint George's Respiratory Questionnaire (SGRQ), the Beck Anxiety Inventory, the Beck Depression Inventory, and the Modified Medical Research Council Dyspnea Scale. Principal component analysis was used in order to reduce the dimensionality of the data, thereby identifying the predictor variables, and multiple linear regression analysis was used in order to identify the explanatory variables. **Results:** Of the 63 patients, 34 were female. The mean age was 60.1 ± 13.3 years, the mean FVC was 64.17 ± 15.54% of predicted, and the mean DLCO was 44.21 ± 14.47% of predicted. All of the patients evaluated had impaired HRQoL, scoring worst for the SF-36 physical functioning and SGRQ activity domains. Of the patients evaluated, 60.3% and 57.1% showed symptoms of anxiety and depression, respectively. The principal component analysis identified one predictor of physical HRQoL and one predictor of mental HRQoL. Depression had a strong influence on the predictor of mental HRQoL, and the degree of dyspnea had a strong influence on both predictors of HRQoL in the patients evaluated. Variables related to lung function, exercise capacity, and anxiety had no impact on these predictors. **Conclusions:** In our sample of patients with ILD, the degree of dyspnea had a major impact on the physical and mental HRQoL, and depression had an impact on mental HRQoL.

Keywords: Anxiety; Depression; Dyspnea; Lung diseases, interstitial; Quality of life; Respiratory function tests.

Resumo

Objetivo: Avaliar fatores preditores da qualidade de vida relacionada à saúde (QVRS) em pacientes com doença pulmonar intersticial (DPI). **Métodos:** Estudo transversal com 63 pacientes, submetidos a provas de função pulmonar e teste de caminhada de seis minutos. Foram aplicados os seguintes instrumentos: *Medical Outcomes Study 36-item Short-form Survey* (SF-36), *Saint George's Respiratory Questionnaire* (SGRQ), os inventários de ansiedade e depressão de Beck e *Modified Medical Research Council Dyspnea Scale*. A análise de componentes principais foi utilizada para reduzir as variáveis em fatores preditivos, e a análise de regressão linear múltipla foi utilizada como um modelo explicativo. **Resultados:** Dos 63 pacientes, 34 eram mulheres. A média de idade foi de 60,1 ± 13,3 anos, média de CVF = 64,17 ± 15,54% do previsto e média de DLCO = 44,21 ± 14,47% do previsto. Todos os pacientes avaliados tinham sua QVRS prejudicada, e os piores escores foram observados nos domínios capacidade funcional do SF-36 e atividade do SGRQ. Dos pacientes avaliados 60,3% e 57,1% apresentaram sintomas de ansiedade e depressão, respectivamente. A análise de componentes principais identificou um fator preditor para QVRS física e um fator preditor para QVRS mental. A depressão apresentou uma forte influência sobre o fator preditor de QVRS mental, e o grau de dispneia apresentou uma influência significativa sobre os dois fatores preditores de QVRS nos pacientes avaliados. Variáveis relacionadas à função pulmonar, capacidade de exercício e ansiedade não apresentaram impactos sobre esses fatores preditores. **Conclusões:** Em nossa amostra de pacientes com DPI, o grau de dispneia teve um impacto importante sobre a QVRS física e mental, e a depressão teve um impacto sobre a QVRS mental nos pacientes com DPI.

Descritores: Ansiedade; Depressão; Dispneia; Doenças pulmonares intersticiais; Qualidade de vida; Testes de função respiratória.

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Introduction

Chronic and progressive diseases that lead to interstitial fibrosis of the lungs are collectively known as interstitial lung disease (ILD), which is associated with increased mortality.[1] The treatment of ILD is one of the greatest challenges in medicine.

The quality of life of patients with ILD has been the subject of various studies and is associated with a number of factors[2-8]: the symptoms of the disease itself; side effects of medications; the natural progression of respiratory dysfunction; and disease-related functional limitation. However, there have been only a few studies evaluating the impact that depression and symptoms of anxiety have on the physical and mental health-related quality of life (HRQoL) of patients with ILD.[5,6,9]

The purpose of this study was to identify predictors of HRQoL in a sample of patients with ILD.

