Quality of Life in Patients with Systemic Sclerosis Compared to the General Population and Patients with Other Chronic Conditions

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ABSTRACT. ***Objective.*** Systemic sclerosis (SSc) affects multiple physical, psychological, and social domains and is associated with impaired health-related quality of life (HRQOL). We compared the HRQOL of SSc patients with individuals in the general population and patients with other common chronic diseases.
Methods. HRQOL of SSc patients in the Canadian Scleroderma Research Group registry was measured using version 2 of the Medical Outcomes Trust Short Form-36 (SF-36). Results were compared to US general population norms and scores reported for patients with other common chronic diseases, namely heart disease, lung disease, hypertension, diabetes, and depression.
Results. SF-36 scores were available for 504 SSc patients (86% women, mean age 56 yrs, mean disease duration since onset of first non-Raynaud's manifestation of SSc 11 yrs). The greatest impairment in SF-36 subscale scores appeared to be in the physical functioning, general health, and role physical domains. SF-36 subscale and summary scores in SSc were significantly worse compared to US general population norms for women of similar ages, except for mental health and mental component summary score, which were not significantly different, and were generally comparable to or worse than the scores of patients with other common chronic conditions.
Conclusion. HRQOL of patients with SSc is significantly impaired compared to that of the general population and is comparable to or worse than that of patients with other common chronic conditions. (J Rheumatol First Release Feb 15 2009; doi:10.3899/jrheum.080281)

Key Indexing Terms:
SYSTEMIC SCLEROSIS HEALTH-RELATED QUALITY OF LIFE CHRONIC DISEASES

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 compared to patients with other acute and chronic conditions, when the same assessment tools and scoring cutoffs are used[3]. As such, the disease encompasses broad multidimensional issues including biological, psychological, and social processes. Thus, it would not be surprising that health-related quality of life (HRQOL) should be impaired in SSc. *A fortiori*, because there is no cure for SSc, understanding the influence 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[4].

The Medical Outcomes Trust Short Form-36 (SF-36)[5] is a widely used generic measure of HRQOL in rheumatology. It is ideal for comparative studies because general population data and population-sampled data for patients with several different and varied chronic diseases are available. We undertook this study to compare the HRQOL of patients with SSc to general population levels and to patients with more common chronic diseases, namely heart disease, lung disease, diabetes, hypertension, and depression, when measured using the SF-36.

MATERIALS AND METHODS

Design. This was a cross-sectional study of a convenience sample of patients with SSc.

Study subjects. The study subjects consisted of those enrolled in the Canadian Scleroderma Research Group (CSRG) Registry. Patients in this

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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 August 2007.

Upwards of 95% of patients approached agreed to participate in the CSRG registry. Certain features of the cohort, including age and female distribution, suggest that patients included in the registry are similar to patients included in other large SSc cohorts as described[6]. Moreover, the cohort includes a mix of patients covering the spectrum of disease severity. Rheumatologists participating in the CSRG include both academic and community rheumatologists, but all have a particular interest in SSc and thus all are perceived as "experts." They thus recruit patients with more severe disease. On the other hand, since the American College of Rheumatology 1980 Preliminary Criteria for the Classification of SSc[7] exclude many patients with limited disease[8], the patients in the CSRG registry do not have to meet those criteria to be included. Thus, participating rheumatologists also recruit patients with probably milder disease. Finally, the patients in the CSRG registry are generally recruited as outpatients and have a mean disease duration since the onset of their first non-Raynaud's disease manifestation of over 10 years. Thus, the cohort probably also includes survivor patients with perhaps less aggressive disease, but who may have accumulated damage over time. Thus, in general, we believe that our patients are representative of the spectrum of SSc seen by the general rheumatology community.

Patients recruited into the registry undergo an extensive standardized evaluation including a history, physical evaluation, patient and physician global assessments, and laboratory investigations. Patients also complete a series of self-report questionnaires, including the SF-36, the Health Assessment Questionnaire (HAQ), and the Center for Epidemiologic Studies - Depression Scale (CES-D). The CES-D is a 20-item scale designed to measure depression in the general population[9,10]. It is also useful in clinical and psychiatric settings. It asks an individual to report the frequency with which each of 20 events was experienced during the previous week. The items are graded on a 4-point scale ranging from 0 to 3 and corresponding to the frequency of each symptom in the past week. It yields a summary score, which ranges from 0 to 60, with higher scores indicating greater depression. The scale is used as a simple indicator of the degree of depression. If the total is 16 or greater, the patient may have experienced some depression in the past week.

