Validity of the Saint George’s Respiratory Questionnaire in the evaluation of the health-related quality of life in patients with interstitial lung disease secondary to systemic sclerosis

L. Beretta, A. Santaniello, A. Lemos¹, M. Masciocchi and R. Scorza

Objectives. Interstitial lung disease (ILD) profoundly affects the health-related quality of life (HRQoL) in patients with systemic sclerosis (SSc). We tested the validity of the Saint George’s Respiratory Questionnaire (SGRQ), a lung-specific HRQoL-evaluation tool, in a population of SSc patients with ILD.

Methods. Twenty-eight consecutive SSc patients with a restrictive pulmonary involvement, defined as a forced vital capacity <80% of the predicted, with no pulmonary hypertension were considered. All the patients filled in the Medical Research Council (MRC) scale for perceived breathlessness, the SGRQ and the Disability Index of the Health Assessment Questionnaire (HAQ DI), and underwent evaluation with complete pulmonary function testing (PFT), 6-minute walk distance (6MWD) and high-resolution computed tomography (HRCT).

Results. The SGRQ ‘activity’ scores inversely correlated with the 6MWD (r = -0.86, P < 0.001) and forced vital capacity percentage of predicted values (r = -0.47) and directly correlated with HRCT (r = 0.41, P < 0.05), MRC (r = 0.64, P < 0.001) or HAQ DI scores (r = 0.62, P < 0.001), independently of disease duration or subset. On the contrary, HAQ DI scores were influenced by those variables and corrected correlations with 6MWD (r = 0.56, P < 0.001) or HRCT scores (r = 0.36, P = NS) were less strong than those observed with the SGRQ.

Conclusions. The SGRQ, although not specifically designed for scleroderma, is a valid respiratory-specific questionnaire for the evaluation of HRQoL in patients with SSc-related ILD. The SGRQ performs better in relation to exercise capacity and lung imaging than other non-respiratory-specific questionnaires widely used in scleroderma studies. Further studies are needed to address its ability to assess changes over time or in response to therapy.

Key words: Systemic sclerosis, Quality of life, Interstitial lung disease.

Introduction

Systemic sclerosis (SSc) is an autoimmune disease characterized by fibrosis, inflammation of the skin and involvement of internal organs, including the heart, the kidney, the gastrointestinal tract and the lung [1]. Interstitial lung disease (ILD) represents the leading cause of morbidity in SSc patients, profoundly affecting survival rates at 8 and 9 yrs [2], and a restrictive pulmonary involvement, with a mild-to-moderate deterioration in lung function, can be observed in up to 40% of scleroderma patients [3]. Functional lung impairment in SSc patients is likely to be accompanied by a decline in patients’ capacity to cope with day-to-day activities, in their emotional well-being and therefore, in their health-related quality of life (HRQoL).

To date, several questionnaires designed to determine the HRQoL in many disease have been developed [4–6]. Some of them specifically addressed the issue of HRQoL in lung diseases, mainly in chronic conditions, such as asthma and chronic obstructive pulmonary disease (COPD) [7–10], but proved reliable in assessing the HRQoL in patients with ILD as well. Namely, the Saint George’s Respiratory Questionnaire (SGRQ) has been successfully evaluated in patients with idiopathic pulmonary fibrosis (IPF) [11] and others with ILD [12, 13]. To date, however, neither the SGRQ nor other lung-specific questionnaires have been applied in SSc patients with interstitial lung involvement and other general measures of the patient’s functional status have been used as substitutes [14].

The aim of the present study was to assess the validity of the SGRQ in a population of patients with SSc-ILD. Indeed, while SSc-ILD and IPF resemble each other in many aspects, they differ in the classification of lung histopathology, pathogenesis, radiographic appearance, prognosis and response to therapy [15]. Our hypothesis was that a worse HRQoL, as determined by the SGRQ, should correlate with an impairment in functional and anatomic lung parameters, such as the 6-min walk distance (6MWD), pulmonary function testing (PFT), dyspnoea scale and high-resolution computed tomography (HRCT) score. The SGRQ has been chosen for this purpose since in IPF it showed better correlations with physiological and functional measures of disease severity than other HRQoL questionnaires [16]. Moreover, this instrument is less prone to produce biased scores than other respiratory-specific HRQoL instruments, such as the chronic...
respiratory questionnaire (CRQ) [12], and covers more domains identified in an ideal—but yet undeveloped—questionnaire to assess the HRQoL in IPF patients, than other respiratory-specific and non-specific HRQoL tools [17].