Methods

This was a cross-sectional study involving 63 patients with ILD, diagnosed according to clinical, radiological, and histopathological criteria.[1,10] The patients were sequentially selected from among those under treatment at an outpatient clinic of the Porto Alegre *Hospital de Clínicas* between January of 2007 and August of 2008. The study was approved by the institutional research ethics committee, and all patients gave written informed consent.

We included patients diagnosed with any ILD and presenting with a restrictive pattern or reduced DLCO, regardless of the pharmacological treatment, the phase of the disease, or histopathological confirmation.

We excluded patients who presented with any of the following: exacerbation of ILD 30 days prior to inclusion in the study; nonparenchymal restrictive lung disease; predominance of obstructive lung disease; use of home oxygen therapy; uncontrolled coronary artery disease; neuromuscular disease; skeletal anomalies; and any other comorbidity that affected ambulation. Patients currently enrolled in pulmonary rehabilitation programs were also excluded.

After their inclusion, all patients underwent lung function testing and functional capacity evaluation. In addition, various questionnaires and scales were applied by an experienced researcher.

We employed spirometry in order to determine FVC, FEV_1, and FEV_1/FVC, whereas we used whole-body plethysmography to measure TLC, RV, and functional residual capacity (FRC). We used the single and sustained breath-hold methods in order to determine DLCO corrected for hemoglobin. The tests were performed with a constant-volume body plethysmograph (MasterScreen Body; Jaeger, Würzburg, Germany), in accordance with the American Thoracic Society (ATS)/European Respiratory Society guidelines,[11-13] and previously established reference values were used.[14-16] Lung volume restriction was classified as mild (TLC = 70-79% of predicted), moderate (TLC = 60-69% of predicted), or severe (TLC < 60% of predicted).[17] We considered DLCO to be reduced when it was < 75% of predicted.[13]

With the patient in a sitting position and breathing room air, we collected a sample of arterial blood (from the radial artery) in order to evaluate PaO_2, $PaCO_2$, and SaO_2%, for which we employed a gas analyzer (Rapidlab 865-2; Bayer, Fernwald, Germany).

We assessed functional capacity using the six-minute walk test (6MWT), in accordance with the ATS guidelines,[18] and the following parameters were evaluated: six-minute walk distance (6MWD); SpO_2% (with pulse oximetry); HR; and perception of dyspnea and leg pain (with the modified Borg scale). The 6MWT was carried out in a 27-m corridor, and standardized verbal incentives were provided once per minute. We continually monitored SpO_2 and HR by means of telemetry, which enabled the identification of the minimal SpO_2 during the test. Desaturation was defined as a resting SpO_2 (the lowest value recorded during a period of at least 30 s) > 4%. The 6MWT was performed twice, with a minimum interval of 30 min between the two tests in order to allow HR to return to its initial resting value. We employed previously described predicted values for the 6MWD.

The HRQoL was assessed by the Medical Outcomes Study 36-item Short-form Health Survey (SF-36)[19] and the Saint George's Respiratory Questionnaire (SGRQ),[20] both of which have been translated to Portuguese and validated for use in Brazil.[21,22] The SF-36 is a generic HRQoL instrument, comprising

36 items, grouped into eight domains: physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health.[19] The scores were converted into a 100-point scale, higher scores indicating better HRQoL.[6,19,21] The SGRQ is a questionnaire with 76 items grouped into three domains (symptoms, activity, and psychosocial impact). The scores for each SGRQ domain are totaled for a maximum of 100 points, lower scores indicating better HRQoL.[6,20,22]

The Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) are scales developed to identify patients with psychosomatic disorders, and both have been validated for use in Brazil.[23-25] The BAI measures the common symptoms of anxiety. It consists of a list of 21 symptoms, with corresponding multiple-choice (four-option) questions, each corresponding to a higher level of anxiety. The level of anxiety is determined by the total BAI score: 0-9 (minimal); 10-16 (mild); 17-29 (moderate); and 30-63 (severe).[23-25] The BDI objectively measures behavioral manifestations of depression. It comprises 21 categories of symptoms and activities. The total BDI score quantifies the severity of depressive symptoms.[23-25] For samples of patients with affective disorders, the Center for Cognitive Therapy recommends the following classification of depressive symptoms,[26] as determined by the total BDI score: 0-9 (absent or minimal); 10-18 (mild to moderate); 19-29 (moderate to severe); and 30-63 (extremely severe).