Outcome measure. The SF-36 consists of 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 Summary (PCS) score and a Mental Component Summary (MCS) score. The PCS and MCS are scored using norm-based scoring based on a general population sample to produce T scores for each patient [mean of 50 and standard deviation (SD) of 10]. Thus, for the 2 summary scores, 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.

Version 2 of the SF-36 was used (SF-36v2) in this study. Major advantages of this second version are first, that norms from version 1 based on surveys from the late 1980s and early 1990s were updated using data collected in 1998, and second, norm-based scoring algorithms were introduced for all 8 subscales. Thus, norm-based scores with means of 50 and SD of 10 are now also available for all 8 SF-36 subscales, whereas previously this was not the case. The official English and French verisons of the SF-36v2, available from the distributors of the instrument, were used.

Statistical analysis. SF-36 subscale and summary scores were compared to those available for the US general population of women of similar ages as well as to those available for patients with other common chronic diseases[11]. The US normative data were derived from the responses of 7069 adults who responded to the 1998 US National Survey of Functional Health Status, which included the SF-36v2. The survey was designed to sample a representative group of noninstitutionalized adults matched to US Census data. Since our SSc sample consisted primarily of women with a mean age of 55 years, and since general population norms were available not only for the whole survey sample but also by sex and age group, we compared the scores in our SSc cohort to those of the general population of women aged 45–64 years. In addition, as part of the 1998 US general population normative data gathering, participants were asked to self-report certain selected diseases. This information was used to generate specific sets of norms for the various diseases. Thus, the SF-36 scores of our patients were compared to the norms available for patients with 5 common chronic conditions: heart disease, lung disease, hypertension, diabetes, and depression.

Descriptive statistics were used to summarize the baseline characteristics of the SSc patients. Comparisons between groups were done with t-tests and one-sample Wilcoxon tests comparing the SSc patients' scores to the mean scores of the other patient groups to account for non-normality of the data. Note that the one-sample tests cannot be directly compared to the 2-sample t-tests, because the Wilcoxon tests do not utilize measures of uncertainty from the samples of patients with other chronic conditions. Statistical significance was evaluated using a Bonferroni correction for multiple comparisons to maintain a family-wise type I error rate of < 0.05. All statistical analyses were performed with SPSS v. 13 and the R statistical package.

Institutional ethics committee approval for this study was obtained at each site, and each patient provided written informed consent to participate.

RESULTS

The study included 504 patients from the CSRG registry with SF-36 data available from their baseline visit (86% women, mean age 56 yrs, mean disease duration since onset of first non-Raynaud's manifestation of SSc 11 yrs; Table 1). The mean SF-36 PCS and MCS scores were 36.7 (SD 11.2) and 49.0 (SD 11.7), respectively.

The results of the individual SF-36 subscale scores for SSc patients are shown in Table 2. The greatest impairments in HRQOL were in the physical functioning, general health, and role physical domains. All subscale scores, except mental health, were significantly lower than those of the US general population of women aged 45–55 years. Similar results were found when comparing the scores of the SSc patients to those of the US general population of women aged 55–64 (data not shown).

Subscale scores in SSc were compared to those of patients with other common chronic diseases, namely heart disease, lung disease, hypertension, diabetes, and depression (Table 2). In most, but not all cases, the subscale scores in SSc were as low as or lower than those in the other chronic diseases. Indeed, scores for physical functioning and general health were the lowest in SSc. Vitality in SSc was as low as in heart disease and lower than in diabetes or hypertension. Finally, scores for role physical, bodily pain, social functioning, role emotional, and mental health in SSc were as low as or lower than for all the other chronic diseases, except for depression.

The SF-36 PCS score in SSc was the lowest, at 36.7, compared to that of the general population (48.5) and those of the 5 selected chronic diseases, which ranged from 38.3

Table 1. Baseline characteristics of the SSc cohort (N = 504).

