Clinical Correlates of Self-reported Physical Health Status in Systemic Sclerosis

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ABSTRACT. ***Objective.*** Systemic sclerosis (SSc) is a multisystem disease associated with impaired health-related quality of life (HRQOL). Our objective was to identify the clinical characteristics that correlate with the physical health status of patients with SSc, as assessed by the Medical Outcomes Trust Short Form-36 (SF-36).

Methods. Cross-sectional, multicenter study of 416 patients from the Canadian Scleroderma Research Group Registry. Patients were assessed with detailed clinical histories, medical examinations, and self-administered SF-36. Multiple linear regression was used to assess the relationship between selected demographic and clinical variables and the SF-36 Physical Component Summary (PCS) score.

Results. The greatest impairments in the SF-36 were in the domains measuring physical health, and the mean SF-36 PCS score was 37.5 (± 11.2). In multivariate analysis, significant clinical predictors of the SF-36 PCS were shortness of breath, number of gastrointestinal problems, skin score, swollen joint count, and age. The final model explained 47% of the variance in the SF-36 PCS.

Conclusion. Clinical characteristics identified as significant correlates of the self-reported physical health status in SSc should each be targets of intervention in order to improve the HRQOL of patients with this disease. (J Rheumatol First Release May 15 2009; doi:10.3899/jrheum.081057)

Key Indexing Terms:
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Systemic sclerosis (SSc) is a multisystem disorder characterized by a disturbance in fibroblast function, microvascular disease, and immune system activation, culminating in fibrosis of skin and internal organs[1]. It is associated with significant morbidity, including disfiguring skin thickening, finger ulcers, joint contractures, pulmonary hypertension, interstitial lung disease, chronic diarrhea, and renal failure. Functional disability is considerable[2] and patients have high rates of clinically significant symptoms of depression, even when compared to patients with other acute and chronic conditions using the same assessment tools and scoring cutoffs[3,4]. As such, the disease encompasses broad multidimensional issues including biological, psychological, and social processes. Thus, it is not surprising that health-related quality of life (HRQOL) is impaired in SSc[5,6]. Moreover, because there is no cure for SSc, understanding the effect of SSc on HRQOL is a priority. However, to date, there has been relatively little work on HRQOL in SSc, and experts have recommended additional research in this area[7].

We undertook this study to identify the demographic and clinical characteristics that correlate with HRQOL in patients with SSc. The Medical Outcomes Trust Short Form-36 (SF-36)[8] is a generic measure of HRQOL widely used in rheumatology and was therefore used as the measure of physical health status.

MATERIALS AND METHODS

Study design. Cross-sectional study of a convenience sample of patients with SSc.

The study subjects consisted of those enrolled in the Canadian Scleroderma Research Group Registry. Patients in this Registry are recruited from 15 centers across Canada. They must have a diagnosis of SSc made by the referring rheumatologist, be ≥ 18 years of age, and be fluent in either English or French. Patients included in the study were those whose baseline visit was between August 2004 and October 2007. Patients recruited into the Registry undergo a standardized evaluation and complete a series of self-report questionnaires, including the SF-36.

Outcome measure. The SF-36 is a self-administered, generic HRQOL questionnaire that covers 8 domains: physical functioning, social functioning, role limitations related to physical problems, role limitations related to emotional problems, mental health, vitality, bodily pain, and general health perceptions. Each domain can be scored separately, with scores ranging from 0, indicating the worst health state, to 100, the best health state. Domain scores can also be summarized into a Physical Component

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Summary (PCS) score. The PCS is scored using norm-based scoring based on a general population sample to produce T scores for each patient (mean of 50 and standard deviation of 10). Thus, for the PCS, HRQOL is worse than average if it is below 50 and better than average if it is above 50, and each point is one-tenth of a standard deviation.

In this study, version 2 of the SF-36 was used (SF-36v2). Major advantages of this second version are 2-fold. First, norms from version 1, which were based on surveys from the late 1980s and early 1990s, were updated using data collected in 1998. Second, norm-based scoring algorithms were introduced for all 8 domains. Thus, norm-based scores with means of 50 and standard deviations of 10 are now also available for all 8 SF-36 domains, whereas previously this was not the case.