The degree of dyspnea was determined by the Modified Medical Research Council (MMRC) Dyspnea Scale, which has been validated for use in Brazil.[27] The MMRC is a simple scale, with only five items, in which patients report the degree of dyspnea and how that limits their activities of daily living.[28]

The sample size was calculated according to the method devised by Bryant & Yarnold, who recommend a subject-to-variable ratio of at least 5:1.[29] Therefore, in order to study the eight SF-36 domains and the three SGRQ domains (eleven HRQoL domains in all), it was necessary to include 55 patients with ILD. Data analysis was performed with the Statistical Package for the Social Sciences, version 14.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used in order to determine the normality of the variables. Quantitative data are presented as number (%), mean ± SD, or median (interquartile range). Values of $p < 0.05$ were considered statistically significant.

Table 1 - Baseline characteristics of the patients with interstitial lung disease (n = 63).

Characteristic	Result
Age, years	60.1 ± 13.3
Body mass index, kg/m^2	27.12 ± 4.72
Female gender	34 (54.0)
Caucasian race	57 (90.5)
Diagnosis	
Idiopathic pulmonary fibrosis	16 (25.4)
Chronic hypersensitivity pneumonitis	13 (20.6)
Other forms of idiopathic interstitial pneumonia[a]	10 (15.9)
Sarcoidosis	8 (12.7)
Pneumoconiosis	8 (12.7)
Connective tissue disease	8 (12.7)

Values expressed as mean ± SD or as n (%). [a]Desquamative interstitial pneumonia (n = 2), nonspecific interstitial pneumonia (n = 2), cryptogenic organizing pneumonia (n = 5), and acute interstitial pneumonia (n = 1).

Principal component analysis was used in order to reduce the dimensionality of the data collected, allowing us to identify the fewest

Table 2 - Lung function and functional capacity of the patients with interstitial lung disease (n = 63).

Variable	Result
Static lung function	
FVC, L	2.15 ± 0.75
FVC, % of predicted	64.17 ± 15.54
FEV_1, L	1.83 ± 0.61
FEV_1, % of predicted	69.08 ± 17.67
FEV_1/FVC	86.95 (81.33-91.79)
TLC, L	4.16 ± 0.93
TLC, % of predicted	75.53 ± 11.82
FRC,L	2,66 ± 0,69
FRC, % of predicted	86.79 ± 18.52
RV, L	1.92 ± 0.37
RV, % of predicted	115.81 ± 25.94
RV/TLC, L	47.40 ± 9.18
DLCO, mL/min/mmHg	12.77 ± 4.84
DLCO, % of predicted	44.21 ± 14.47
PaO_2, mmHg	83.21 ± 12.48
Six-minute walk test	
Walk distance, m	437.2 ± 108.4
Walk distance, % of predicted	86.3 ± 22.41
Minimal SpO_2, %	87 (83-92)
Dyspnea on exertion (Borg scale)	3 (0-4)
Desaturation, n (%)	53 (84)

Values expressed as mean ± SD or median (interquartile range), except where otherwise indicated. FRC: functional residual capacity.

number of factors related to the variables in question. To determine the number of factors, we used the criterion of an eigenvalue > 1. To select the variables for each factor, we used factor loadings, the variable being assigned to the factor with the highest loading. We employed varimax rotation with Kaiser normalization.[29]

We used multiple linear regression analysis in order to identify the explanatory variables, comparing the relative influence of each independent variable on the dependent variable, rather than as a predictive model. A single model including all independent variables was tested in order to identify variables associated with the physical HRQoL and mental HRQoL of patients with ILD (dependent variables). The dependent and the minimal number of independent variables are represented by the factors determined through the principal component analysis described above.[29]

Results

A total of 63 patients with ILD were included in the study. The baseline characteristics of the patients are shown in Table 1. The most common diagnoses were idiopathic pulmonary fibrosis (IPF) and chronic hypersensitivity pneumonitis. The diagnosis of ILD was made according to clinical and radiological criteria in 44.4% of the patients, open lung biopsy findings in 36.5%, transbronchial biopsy findings in 15.9%, and mediastinal biopsy findings in 3.2%.