Demographic data	N	% or mean (SD)
Women	504	86
Age, yrs	504	55.5 (12.5)
Education (more than high school)	501	46
Currently employed/in school	504	39
Yearly family income ≥ $50,000	440	47
Disease characteristics		
Disease duration since onset of first non-Raynaud's manifestation of SSc, yrs	504	10.5 (8.6)
Diffuse skin involvement	504	44
Meet American College of Rheumatology criteria for SSc	501	81
Physician global assessment of disease severity (range 0–10)	504	2.8 (2.3)
Patient global assessment of disease severity (range 0–10)	502	3.6 (2.6)
Health Assessment Questionnaire-Disability Index (range 0–3)	504	0.82 (0.70)
Center for Epidemiologic Studies — Depression scale (range 0–60)	504	14.2 (10.6)
SF-36 physical component summary score	504	36.7 (11.2)
SF-36 mental component summary score	504	49.0 (11.7)

Table 2. Comparison of the mean (SD) SF-36 domain and summary scores for patients with SSc, US women from the general population, and patients with selected chronic diseases.

	SSc, n = 504	US Population Norms (women aged 45–54) n = 911	Heart Disease, n = 660	Lung Disease, n = 328	Hypertension, n = 1729	Diabetes, n = 545	Depression, n = 942
Physical function	36.4 (11.8)	48.7 (8.4)*†	38.9 (11.2)*	38.3 (11.6)	43.9 (10.5)*	41.4 (12.3)*	44.3 (12.0)*
Role physical	40.1 (12.1)	49.6 (8.4)*†	40.1 (10.7)	39.3 (11.6)	45.0 (9.9)*	42.6 (11.7)*	42.9 (11.9)*
Bodily pain	43.0 (10.0)	48.2 (8.5)*†	43.5 (9.9)	43.1 (10.0)	46.0 (11.1)*	44.2 (10.2)†	42.9 (10.6)
General health	37.7 (10.7)	49.3 (8.8)*†	40.9 (9.9)*	38.3 (10.2)	45.5 (11.0)*	41.4 (10.5)*	41.0 (10.9)*
Vitality	45.5 (10.9)	49.5 (8.3)*†	45.4 (9.5)	42.7 (9.3)*†	48.4 (9.7)*	46.0 (10.6)	40.1 (9.8)*
Social function	42.8 (11.8)	49.7 (8.4)*†	44.2 (11.4)	41.8 (11.8)	47.5 (9.6)*	44.5 (11.7)	38.7 (11.9)*
Role emotional	44.9 (12.4)	50.3 (8.2)*†	43.6 (12.7)	42.5 (13.5)†	47.3 (9.5)*	44.7 (13.1)	38.9 (13.0)*
Mental health	47.6 (10.3)	49.7 (8.3)	48.5 (10.1)†	45.8 (10.6)†	49.0 (10.6)	47.7 (10.8)	36.7 (11.1)*
PCS score	36.7 (11.2)	48.5 (8.7)*†	38.9 (10.1)*	38.3 (10.9)	44.0 (11.3)*	41.1 (11.2)*	45.4 (11.6)*
MCS score	49.0 (11.7)	50.2 (8.1)	48.3 (10.7)	45.6 (11.5)*	49.7 (9.8)	47.8 (11.5)	36.3 (11.9)*

* Significant p values for comparisons between scores for the given category and SSc using a standard 2-sample t-test. † Significant p values for comparisons using a one-sample Wilcoxon test to account for non-normality. Both utilize a simple Bonferroni correction for multiple comparisons to maintain a family-wise type I error rate of < 0.05. PCS: physical component summary, MCS: mental component summary.

to 45.4, although the difference was not statistically significant between SSc and lung disease. The SF-36 MCS score in SSc was close to average at 49.0, as were those in heart disease (48.3), hypertension (49.7), and diabetes (47.8).

DISCUSSION

In this study of over 500 patients with SSc, we found that HRQOL in SSc was significantly below that of the general population and in many cases was impaired to a similar or greater degree than in other common chronic diseases. Indeed, the SF-36 PCS score in SSc was almost 1.5 SD below that of the general population, when those of patients with heart disease, lung disease, hypertension, diabetes, and depression were roughly 0.5 to 1 SD below that of the general population.

Studies have shown that HRQOL of other systemic autoimmune diseases similar to SSc is significantly lower than that of the general population and of patients with other common chronic diseases[12]. However, few such comparisons are available in SSc. In perhaps the largest study comparing patients with SSc to the general population and to patients with a more common chronic disease, Khanna and colleagues compared the SF-36 scores of 158 SSc patients with lung disease to that of the general US population and patients with chronic obstructive lung disease[13]. They found that the SF-36 subscale scores were all significantly below those of the general population and comparable to those of patients with chronic obstructive lung disease. Our results are consistent with these data.