Predictor variables. Patients recruited into the Registry underwent an extensive medical evaluation with standardized reporting of history, physical evaluation, and laboratory investigations. Skin involvement was assessed using the modified Rodnan skin score ranging from 0 to 51[9], and participating rheumatologists counted the number of fingertip ulcers using standardized definitions. Joint examinations were done using the simplified 28-jount count[10], and tender points of fibromyalgia were assessed using American College of Rheumatology criteria[11]. Fingertip to palm distance was measured as described[12]. Shortness of breath was assessed using the disease-specific question of the Scleroderma-Health Assessment Questionnaire (S-HAQ)[2]. For this question, patients were asked to rate the severity of their shortness of breath in the past week. The question was anchored by the following statements: "Does not interfere" and "Very severe limitation". Unlike the visual analog scales originally used for the S-HAQ, the assessment in this study was made using 11-point numerical rating scales ranging from 0 to 10[13,14]. Patients also self-reported on a number of different gastrointestinal (GI) symptoms, namely weight loss, anorexia, dysphagia, pyrosis, choking at night, early satiety, bloating, nausea/vomiting, constipation, diarrhea, malabsorption, and fecal incontinence. They also reported on whether they required either antibiotics for bacterial overgrowth or hyperalimentation.

Statistical analysis. Descriptive statistics were used to summarize the patients' baseline characteristics. Bivariate analyses were performed to identify clinical correlates of disease with the SF-36 PCS. Kendall's tau was used for continuous variables and Mann-Whitney test for categorical variables. Multiple regression analysis was performed to identify the independent predictors of HRQOL in patients with SSc as measured by the SF-36 PCS. The variables entered into the models included sociodemographic variables (age, sex, and education status) and disease duration (measured from the onset of the first non-Raynaud's disease manifestation). The clinical variables of interest were chosen to represent a spectrum of common disease manifestations that could potentially influence HRQOL in SSc. These were the modified Rodnan skin scores, fingertip to palm distance, number of fingertip ulcers, shortness of breath (assessed by the patient on the S-HAQ), number of GI symptoms, swollen joint count, tender joint count, and number of tender points of fibromyalgia. We did not include variables such as working status, income, and function because they likely represent outcomes of SSc for many patients and their inclusion could artifactually underestimate the role of the selected clinical variables in the evaluation of the patients' HRQOL. Separate models were run for the entire cohort and for patients with limited and diffuse skin involvement[15].

Model selection was based primarily on clinical reasoning and optimizing the value of the Bayesian Information Criterion (BIC)[16,17]. The BIC overcomes many of the difficulties associated with using p values for model selection and can be interpreted as a criterion similar to adjusted R^2 in that it penalizes the fit of a regression model by a measure of its complexity[17]. Models that contain many regression parameters that do not significantly improve the fit of the model will yield worse values of the BIC than similarly fitting, but less complicated regression models. The BMA package in R was used to perform an exhaustive search of all possible regression models[18]. Transformations for the data were performed to improve fidelity to standard multiple linear regression assumptions (constant variance and normality of the regression errors).

Statistical analyses were performed with the R statistical package[19].

Ethical considerations. Ethics committee approval for this study was obtained at each site and each patient provided written informed consent to participate.

RESULTS

There were 416 patients included in this study, of which 86% were women. The mean age was 56 (± 13) years and the mean disease duration since the onset of the first non-Raynaud's disease manifestation was 11 (± 8) years (Table 1). The greatest impairments in the SF-36 were in the domains measuring physical health. Mean SF-36 PCS score was 37.5 (± 11.2).

In bivariate analyses with the SF-36 PCS (Table 2), the only significant demographic variable was education ($p = 0.0164$). Several disease characteristics correlated significantly with the SF-36 PCS: skin score, number of fibromyalgia tender points, fingertip to palm distance, shortness of breath, number of swollen joints, number of tender joints, and number of GI symptoms (all $p < 0.0001$). The negative correlation coefficients are due to the fact that for the SF-36, lower scores represent worse quality of life.

In multivariate analysis, the significant clinical predictors of the SF-36 PCS were, in descending order of importance, shortness of breath, number of GI problems, skin score, swollen joint count, and age (Table 3). The final model explained 47% of the variance in the SF-36 PCS. The results of the analysis stratified by limited and diffuse skin involve-

Table 1. Baseline characteristics of patients with systemic sclerosis enrolled in the Canadian Scleroderma Research Group Registry (N = 416).

Characteristic	% or mean (SD)
Women, %	86.3
Mean age, yrs	56.0 (12.8)
Education (more than high school), %	45.2
Mean disease duration, yrs*	10.5 (8.3)
Patients with diffuse skin involvement, %	35.8
Modified Rodnan skin scores (range 0–51)	10.6 (10.0)
Fingertip to palm distance, centimeters	1.1 (1.8)
No. of fingertip ulcers	1.3 (2.3)
Shortness of breath (range 0–10)	2.1 (2.6)
No. of swollen joints	0.9 (2.9)
No. of tender joints	1.8 (4.4)
No. of gastrointestinal symptoms (range 0–14)	3.9 (3.0)
No. of tender points of fibromyalgia (range 0–18)	3.0 (5.0)
SF-36 domains**	
Physical functioning	36.9 (11.9)
Social functioning	44.2 (11.4)
Role physical	40.6 (12.0)
Role emotional	44.8 (12.7)
Mental health	48.4 (10.6)
Vitality	46.1 (10.6)
Bodily pain	43.2 (9.4)
General health	38.9 (10.9)
SF-36 Physical Component Summary score	37.5 (11.2)

*Since onset of first non-Raynaud's manifestation of SSc. **Lower scores represent worse and higher scores, better HRQOL.