Materials and methods

Patients

Patients referring to our outpatient clinic between May 2005 and November 2005 with a diagnosis of SSc made according to the preliminary American College of Rheumatology (ACR) criteria for the classification of SSc [18], and with a restrictive lung disease, defined by a forced vital capacity (FVC) <80% of the predicted values [19] were considered for the study. Patients were excluded if they had any of the following: (i) inability to perform the 6-minute walk test (6MWT) due to skeletal-muscle impairment or other illness; (ii) presence of other diseases contraindicating the execution of the test (i.e. hypertension, history of myocardial infarction or unstable angina) and (iii) pulmonary hypertension (PAH) on echocardiogram, defined as a right-ventricular systolic pressure (RVSP) >40 mmHg. RVSP was estimated by adding the transthoracic apical systolic pressure, determined by the modified Bernoulli formula \( P = 4V^2 \), to the mean atrial pressure, nominally set at 5 mmHg.

Patients were categorized as having the limited cutaneous SSc (lcSSc) or the diffuse cutaneous SSc (dcSSc) form of the disease [20]. Disease duration was defined as the number of years elapsing from the first non-Raynaud symptom that was clearly attributable to scleroderma up to the day the patients entered the study [21]. A total of 194 SSc patients were evaluated at our Institution in the considered period (Fig. 1); among these, 72 (37%) had an FVC <80% of the predicted values on former PFT and were thus considered eligible. Eighteen were not willing to participate in the study, 26 patients were further excluded due to: increased RVSP (\( n = 17 \)), inability to perform the 6MWT (\( n = 5 \)), inability to fill-in the Italian version of the SGRQ since they were non-natives (\( n = 3 \)), two patients were further excluded from the analysis due to the occurrence of an FVC ≥80% of the predicted values on confirmatory PFT.

Overall, 28 patients completed the study procedures and fulfilled the inclusion/exclusion criteria. All of them provided written consent for the research.

Saint George’s respiratory questionnaire

The SGRQ is a standardized, self-administered questionnaire for measuring impaired health and perceived HRQoL in airways disease [22]. It consists of 76 items, producing a ‘symptoms’, an ‘activity’, an ‘impacts’ and a ‘total score’. The ‘symptoms score’ assesses the patients’ perception of their recent (4 weeks) respiratory problems; the ‘activity’ score measures the patients’ current disturbance to perform daily physical activity; the ‘impacts’ score evaluates the whole range of disturbances the patients currently experience in their life due to respiratory problems and the ‘total’ score sums and weights all the former components.

Scores can range from 0 (no impairment) to 100 (the worst impairment) for each component; higher scores connote greater distress and thus, worse HRQoL. The questionnaire was administered and scored according to the instruction manual before the execution of the 6MWT and PFT.

The face and content validity of the SGRQ in ILD has been previously tested [12, 16], and while some authors raised some concerns about its face validity, especially as far as the questions included in the ‘symptoms’ domain (i.e. those more specific for COPD-related manifestations) were concerned [23], others had the instrument rate by ILD patients for relevance, obtaining a highly positive feedback [12].

MRC dyspnoea scale

Before filling in the SGRQ, all the patients were asked to grade their perceived breathlessness on the Medical Research Council (MRC) scale: grade 1, ‘I only get breathless with strenuous exercise’; grade 2, ‘I get short of breath when hurrying or walking up a slight hill’; grade 3, ‘I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level’; grade 4, ‘I stop for breath after walking 100 yards or after a few minutes on the level’ and grade 5, ‘I am too breathless to leave the house’.

HAQ DI

The Disability index of the Health Assessment Questionnaire (HAQ DI) has been developed as an instrument to measure the patient’s functional status in rheumatoid arthritis, but it has successfully been used in SSc, correlating with the cutaneous and the visceral involvement [24]. The HAQ DI has been extensively utilized in SSc patients with ILD [14]. All the 20 items included in the eight original domains of the HAQ DI were administered to the patients. Each item is assessed on a 0–3 scale and the highest scores in each of the eight domains were summed and divided by eight to derive the HAQ DI score (range 0–3).