Regarding the severity of lung function impairment, the restriction was found to be mild in 21 patients (33.3%), moderate in 11 (17.5%), and severe in 6 (9.5%). As can be seen in Table 2, reduced DLCO was found in 51 patients (81.0%). The mean RV was 115.81 ± 25.94% of predicted, and the mean TLC was 75.53 ± 11.82% of predicted; therefore, the RV/TLC ratio was slightly elevated (47.40 ± 9.18 L). The mean 6MWD was 437.2 ± 108.4 m, and 84.1% of the patients presented significant desaturation during the 6MWT.

At the time of the interviews, 28 (44.4%) of the patients were not receiving any pharmacological treatment, 23 (36.5%) were receiving oral corticosteroids, 8 (12.7%) were receiving oral immunosuppressants (cyclophosphamide, azathioprine, methotrexate, or combinations of those), and 4 (6.3%) were receiving a combination of oral corticosteroids and immunosuppressants. Of the 63 patients interviewed, 31 (49.2%) were nonsmokers, 30 (47.6%) were former smokers, and 2 (3.2%) were current smokers. The median smoking history was 18.8 pack-years (range: 0.1-120 pack-years).

We found that HRQoL was impaired in all of the patients evaluated (Table 3). The worst scores were found in the SF-36 physical functioning and SGRQ activity domains. There was a high prevalence of depressive and anxiety symptoms. We found that 36 patients (57.1%) presented with depressive symptoms, which were mild-to-moderate in 27, moderate-to-severe in 8, and severe in 1. We also found that 39 patients (60.3%) presented with anxiety symptoms, which were mild in 23, moderate in 12, and severe in 4.

In relation to the data collected in the interviews (SF-36 and SGRQ), the principal component analysis identified two factors, which were designated physical HRQoL and mental HRQoL. These factors explained 64.8% of the total variance. The domains that correlated most strongly with the physical HRQoL factor (shown here with their respective factor loadings) were the following: the SF-36 functional capacity domain

Table 3 - Dyspnea, anxiety, depression, and health-related quality of life of the patients with interstitial lung disease (n = 63).

Variable	Result
Dyspnea (MMRC score)	2 (1-2)
BAI score	11 (6-17)
BDI score	11 (5-16)
SF-36, domain scores	
Physical functioning	45 (20-70)
Role-physical	75 (0-100)
Bodily pain	72 (41-84)
General health	62 (40-82)
Vitality	60 (45-80)
Social functioning	100 (75-100)
Role-emotional	100 (33-100)
Mental health	76 (60-96)
SGRQ, domain scores	
Symptoms	39.6 (26.0-60.4)
Activity	59.5 (49.9-73.9)
Psychosocial impact	31.4 (18.9-53.8)
Total	41.9 (31.1-64.4)

Values expressed as median (interquartile range). MMRC: Modified Medical Research Council scale; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; SF-36: Medical Outcomes Study 36-item Short-form Survey; SGRQ: Saint George's Respiratory Questionnaire.

Table 4 - Multiple linear regression with the physical health-related quality of life factor as the dependent variable (n = 63).

Factor model: physical HRQoL	Loading	SE	β	p
Constant	1.241	0.267	-	< 0.001
Factor 1 – Lung function	–0.045	0.100	–0.048	0.656
Factor 2 – Lung function	0.192	0.122	0.209	0.122
Factor 1 – 6MWT	–0.189	0.134	–0.192	0.166
Factor 2 – 6MWT	–0.098	0.145	–0.098	0.504
BAI score	–0.019	0.016	–0.170	0.241
BDI score	–0.003	0.020	–0.022	0.895
Degree of dyspnea (MMRC score)	–0.536	0.134	–0.532	< 0.001

HRQoL: health-related quality of life; 6MWT: six-minute walk test; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; and MMRC: Modified Medical Research Council scale. Factor 1 – Lung Function: TLC % of predicted and FVC % of predicted; Factor 2 – Lung Function: DLCO % of predicted and PaO_2; Factor 1 – 6MWT: dyspnea at exercise and minimal SpO_2; and Factor 2 – 6MWT: six-minute walk distance.

