Work Disability in Systemic Sclerosis

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ABSTRACT. ***Objective.*** Systemic sclerosis (SSc) is a multisystem disease associated with significant morbidity and increased mortality. Little is known about work disability in SSc. We undertook this study to determine the prevalence and demographic and clinical correlates of work disability in a large cohort of patients with SSc.

Methods. Cross-sectional, multicenter study of patients from the Canadian Scleroderma Research Group Registry. Patients were assessed with detailed clinical histories, medical examinations, and self-administered questionnaires. The primary outcome was self-reported work disability. Multiple logistic regression was used to assess the relationship between selected demographic and clinical variables and work disability.

Results. Of the 643 patients available for this study, 133 (21%) reported that they were work disabled. Work disability in SSc was common, even in people with short disease duration, and increased steadily with increasing disease duration: among those who were ≤ 65 years and who reported being either disabled or working, 28.0% and 44.8% of patients with disease duration of < 2 and 10–15 years, respectively, reported that they were work-disabled. The significant correlates of work disability included comorbidities, disease duration, diffuse disease, disease severity, pain, fatigue, and physical function.

Conclusion. Work disability is prevalent, occurs early, and is associated with markers of disease severity and functional status. Further research is needed to identify other, potentially modifiable, risk factors for work disability in SSc. (First Release Oct 1 2009; J Rheumatol 2009;36:2481–6; doi:10.3899/jrheum.081237)

Key Indexing Terms:
SYSTEMIC SCLEROSIS WORK DISABILITY PREVALENCE
CLINICAL CORRELATES EPIDEMIOLOGY

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].

Work disability has become an important outcome of interest in rheumatic diseases, largely as a result of high prevalence rates and costs[5]. Indeed, arthritis and musculoskeletal conditions are the leading cause of long term work disability in Canada and the US[6], and the annual indirect costs of musculoskeletal diseases were estimated to be $13.7 billion in Canada (in 1998)[7], and up to $339 billion per year in the US (in the 2002–2004 period)[8]. Most research to date on work disability in the rheumatic diseases has focused on rheumatoid arthritis. Several risk factors for work disability have been documented in that disease, including demographic variables such as age and level of education, and markers of disease severity, pain, fatigue, and functional status[9,10].

Little is known on the subject of work disability in SSc. The objective of our study was thus to determine (1) the prevalence, and (2) the demographic and clinical correlates of work disability in a large cohort of patients with SSc.

MATERIALS AND METHODS

Design. We performed a cross-sectional study of a national cohort of patients with SSc.

Study subjects. Study subjects consisted of those enrolled in the Canadian Scleroderma Research Group Registry (CSRG). The CSRG is a unique consortium of the major Canadian stakeholders in SSc research, including rheumatologists, basic scientists, and patient representatives, who have established a multicentered registry to recruit large numbers of patients for longitudinal studies in SSc. Patients in this registry are recruited from 15 centers across Canada, with over 18 participating rheumatologists and numerous other referring rheumatologists. Patients must have a diagnosis of SSc made by the participating rheumatologist, be > 18 years of age, and

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be fluent in either English or French. Since patients began to be recruited into the Registry in August 2004, upwards of 95% of patients approached have agreed to participate, and on average over 150 patients have been recruited yearly to date. Patients recruited into the Registry undergo an extensive yearly medical evaluation with standardized reporting of history, physical evaluation, and laboratory investigations. Those included in our study were those whose baseline visit was entered in the database up until April 2008.

Certain features of the cohort, including age and female distribution, suggest that the patients included in the Registry are similar to patients included in other described large SSc cohorts[11]. Moreover, the cohort includes a mix of patients whose disease covers the spectrum of disease severity. Although the participating rheumatologists in the CSRG include both academic and community rheumatologists, 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 exclude many patients with limited disease, 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.