Some of our findings are statistically significant, and they also likely represent differences that are clinically meaningful. Since statistical differences, although significant, may be too small to be clinically meaningful, it has been suggested that changes be interpreted by a standard that takes

into account the smallest change that is perceptible by the patient: the minimal important clinical difference (MICD)[14]. Differences of 5 to 10 points on the SF-36 subscales and 2.5 to 5 in the SF-36 summary scores have been proposed as clinically meaningful in SSc[15]. Assuming that to be so, SF-36 subscale scores of the SSc patients in our study all represented differences that were clinically meaningful compared to those of the general population, except perhaps for mental health. In most cases, they were also comparable to or worse than the scores of patients with other chronic diseases.

Our finding that the SF-36 MCS in SSc appears near normal remains perplexing. There are at least 3 possible explanations for this. First, since our cohort consisted of a Canadian sample, we may be comparing to the wrong norms. Some Canadian normative data are available for version 1 of the SF-36. These data come from a multicenter prospective cohort study on the incidence and prevalence of osteoporosis and osteoporotic fractures in Canada. The data involved 9423 randomly selected community-dwelling men and women aged 25 years and older. In that cohort, the SF-36 MCS was 51.4 (SD 9.2) for women aged 45–54 years [and the PCS was 51.3 (SD 9.0)]. When compared to those norms, the SF-36 MCS scores for our SSc patients were significantly lower ($p < 0.01$) than that of the general Canadian population of women of similar ages (as were those of the PCS scores, $p < 0.0001$).

Second, the fact that mental health in SSc appears to be relatively preserved when measured with the SF-36 MCS has been observed in another study of SSc[15]. This has been interpreted as possibly suggesting that, despite significant impairments in physical health, SSc patients adapt well to their slowly progressing disease. This is incongruent, however, with reports of high rates of depressive symptoms in SSc[3].

Thus, a third interpretation of the near-normal scores for the SF-36 MCS may relate more to the way the SF-36 PCS and MCS are scored. Indeed, the SF-36 MCS and PCS scores are designed to be uncorrelated (orthogonal) measures of mental and physical function, respectively. To achieve this, scoring algorithms were designed using general population data to control for physical health in rating mental health and vice versa. As a result, some subscales load negatively on the composite score. For example, the physical functioning subscale loads negatively on the MCS. In the general population, this is a minor adjustment. In SSc patients, however, very low physical functioning scores may result in potentially large upward "adjustments" in mental health estimates. Alternatively, by definition, improvements in physical condition will result in scoring reductions for the MCS. Indeed, the shortcomings of the SF-36 population-based scoring system have been criticized in terms of its usefulness for patients with chronic disease due to strong links between physical and mental health in patients with such conditions[16]. Farivar, *et al*[17] demonstrated that when physical subscale scores are well below the mean and mental subscale scores somewhat less below the mean, this scoring method will result in an artifactual migration of the aggregate PCS score away from the mean and a migration of the aggregate MCS score toward the mean. Thus, at this point, it is clear that further research into the mental health and coping capabilities of SSc patients who are affected by this chronic, disfiguring, and disabling disease will be necessary to understand the relationship of physical and mental health, and their respective effects on HRQOL.

The major limitation of our study is that the data available on the reference groups were insufficient to assess and control for numerous potentially confounding variables. Also, we were unable to use a Canadian comparison group, because Canadian normative data were available only for an earlier version of the SF-36. Nevertheless, the strength of the study lies in its large sample size and its ability to situate the HRQOL of patients with a rare and little known disease compared to that of the general population and of patients with better known chronic diseases.

The significance of the study is several-fold. First, since SSc is rare, by comparing SSc to the general population and to patients with other more common chronic diseases it provides perspective on the considerable burden that SSc imposes on patients. Second, comparative data such as these can be used by patient groups to advocate for better allocation of healthcare resources. Indeed, SSc is rare and probably little known by policy-makers. However, showing that it affects patients as much as if not more than conditions such as heart disease, hypertension, and diabetes is a powerful argument in the hands of patient advocacy groups. Although our study remains hypothesis-generating, our results bring to light the severe impairments in HRQOL of patients with SSc. Our findings allow us to raise awareness about the influence of SSc on patients' HRQOL and provide impetus for further research on the HRQOL of patients with this devastating disease.

APPENDIX

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