Six-minute walk test

The 6MWT measures the distance a patient can quickly walk on a flat, hard surface in a period of 6 min and is thought to reflect well a person’s functional activity level for daily physical activities. The 6MWT was conducted according to the American Thoracic Society guidelines [25] and it was performed in a quiet corridor between two cones placed 30 m apart. Before, during and after the test, oxygen saturation (SpO2) was measured by a pulse oximeter carried by an assistant and with a probe placed on the patient’s forehead to minimize and compensate motion artefacts and misreading due to peripheral low blood perfusion or SSc cutaneous involvement. Borg scores for perceived

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**Fig. 1.** Inclusion/exclusion flow chart. SSc, systemic sclerosis; FVC, forced vital capacity; PFT, pulmonary function testing; RVSP, right-ventricular systolic pressure; 6MWT, 6-minute, walk test.
breathlessness [26] were measured after the 6MWT, with a score of 0 being no breathlessness at all and a score of 10 being the maximal breathlessness.

Pulmonary function tests

PFTs were performed the same day of the 6MWT, according to the recommendations of the American Thoracic Society [27]; normal values for FVC, total lung capacity (TLC), forced expiratory volume in one second (FEV₁) and diffusing capacity of the lung for carbon monoxide (DLCO) were derived from those previously published [28, 29]. The DLCO values were corrected of the lung for carbon monoxide (DLCO) were derived from those by means of Pearson’s during the 6MWT), Borg scores and MRC scores were compared (67.9%) form of the disease and the Scl70 antibody (78.6%), and the majority of the patients were females (82.1%) with the dcSSc form of the disease and the Scl70 antibody (78.6%), and the majority of the patients were females (82.1%) with the dcSSc form of the disease and the Scl70 antibody (78.6%).

High-resolution computed tomography

HRCT was performed within 1 week from the completion of the SGRQ and the execution of PFT and the 6MWT. Scans were performed at full inspiration, in a prone position with a slice thickness of 1.5 mm and a table increment from apex to base of 10 mm. The images were viewed with the optimal windows setting according to the patient’s morphology. Scans were scored by an experienced radiologist (A.L.), blind to clinical and other investigational data, according to Warrick et al. [30]. A point value was assigned to each abnormality (ground-glass appearance = 1; irregular pleural margins = 2; septal/subpleural lines = 3; honeycombing = 4 and subpleural cyst = 5); a ‘severity of disease’ score was generated by adding these point values. An ‘extent of disease’ score was generated by localizing the number of bronchopulmonary segments (up to 18) with the above abnormalities (1–3 segments = 1; 4–9 segments = 2; >9 segments = 3). A total HRCT scores with a possible range from 0 (no involvement) to 30 (the worst involvement) was computed by adding the severity and the extent score.

Statistical analysis

Statistical analysis was performed with the SPSS package software (ver 12.0, SPSS Inc). Clinical parameters (age, disease duration, total skin score, anticorpal status, disease subset and gender), HRCT scores, SGRQ scores, 6MWD, PFT percentage of predicted values, SpO₂ (at rest, maximum and mean desaturation during the 6MWT), Borg scores and MRC scores were compared by means of Pearson’s r, Spearman’s p or Mann–Whitney’s U-test when appropriate. The relationship between SGRQ scores, HAQ DI, HRCT scores or lung physiology and the 6MWD was determined by using partial correlation coefficients, controlling for age, gender and smoking habit, since these variables have been shown to influence the 6MWD [25]. To analyse the contributive factors to the SGRQ and to the HAQ DI scores, the 6MWD, the lung physiology (the FVC, TLC and DLCO percentage of predicted values) the HRCT score, the maximum SpO₂ desaturation, age, disease subset and disease duration, were inserted in a multiple regression model as independent variables and stepwise multivariate analysis was performed.

Results

Patient’s demographic and clinical data are reported in Table 1. The majority of the patients were females (82.1%) with the dcSSc (67.9%) form of the disease and the Scl70 antibody (78.6%), and with a long-lasting disease duration (12.6 ± 7.3 yrs). Lung-related and HRQoL-related parameters are reported in Table 2. All the patients had signs of interstitial lung involvement with a mean HRCT score of 9.8 ± 4.3.

Correlations between questionnaires (SGRQ and HAQ DI) and the MRC scale for perceived breathlessness or the selected lung parameters are reported in Table 3.

All the four components of the SGRQ inversely correlated with the 6MWD (Fig. 2), the strongest correlations were observed with the ‘activity’ component. The same results (Table 3) were confirmed when the 6MWD was corrected for age, gender and smoking habit (‘activity’ r = −0.86, P < 0.001; ‘impact’ r = −0.59, P < 0.005; ‘total’ SGRQ r = −0.77, P < 0.001), with the exception of the symptoms component (r = −0.37, P = NS).