Primary outcome. In their self-reported case report forms, patients were asked their current employment status and were provided with the following options: Currently working: part-time, full-time, or self-employed; or Currently retired, student, disabled, on sick leave, unemployed, homemaker, or other (please specify). The option for "disabled or on sick leave" did not require that the patient ascribe a cause for the disability. We divided patients into 3 groups: (1) Those considered work disabled were ≤ 65 years and chose the response option: "I am currently disabled or on sick leave"; (2) those considered to be working were ≤ 65 years and reported that they were working either part-time, full-time, or self-employed; and (3) all other patients, namely all patients > 65 years or those who answered that they were retired, student, unemployed, homemaker, or other (specify). We excluded those in group 3 from further analysis and proceeded to study only those who were work disabled (group 1) and working (group 2).

Predictor variables. Demographic variables, namely age, gender, race, and education, were reported by patients. Disease duration was recorded by the participating rheumatologist and determined from onset of the first non-Raynaud's disease manifestation. Comorbidity was measured using the Self-Administered Comorbidity Questionnaire (SCQ)[12]. The SCQ lists 12 common medical conditions and provides space to specify 3 optional health conditions. The patient indicates for each condition if it is present, being treated, and/or imposes functional limitation. Every "yes" response is given 1 point for a maximum score of 45. Skin involvement was assessed using the modified Rodnan skin score ranging from 0 to 51[13], and patients were classified into limited and diffuse subsets, based on the definition of Leroy et al[14]. The Scleroderma-Health Assessment Questionnaire (S-HAQ) consists of the HAQ-Disability Index (DI)[15] and visual analog scales (VAS) to measure severity of symptoms specific for SSc, including pain in the past week[2]. Unlike the VAS originally used for the S-HAQ, we assessed patients using an 11-point numerical rating scale (NRS). Physical function was measured using the HAQ-DI and pain using the patient NRS for pain. Fatigue was measured using the Vitality subscale of the Medical Outcome Study Short Form-36 item Survey (SF-36)[16,17]. Finally, the participating rheumatologist completed a global assessment of disease severity, also using an 11-point NRS.

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

Role of the funding sources. Funding sources had no role in the design of the study, analysis of the data, preparation of the manuscript and decision to submit for publication.

Statistical analysis. Descriptive statistics were used to summarize the baseline characteristics of the working and work disabled patients. Generalized linear mixed models were used to identify the demographic and clinical predictors of work disability in work disabled compared to working patients, in order to account for the cluster sampling design of the study. Potential predictor variables included in the main model were age, female (vs male), white race (vs other), more than high school education (vs high school or less), disease duration, SCQ comorbidity score, diffuse skin involvement (vs limited), and physician global assessment of disease severity score (range 0–10). Patients were clustered by study center, so we included study center as a random effect in the models. Pain, fatigue, and physical function have been identified as correlates of work disability in other rheumatic diseases. However, it is possible that those variables could be correlates of work disability, but acting as mediators (i.e., lying in the causal pathway) of clinical causes of disability included in the main model (such as disease severity) and the outcome of work disability[18,19]. Thus, rather than performing a single analysis to estimate the effects of all of the parameters of the model, we ran a number of nested models to allow us to explore the association of particular clinical characteristics and the outcome of interest. Model fit was assessed using the area under the curve (AUC) for a receiver operating characteristic (ROC) curve using the fitted probabilities from the generalized linear mixed models as classification probabilities and the Bayesian information criterion (BIC) to compare evidence for the models fit[20,21]. For purposes of interpretation, higher AUC and lower BIC values indicate better model fit. AUC of 0.7 are typically regarded as good, and the maximum AUC is 1.0. BIC are interpreted as a difference of 0–2 showing weak evidence, a difference of 2–6 positive evidence, a difference of 6–10 strong evidence, and a difference of > 10 very strong evidence of better fit[21]. All statistical analyses were performed with SAS 9.1 TS Level 1M3 and the R statistical package lme4, and all statistical tests were 2-sided with a $p < 0.05$ significance level.