(0.868); the SGRQ activity domain (–0.848); the SGRQ psychosocial impact domain (–0.811); the SGRQ symptoms domain (–0.806); and the SF-36 vitality domain (0.620). The domains that correlated most strongly with the mental HRQoL factor (and their respective factor loadings) were as follows: the SF-36 role-emotional domain (0.778); the SF-36 role-physical domain (0.730); the SF-36 general health domain (0.714); the SF-36 mental health domain (0.713); the SF-36 social functioning domain (0.638); and the SF-36 bodily pain domain (0.435).

The principal component analysis of the lung function testing data identified two factors that explained 80.2% of the total variance. The variables that best correlated with factor 1 for lung function testing were TLC, % of predicted (0.937) and FVC, % of predicted (0.922), whereas those that best correlated with factor 2 for lung function testing were DLCO, % of predicted (0.836) and PaO_2 (0.824).

In the analysis of the 6MWT data, we identified two factors that explained 76.1% of the total variance. The variables that best correlated with factor 1 for the 6MWT were dyspnea at the end of the test (0.858) and minimal SpO_2% (–0.706), whereas the variable that best correlated with factor 2 for 6MWT was the 6MWD (0.955).

In the multiple linear regression analysis, the independent variables were factors 1 and 2 for lung function testing, factors 1 and 2 for 6MWT, degree of dyspnea (MMRC score), level of anxiety (BAI score) and severity of depression (BDI score). Tables 4 and 5 show the multiple linear regression model.

Table 4 shows the multiple linear regression analysis with the physical HRQoL factor as the dependent variable. The p value indicates which variables were significantly correlated. The variable that made the greatest contribution to the physical HRQoL factor was the degree of dyspnea ($p < 0.001$; $\beta = -0.532$). However,

Table 5 - Multiple linear regression with the mental health-related quality of life factor as the dependent variable (n = 63).

Factor model: mental HRQoL	Loading	SE	β	p
Constant	0.406	0.315		0.204
Factor 1 – Lung function	–0.064	0.117	–0.063	0.591
Factor 2 – Lung function	–0.023	0.144	–0.023	0.871
Factor 1 – 6MWT	0.044	0.158	0.041	0.783
Factor 2 – 6MWT	0.229	0.171	0.211	0.187
BAI score	–0.007	0.019	–0.055	0.724
BDI score	–0.089	0.024	–0.665	< 0.001
Degree of dyspnea (MMRC score)	0.342	0.158	–0.311	0.035

HRQoL: health-related quality of life; 6MWT: six-minute walk test; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; and MMRC: Modified Medical Research Council scale. Factor 1 – Lung Function: TLC % of predicted and FVC % of predicted; Factor 2 – Lung Function: DLCO % of predicted and PaO_2; Factor 1 – 6MWT: dyspnea at exercise and minimal SpO_2; and Factor 2 – 6MWT: six-minute walk distance.

the β coefficients reveal that, although the influence of factor 2 for lung function testing and of factor 1 for 6MWT were not significant for the physical HRQoL, these variables had a reasonably relevant importance. In relation to depression, we did not observe any influence on the physical HRQoL.

In the multiple linear regression analysis with the mental HRQoL factor as the dependent variable (Table 5), depressive symptoms and the degree of dyspnea were the main factors ($p < 0.001$; $\beta = -0.665$, and $p = 0.035$; $\beta = -0.311$, respectively). However, the β coefficients reveal that, in addition to these two variables, factor 2 for 6MWT also exerted a certain influence on the mental HRQoL. For all of the other variables, the β coefficients indicated almost no influence on the mental HRQoL.

By comparing the two models, we can see that depression had a strong influence on the mental HRQoL but almost none on the physical HRQoL, whereas the degree of dyspnea had a significant influence on the physical and mental HRQoL.