Significant correlations were also observed among the ‘activity’ component of the SGRQ and HRCT scores (r = 0.41, P < 0.05), the MRC scale (r = 0.64, P < 0.001) or FVC percentage of predicted values (r = −0.47, P < 0.05); or between the SGRQ ‘total’ score and HRCT scores (r = 0.52, P < 0.005) or the MRC scale (r = −0.41, P < 0.05), and between the ‘impact’ component of the SGRQ and HRCT scores (r = 0.499, P < 0.01). No correlations were found between SGRQ scores and SpO₂ (at rest or maximum desaturation) or Borg index. Disease duration, age, gender, smoking habit, Rodman’s total skin score (TSS) or the anticorpal status did not influence the SGRQ scores.

Stepwise multiple regression analysis (Table 4) showed that only the 6MWD significantly contributed to the ‘activity’ (R² = 0.77, t = −9.34, P < 0.0001), to the ‘impact’ (R² = 0.34,
The HAQ DI scores were correlated with disease duration (Spearman’s $r = 0.51$, $P < 0.01$) and were significantly higher in dcSSc patients as compared with lcSSc patients ($0.5 \pm 0.5$ vs $0.37 \pm 0.56$, $P < 0.05$). Correlations between the HAQ DI scores and the selected lung parameters were therefore corrected for disease duration and disease subset, obtaining values and probabilities largely comparable, but weaker than those observed with the SGRQ scores (Table 3). Stepwise multiple regression analysis (Table 4) showed that exercise tolerance (6MWD) was the main contributing factor to the HAQ DI scores, but its effect was weaker than the one exerted on the ‘activity’ and the ‘total’ SGRQ scores ($R^2 = 0.39$, $t = -4.1$, $P = 0.0002$).
**Table 5. Correlations among lung parameters**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>FVC</th>
<th>TLC</th>
<th>DLCO</th>
<th>HRCT</th>
<th>6MWD</th>
</tr>
</thead>
<tbody>
<tr>
<td>SpO2</td>
<td>-0.48**</td>
<td>-0.64*</td>
<td>-0.42*</td>
<td>-0.31</td>
<td>0.25</td>
</tr>
<tr>
<td>FVC</td>
<td>-0.59*</td>
<td>0.44*</td>
<td>0.25</td>
<td>0.64*</td>
<td></td>
</tr>
<tr>
<td>TLC</td>
<td>0.49**</td>
<td>0.42*</td>
<td>0.64*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLCO</td>
<td>-0.18</td>
<td>0.47*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRCT</td>
<td>-0.47*</td>
<td></td>
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</tbody>
</table>

Correlations by means of Pearson’s r are shown, except where otherwise indicated. FVC, forced vital capacity; TLC, total lung capacity; DLCO, diffusing capacity of the lung for carbon monoxide; HRCT, high-resolution computed tomography scored according to Warrick et al. [30]; 6MWD, 6-minute walk distance; SpO2, maximum oxygen desaturation during the 6MWD.

*Partial correlation, corrected for age, gender and smoking habit.

**P < 0.05, ***P < 0.01, *P < 0.001, ^P < 0.0001.

Medium-strength correlations were found among the HAQ DI scores and the ‘activity’ (r = 0.62, P < 0.001), the ‘impact’ (r = 0.4, P < 0.05) and the total SGRQ scores (r = 0.5, P < 0.01).

Correlations among lung physiology, HRCT scores, 6MWD and SpO2 during the 6MWT are reported in Table 5. On univariate analysis, the maximum SpO2 desaturation during the 6MWT inversely correlated with FVC (r = -0.48, P < 0.01), TLC (r = -0.64, P < 0.001) or DLCO (r = -0.42, P < 0.05) percentage of predicted values; stepwise multivariate linear analysis showed that only TLC influenced SpO2 desaturation during exertion (r = -2.48, P < 0.001). TLC percentage of predicted values showed also a medium inverse correlation with HRCT scores (r = -0.42, P < 0.05).

The 6MWD directly correlated with FVC (r = 0.64, P = 0.001), TLC (r = 0.41, P < 0.05) or DLCO (r = 0.47, P < 0.05) percentage of predicted values, and inversely correlated with HRCT scores (r = -0.47, P < 0.05).

No significant differences were observed between lcSSc and dcSSc patients for all the variables considered, except for the TSS (3.2 ± 4.3 vs 8.6 ± 5.3, P < 0.005) and the HAQ DI (see earlier observation).