RESULTS

Of the 643 patients available for our study, 232 (36%) were currently working (whether full-time, part-time or self-employed), and 133 (21%) were work disabled, as defined in this study (Table 1). The remainder were either > 65 years or reported being retired, homemakers, students or unemployed and were excluded from further analyses. The work disabled patients were different from the working patients: they were slightly older and less likely to have education beyond high school; they had longer disease duration; they were more likely to have diffuse skin involvement and more severe disease; and they reported more pain and worse physical functioning.

Work disability was common even in people with short disease duration, suggesting that work disability occurs early in the course of SSc. Almost one-third of patients with less than 2 years' disease duration reported they were work disabled (Figure 1). The cross-sectional estimates of work disability continued to increase steadily thereafter, with 36.1% and 44.8% of those with 5–10 years and 10–15 years of disease duration, respectively, reporting they were work disabled. Almost one-half of patients with disease duration > 20 years reported they were work disabled. For every additional year of disease, the odds ratio (OR) of being work disabled (vs working) was 1.03 [95% confidence interval

Table 1. Baseline characteristics of the working and work disabled patients.

	Working	Work Disabled
N	232	133
Age, yrs (SD)	48.4 (9.4)	50.2 (8.2)
Female, %	83	84
White, %	90	89
Education beyond high school, %	58	43
Comorbidity, range 0–45 (SD)	3.3 (3.7)	5.8 (5.6)
Disease duration since onset of first non-Raynaud's disease manifestation, yrs (SD)	9.0 (7.7)	11.0 (8.6)
Diffuse skin involvement, %	42	59
PGA of disease severity, range 0–10 (SD)	2.3 (1.9)	3.6 (2.4)
Pain, range 0–10 (SD)	3.1 (2.6)	4.9 (2.7)
Fatigue, range 0-100* (SD)	47.6 (10.7)	40.4 (11.0)
Health Assessment Questionnaire, range 0–3 (SD)	0.55 (0.57)	1.36 (0.72)

* Lower scores indicate worse fatigue. PGA: physician global assessment.

(CI) 1.003, 1.058]. This suggests that, for example, the odds of becoming work disabled increases by about 15% after 5 additional years of disease.

Generalized linear mixed models were used to assess the association between disease severity and work disability (Model 1, Table 2). Worsening comorbidity score (OR 1.135, 95% CI 1.072, 1.202), disease duration (OR 1.033, 95% CI 1.001, 1.066), diffuse skin involvement (OR 1.890, 95% CI 1.134, 3.151), and physician global assessment of disease severity (OR 1.312, 95% CI 1.162, 1.481) were significant correlates of outcome. The observed area under the ROC curve (AUC) was 76.7%, which indicates good predictive ability of the model. The value of the BIC was 467.4. In considering potential mediators, pain (Model 2, OR 1.212, 95% CI 1.102, 1.333) and fatigue (Model 3, OR 0.967, 95% CI 0.942, 0.993) were also found to be significant correlates of work disability, but did not have an obvious mediating effect on the covariates from Model 1, in particular disease duration, diffuse disease, or disease severity. Therefore, we did not observe strong evidence of potential mediation of our covariates from pain or fatigue. Note that the estimates and intervals of less than 1 for fatigue reflect the fact that low scores of fatigue on the SF-36 represent worse levels of fatigue and high scores indicate lower levels of fatigue. The AUC for Models 2 (+ pain) and 3 (+ fatigue) were 79.2% and 80.1%, respectively, which indicates that Model 2 improved on Model 1, but that the difference between Model 2 and 3 in predictive ability was minimal. This was also shown by the BIC values, as the BIC for Model 2 (457.3) indicated strong evidence of better fit for Model 2 compared to Model 1, but the BIC value for Model 3 (456.8) did not provide much more evidence for Model 3 over Model 2.