Discussion

Our study investigated predictors of HRQoL in patients with ILD regarding their physical and mental aspects. The scores that indicated the greatest impairment of HRQoL were those related to physical aspects. The variable that contributed the most to the physical HRQoL was the degree of dyspnea, whereas the degree of dyspnea and the severity of depression were the variables that contributed the most to the mental HRQoL.

In our study, the prevalence of depressive symptoms was high (57.1%) but similar to that found by other investigators. In one study, the prevalence of depressive symptoms in a sample of patients with sarcoidosis was 66%,[6] which is similar to that found in another study of such patients (60%).[9] Although anxiety symptoms did not significantly influence the HRQoL in our sample of patients with ILD, the prevalence of anxiety was high (60.3%). Studies on the prevalence of anxiety in patients with ILD are still scarce, and further studies are therefore warranted.

One group of authors evaluated the HRQoL of patients with ILD, using the same instruments that we used, and obtained similar results[7]: the median score for the SGRQ activity domain was 54.4 (range: 39.9-72.9); and the median score for the SF-36 physical functioning domain was 55 (range: 30.0-71.3). The authors demonstrated that both the SGRQ and the SF-36 are sensitive instruments for the evaluation of HRQoL in patients with ILD, as well as that FVC, FEV_1, DLCO, 6MWD, and the degree of dyspnea (Borg scale) correlate significantly with the scores on those questionnaires.

There have been two studies conducted in Brazil and evaluating the HRQoL of patients with IPF.[4,8] The authors of both of those studies obtained results similar to ours. The first study validated the SF-36 questionnaire for use in patients with IPF. The authors of that study found that the patients with IPF scored significantly worse than did the control subjects for the SF-36 physical functioning, role-emotional, and mental health domains.[4] In the second study,[8] the SGRQ domain that was most affected was the activity domain (highest mean value, 62.4 ± 19.0); for the SF-36, the domain that was least affected was the mental health domain, the most affected domains being the physical functioning, vitality and role-emotional domains (46.0 ± 18.3, 49.2 ± 24.3, and 46.6 ± 39.5, respectively). In addition, TLC presented a strong correlation with HRQoL in the population evaluated in that study. The authors concluded that a specific questionnaire (the SGRQ) rather than a generic one (the SF-36) is a more appropriate instrument to evaluate HRQoL in patients with IPF.[8]

In the principal component analysis of the data collected with the HRQoL questionnaires used in our study, all of the SGRQ domains were included in the physical HRQoL factor, and most of the SF-36 domains were included in the mental HRQoL factor. Consequently, the SGRQ seems to reflect the physical aspects better, and the SF-36 seems to reflect the mental aspects better. The SF-36 role-physical and bodily pain domains, which are classified as physical domains for the general population,[4,7] were included in the mental HRQoL factor in our study, perhaps reflecting this aspect better than does the SGRQ, which has no predefined classification for the physical or mental aspects.[7]

In the multiple linear regression analysis, depression had a strong influence on the mental HRQoL but no influence on the physical

HRQoL, whereas the degree of dyspnea had a significant influence on both aspects of HRQoL. One group of authors analyzed studies related to the HRQoL of patients with IPF.[2] Those authors found a strongly significant association between dyspnea and physical health. However, they identified no relationship between dyspnea and mental health. In addition, they found that lung function and oxygenation variables were not related to HRQoL, a result similar to that obtained in our study.

Another group of authors employed the SGRQ to evaluate and identify factors related to the HRQoL of patients with IPF.[3] In the multiple linear regression analysis, the dyspnea score (baseline dyspnea index) was the factor that contributed the most to explaining the variance in the HRQoL of these patients. However, the authors did not investigate the influence that anxiety and depression had on HRQoL. In another study, involving patients with sarcoidosis, a moderate but significant association was found between depression and the SF-36 mental health domain score ($r = 0.58$; $p < 0.001$).[6] In that study, the degree of dyspnea did not make a significant contribution to HRQoL. However, variables such as 6MWD, DLCO, TLC, and anxiety were not considered in the analysis.

For patients with ILD, treatment strategies are most often established on the basis of physiological variables, such as lung function and PaO_2.[1] However, the results of our study suggest that findings related to the individual perception of the patients, such as the degree of dyspnea, depression and HRQoL, are more strongly interrelated than are lung function test results. Consequently, the management of dyspnea and depressive symptoms could be an important tool for optimizing the HRQoL of patients with ILD.