**Discussion**

Our data demonstrate the validity of the SGRQ in assessing the HRQoL in SSC patients with ILD. Indeed, the SGRQ showed a good correlation with the 6MWD, HRCT scores and other validated measures for perceived breathlessness, such as the MRC scale, but not with PFT except for the significant relationship between the SGRQ ‘activity’ score and FVC (Table 3). The strongest correlations were found between the 6MWD and the SGRQ scores, with an almost linear association with the ‘activity’ score (Fig. 2); stepwise multiple regression analysis showed also that the 6MWD was the main contributing factor to the ‘activity’, ‘impact’ and ‘total’ SGRQ scores. Our data confirm previously published correlation between the SGRQ and the 6MWD in ILD [12] and in other airway diseases [8]. The 6MWD is a standardized measure that is thought to reflect well a one person’s functional level for daily physical activities [25]. The SGRQ appears thus as an adequate instrument to measure the patient’s exercise tolerance in subject with ILD secondary to SSC and it may represent an adequate substitute for the 6MWD in those patients with any physical impairments or pathologic condition contraindicating the execution of the 6MWT.

In our study, we did not find significant correlations between the ‘symptoms’ score and the selected lung parameters. This result is not completely unexpected, since the items composing the ‘symptoms’ score specifically address to COPD-related manifestations, such as wheezing, productive cough or lower respiratory tract infections, that are virtually absent or marginally important in ILD patients.

One of the main findings of our research is the ability of the SGRQ to evaluate the HRQoL in all SSC patients with ILD, regardless of other non-lung-related parameters, such as disease subset or disease duration. Our data also indicate that in SSC-ILD, the SGRQ performs better in relation to lung imaging and exercise capacity than other general measures of the patient’s functional status. The observation that the HAQ DI scores more strongly correlated with FVC than with the SGRQ scores is of little interest in this context, since in our population of SSC patients with ILD, multiple regression analysis showed that the patient’s exercise tolerance (i.e. 6MWD) was the main contributing factor both to the HAQ DI and to the SGRQ scores.

In the present work, we also confirmed the previous observation by Diot et al. [31] on an association between HRCT scores and TLC percentage of predicted values, while we weren’t able to confirm the correlation they observed between DLCO and HRCT scores. In our study, TLC was the sole variable related to oxygen desaturation during exertion (i.e. 6MWT), while SpO2 maximum desaturation did not correlate to the SGRQ scores, as similarly observed by Chang et al. [12] in subjects with ILD. Providing different information from PFT, the SGRQ can thus be considered as an useful and adequate complement to traditional measures of lung involvement in SSC patients. The complementarity between the SGRQ and PFT is also confirmed by the poor correlation we observed between them. This result is somewhat in contrast with the results obtained by Chang et al. [12] but is very similar to those described by Nishiyama et al. [11] in 41 subjects with IPF.

Some limitations/unsolved questions must be addressed in our study. First, on the basis of our results it is not possible to determine whether the SGRQ is an adequate tool to evaluate the change or the evolution of SSC-related ILD over time and its response to therapy. Second, it is not possible to determine whether our results can be applied to all scleroderma patients with ILD, comprising those with secondary pulmonary hypertension; indeed, we deliberately excluded from the analysis subjects with a RVSP >40 mmHg to obtain an as homogeneous as possible population of patients without concomitant confounding variables that might have further influenced the 6MWD or SpO2 values regardless of the severity of fibrosis (i.e. HRCT scores). Third, in this study, the number of patients involved is relatively low due to inclusion/exclusion criteria and to the low prevalence of SSC-related ILD in the general population. Fourth, the FVC threshold we chose as inclusion criterion might seem too loose to define the presence of a restrictive lung physiology; however, this value has previously been used in a parallel radiographic/functional study in SSC patients with interstitial lung involvement [19] and all of our patients had indeed radiographic signs of ILD with a high mean HRCT scores.

In summary, the SGRQ, although not specifically designed for scleroderma, proved to be a valid respiratory-specific questionnaire for the evaluation of the HRQoL in patients with SSC-related ILD, strongly correlating with standardized tools.
to measure the patient’s lung involvement, its physical tolerance to exertion or perceived breathlessness and providing additional information to traditional measures of lung involvement. Further studies are needed to address the ability of the SGRQ to assess changes over time or in response to therapy.

### Key messages

- The HRQoL is impaired in SSc-ILD.
- No specific respiratory HRQoL questionnaire has been validated in SSc-ILD.
- The SGRQ is a valid instrument for the evaluation of the HRQoL in SSc-ILD.

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### References