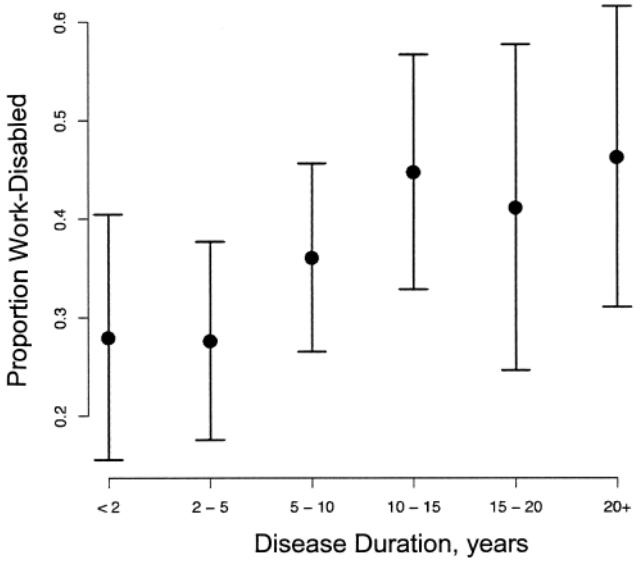

Figure 1. Relationship between the proportion of SSc patients reporting work disability and disease duration. Shown are percentages of work disabled individuals among those who were 65 years and younger and who reported either being disabled or working in 6 categories of disease duration.

Physical function, as measured by the HAQ, was strongly associated with increased risk of work disability (Model 4, OR 4. 881, 95% CI 2.854, 8.348). When it was added to the model, estimates of disease duration and comorbidity were not significantly affected, but the effects of diffuse disease, disease severity, pain, and fatigue were greatly attenuated. This would indicate potential mediation of those variables by decreased physical function. Both the AUC (84.7%) and the BIC (423.63) indicated that Model 4 provided a significantly better fit to the data than Models 1, 2 and 3, although one must be careful when interpreting this result as indicating a "best" model due to the potentially mediating effect of function.

In each of the 4 models, we found some evidence of heterogeneity in work disability between centers, after adjusting for the covariates. Most of this heterogeneity was driven by 2 centers, one with higher and the other with lower than expected work disability rates. However, the interpretation of the results of the generalized linear mixed models were quite similar to multivariate logistic regression models that did not account for between-center variability. Using model selection criteria like Akaike's information criterion and BIC, we were unable to clearly ascertain whether there was a statistically significant amount of heterogeneity between centers, and so we have presented the slightly more conservative analyses that include center as a random effect in the model.

DISCUSSION

In this large cohort of SSc patients, 21% were ≤ 65 years old and reported currently not working and being work disabled. Work disability was common even in people with short disease duration, suggesting that work disability occurred early

Table 2. Generalized linear mixed models to identify demographic and clinical predictors of self-reported work disability in SSc.

	Model 1		Model 2		Model 3		Model 4	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Age	1.008	0.979 1.037	1.014	0.984 1.046	1.014	0.983 1.047	0.999	0.966 1.033
Female	1.246	0.649 2.392	1.365	0.701 2.659	1.377	0.702 2.701	1.109	0.538 2.284
White	1.163	0.533 2.539	1.331	0.606 2.923	1.220	0.552 2.694	1.232	0.523 2.902
Education	0.618	0.377 1.012	0.668	0.401 1.111	0.630	0.376 1.056	0.622	0.355 1.089
Comorbidity score	1.135	1.072 1.202	1.101	1.036 1.169	1.077	1.012 1.147	1.075	1.005 1.151
Disease duration	1.033	1.001 1.066	1.041	1.007 1.076	1.042	1.008 1.077	1.050	1.013 1.088
Diffuse skin involvement	1.890	1.134 3.151	1.843	1.090 3.116	1.772	1.042 3.016	1.290	0.724 2.300
PGA of disease severity	1.312	1.162 1.481	1.257	1.109 1.424	1.252	1.104 1.420	1.093	0.948 1.260
Pain			1.212	1.102 1.333	1.152	1.040 1.277	1.000	0.886 1.128
Fatigue*					0.967	0.942 0.993	0.987	0.959 1.016
HAQ							4.881	2.854 8.348
	AUC 76.6%, BIC 467.4		AUC 79.2%, BIC 457.3		AUC 80.1%, BIC 456.87		AUC 84.7%, BIC 423.6	