Our study has some limitations. First, it is necessary to consider the heterogeneity of the sample. The different types of ILD and the limited number of patients in each subgroup did not allow a more detailed analysis of the impact that the underlying disease had on the HRQoL of the patients evaluated. In addition, this was a cross-sectional study, and our findings therefore allow us only to describe the associations among the variables that were studied in patients with ILD. The second aspect to be considered is related to the diagnostic criteria for ILD. In most cases, the diagnosis was made according to clinical and radiological criteria, only 39.7% of the diagnoses having been obtained through surgical biopsy. However, surgical biopsy is not considered the gold standard for the diagnosis of ILD. The current consensus is that the diagnosis should be made on the basis of a multidisciplinary assessment and a mutually agreeable conclusion.[1] In addition, our sample was more homogeneous than were those evaluated in other studies.[7] Furthermore, we included patients with ILD and restrictive lung function or reduced DLCO. Patients with reduced DLCO, in the absence of a restrictive pattern, were included in this study in order to enhance the functional spectrum of the disease, adding cases of milder lung function impairment to the sample. Moreover, former smokers and current smokers accounted for more than half of our sample, and the overall mean RV/TLC ratio was 47.4 ± 9.2 L. It is also noteworthy that the mean TLC was low (75.53 ± 11.82% of predicted), and that the RV was slightly elevated (115.81 ± 25.94% of predicted).[17] Low TLC is usually associated with reduced VC. With intrapulmonary restriction, RV is usually normal, and the RV/TLC ratio is consequently high. In this context, this does not necessarily imply airway obstruction. However, considering that the sample was mainly composed of former smokers and current smokers, and that a mixed obstructive and restrictive ventilatory defect is not uncommon in such patients, it is possible that smoking had contributed to the abnormality in the small airways, which could have contributed to early airway closure, resulting in a high RV/TLC ratio.[30]

In conclusion, our results suggest that, in patients with ILD, depression has a strong influence on the mental HRQoL and that the degree of dyspnea has a significant influence on both aspects (physical and mental) of the HRQoL. Variables related to lung function, 6MWT, and anxiety had no impact on HRQoL in this sample of patients with ILD.