Table 2. Correlations between SF-36 PCS scores and sociodemographic and disease related variables.

Characteristic	Correlation Coefficient	p
Male (compared to female)		0.1818
Age	–0.0519	0.0693
More than high school education vs high school or less		0.0164
Disease duration	0.0204	0.4785
Skin score	–0.1326	< 0.0001
Number of fibromyalgia tender points	–0.1559	< 0.0001
Fingertip to palm distance	–0.1386	< 0.0001
No. of fingertip ulcers	–0.0451	0.1622
Shortness of breath	–0.4102	< 0.0001
No. of swollen joints	–0.1578	< 0.0001
No. of tender joints	–0.2039	< 0.0001
No. of gastrointestinal symptoms	–0.2854	< 0.0001

Table 3. Final multivariate regression model to determine clinical correlates of SF-36 PCS.

Characteristic	Standardized Estimates	Lower CI	Upper CI
Age	–1.59	–2.42	–0.76
Skin score	–2.28	–3.10	–1.46
Shortness of breath*	–5.10	–5.97	–4.23
No. of gastrointestinal symptoms*	–2.64	–3.52	–1.76
No. of swollen joints*	–1.74	–2.55	–0.92

*Square root transformation of variables was performed to improve fidelity to the regression assumptions. Coefficients are standardized by the standard deviations of the transformed variables in the regression (e.g., the coefficient for number of gastrointestinal symptoms is standardized by the standard deviation of the number of gastrointestinal symptoms).

ment were very similar (data not shown). The final model presented was the best regression model according to the BIC. This criterion provides strong evidence that one should include at least the selected covariates in the model. Less parsimonious models including other demographic and clinical variables did not improve fit substantively compared to the model presented.

DISCUSSION

In this large study of patients with SSc, we found that shortness of breath, number of GI symptoms, skin involvement, number of swollen joints, and age were independent correlates of HRQOL, as measured by the SF-36 PCS. The variables selected for this model explained a large amount of the variance in the SF-36 PCS (47%), validating our *a priori* selection of variables and suggesting that we have identified some of the most important factors that contribute to physical health status in SSc.

Our study confirms some of the previously identified clinical correlates of HRQOL in a large cohort of patients with SSc using multivariate analysis and a widely known HRQOL instrument. Indeed, some smaller studies (all N < 200) had previously attempted to identify clinical correlates of HRQOL in SSc but their findings were the result of univariate analyses[6,20] or were restricted to patients with limited SSc[21]. We had previously identified similar correlates of HRQOL in SSc in multivariate analysis[22], but using the *World Health Organization Disability Assessment Schedule II* (WHODAS II)[23,24]. The WHODAS II is a new generic HRQOL instrument that remains relatively unknown to many in the scleroderma research community. This study thus provides robust data on the clinical correlates of HRQOL in SSc using a large SSc cohort, more advanced statistical modeling, and the most widely used generic HRQOL instrument, the SF-36[25].

The significance of this study is that the identification of clinical correlates of disease provides foci of intervention for SSc. Although there is considerable interest in developing and testing treatments for skin and pulmonary disease, there has been little work on GI and joint disease in SSc. This remains a serious lacuna. Identifying these contributors of HRQOL in SSc gives a strong signal to the research community that, short of curative treatments, we need to develop better symptomatic treatments for this devastating disease.

This study has some limitations. Most importantly, the cross-sectional design prevents us examining the mechanisms by which some variables may relate and how this influences outcome. In other words, how are skin involvement, GI symptoms, dyspnea, and joint disease related to HRQOL? Longitudinal studies examining these relationships are currently under way. Second, given the older age and female preponderance of our sample, the SF-36 PCS score of 37.5 in this study cannot be directly compared to the general population norms of the SF-36 (where 50.0 is the norm for the overall general population and 46.7 that of women aged 55–64)[26]. Nevertheless, without a precise estimate of a general population norm for a sex and aged-matched sample similar to ours, it provides a strong clue that physical health status in SSc is in the range of 1 standard deviation below that of the general population.

Our study allowed us to identify important clinical correlates of physical health status in SSc, namely skin, GI, and joint involvement, as well as dyspnea. Such studies identify targets of intervention and help set the research agenda in the field of SSc, with the hope of effectively improving the HRQOL of patients with this disease.

APPENDIX

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