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References

1. Bradley B, Branley HM, Egan JJ, Greaves MS, Hansell DM, Harrison NK, et al. Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. Thorax. 2008;63 Suppl 5:v1-58.
2. Swigris JJ, Kuschner WG, Jacobs SS, Wilson SR, Gould MK. Health-related quality of life in patients with idiopathic pulmonary fibrosis: a systematic review. Thorax. 2005;60(7):588-94.
3. Nishiyama O, Taniguchi H, Kondoh Y, Kimura T, Ogawa T, Watanabe F, et al. Health-related quality of life in patients with idiopathic pulmonary fibrosis. What is the main contributing factor? Respir Med. 2005;99(4):408-14.
4. Martinez TY, Pereira CA, dos Santos ML, Ciconelli RM, Guimarães SM, Martinez JA. Evaluation of the short-form 36-item questionnaire to measure health-related quality of life in patients with idiopathic pulmonary fibrosis. Chest. 2000;117(6):1627-32.
5. Drent M, Wirnsberger RM, Breteler MH, Kock LM, de Vries J, Wouters EF. Quality of life and depressive symptoms in patients suffering from sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis. 1998;15(1):59-66.
6. Cox CE, Donohue JF, Brown CD, Kataria YP, Judson MA. Health-related quality of life of persons with sarcoidosis. Chest. 2004;125(3):997-1004.
7. Chang JA, Curtis JR, Patrick DL, Raghu G. Assessment of health-related quality of life in patients with interstitial lung disease. Chest. 1999;116(5):1175-82.
8. Zimmermann CS, Carvalho CR, Silveira KR, Yamaguti WP, Moderno EV, Salge JM, et al. Comparison of two questionnaires which measure the health-related quality of life of idiopathic pulmonary fibrosis patients. Braz J Med Biol Res. 2007;40(2):179-87.
9. Chang B, Steimel J, Moller DR, Baughman RP, Judson MA, Yeager H Jr, et al. Depression in sarcoidosis. Am J Respir Crit Care Med. 2001;163(2):329-34.
10. American Thoracic Society; European Respiratory Society. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. This joint statement of the American Thoracic Society (ATS), and the European Respiratory Society (ERS) was adopted by the ATS board of directors, June 2001 and by the ERS Executive Committee, June 2001. Am J Respir Crit Care Med. 2002;165(2):277-304. Erratum in: Am J Respir Crit Care Med. 2002;166(3):426.
11. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005;26(2):319-38.
12. Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, et al. Standardisation of the measurement of lung volumes. Eur Respir J. 2005;26(3):511-22.
13. Macintyre N, Crapo RO, Viegi G, Johnson DC, van der Grinten CP, Brusasco V, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. Eur Respir J. 2005;26(4):720-35.
14. Neder JA, Andreoni S, Castelo-Filho A, Nery LE. Reference values for lung function tests. I. Static volumes. Braz J Med Biol Res. 1999;32(6):703-17.
15. Crapo RO, Morris AH, Gardner RM. Reference spirometric values using techniques and equipment that meet ATS recommendations. Am Rev Respir Dis. 1981;123(6):659-64.
16. Neder JA, Andreoni S, Peres C, Nery LE. Reference values for lung function tests. III. Carbon monoxide diffusing capacity (transfer factor). Braz J Med Biol Res. 1999;32(6):729-37.
17. Pennock BE, Cottrell JJ, Rogers RM. Pulmonary function testing. What is 'normal'? Arch Intern Med. 1983;143(11):2123-7.
18. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166(1):111-7.
19. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care. 1992;30(6):473-83.
20. Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation. The St. George's Respiratory Questionnaire. Am Rev Respir Dis. 1992;145(6):1321-7.
21. Ciconelli RM, Ferraz MB, Santos W, Meinão I, Quaresma MR Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36). Rev Bras Reumatol. 1999;39(3):143-50.
22. Sousa TC, Jardim JR, Jones P. Validação do Questionário do Hospital de Saint George na Doença Respiratória (SGRQ) em pacientes portadores de doença pulmonar obstrutiva crônica no Brasil. J Pneumol. 2000;26(3):119-28.
23. Gorenstein C, Pompéia S, Andrade L. Scores of Brazilian University students on the Beck Depression and the State Trait Anxiety Inventories. Psychol Rep. 1995;77(2):635-41.
24. Gorenstein C, Andrade L. Validation of a Portuguese version of the Beck Depression Inventory and the State-Trait Anxiety Inventory in Brazilian subjects. Braz J Med Biol Res. 1996;29(4):453-7.
25. Andrade L, Gorenstein C, Vieira Filho AH, Tung TC, Artes R. Psychometric properties of the Portuguese version of the State-Trait Anxiety Inventory applied to college students: factor analysis and relation to the Beck Depression Inventory. Braz J Med Biol Res. 2001;34(3):367-74.
26. Beck AT, Steer RA, Garbin MG. Psychometric properties of the Beck Depression Inventory: Twenty-five years of evaluation. Clin Psychol Rev. 1988;1(8):77-100.
27. Kovelis D, Segretti NO, Probst VS, Lareau SC, Brunetto AF, Pitta F. Validation of the Modified Pulmonary Functional Status and Dyspnea Questionnaire and the Medical Research Council scale for use in Brazilian patients with chronic obstructive pulmonary disease. J Bras Pneumol. 2008;34(12):1008-18.
28. Baydur A, Alsalek M, Louie SG, Sharma OP. Respiratory muscle strength, lung function, and dyspnea in patients with sarcoidosis. Chest. 2001;120(1):102-8.
29. Bryant FB, Yarnold PR. Principal-components analysis and exploratory and confirmatory factor analysis. In: Grimm LG, Yarnold PR, editors. Reading and understanding multivariate statistics. Washington: American Psychological Association; 2001. p. 99-136.
30. Gibson GJ. Lung volumes and elasticity. Clin Chest Med. 2001;22(4):623-35, vii.

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