* Lower scores indicate worse fatigue. PGA: physician global assessment; HAQ: Health Assessment Questionnaire; CI: confidence interval; AUC: area under the ROC curve; BIC: Bayesian information criterion.

after disease onset and increased steadily thereafter. In addition to disease duration and comorbidities, diffuse disease, disease severity, pain, fatigue, and physical function were significant correlates of work disability.

It is possible that the effects of diffuse disease, disease severity, pain, and fatigue were, at least in part, mediated by the effect of physical function. However, we could not partition the associations of those variables into direct and indirect effects due to equivalent specifications of the causal model and the potential for unmeasured confounding of the mediator variable (i.e.. physical function as measured by the HAQ). Kaufman, *et al*[19] discuss a situation very similar to ours in which the existence of an unmeasured confounder that causes change both in the mediator (in our case, physical function) and in the outcome (in our case, work disability) can yield results similar to those we obtained, even if the mediator had no direct causal effect on the outcome (which would preclude true mediation of the outcome). Since we cannot exclude this possibility, we cannot conclude that physical function is the definite mediator of the effect of disease severity, diffuse disease, pain, and fatigue. Nevertheless, it remains highly plausible from a clinical standpoint that the effects of diffuse disease, disease severity, pain and fatigue are mediated, at least in part, through physical function, as suggested by Models 2 through 4.

The rates of work disability in SSc reported in our study are consistent with those reported in other systemic rheumatic diseases. In one study of 1824 patients with rheumatoid arthritis, rates of work disability of 7.5%, 18%, and 27% at 1, 5, and 10 years were reported[22]. Other studies in RA have reported rates of 32–50% after 10 years of disease[6]. In 159 patients with systemic lupus erythematosus, 40% were work disabled after an average of 3.4 years since diagnosis[23]. In addition, the correlates of work disability identified in our present study, namely disease severity, pain, fatigue, and function, have also been identified as correlates of work disability in other rheumatic diseases[5,10].

Little is known about the prevalence of work disability in SSc. A recent study reported that work disability affected over half of SSc patients surveyed, although that study was limited by small numbers (n = 61) and a possible response bias (less than half of those surveyed responded), but work disability was related to higher HAQ scores and a trend towards more disability in diffuse SSc[24]. In another study conducted in Germany, employment rates of patients included in a large rheumatological outpatient database were compared to general population figures to produce standardized employment rates (SER)[25]. The SER for patients with SSc in that study was 0.77. However, at least in rheumatoid arthritis, work disability prevalence has generally been higher in European compared to US samples, and results among countries have been found to be difficult to compare head-to-head[25].

It should be noted that there is no accepted definition of work disability used across studies and this may, at least in part, account for variations in estimates. Some definitions used in the past include work cessation prior to the age of 65 years (also called premature work cessation)[26], work cessation prior to the age of 65 attributed to a specific condition[26], work cessation for at least 6 months' duration[22], receiving work disability benefits, or working less than full time[10]. Definitions that have included a reason for the work cessation, as opposed to simple premature work cessation, have provided lower estimates of work disability[26]. We defined work disability as someone who was ≤ 65 years old and answered yes to the following question: "I am not working. I am currently disabled or on sick leave" [with the other options being currently not working because retired, student, homemaker, unemployed, or other (please specify)]. We believe that this definition attributing work cessation to disability may, as in other studies, have provided a conservative estimate[26]. Moreover, as mentioned above, our estimates are in the range of other estimates reported for SSc and other rheumatic diseases.

Age and education level have been significant predictors of work disability in some but not all studies of patients with other rheumatic disease[9,27], and not in our current SSc sample. Although it is difficult to demonstrate, we suspect that these discrepancies, both within and between diseases, are likely related to differences in demographic, disease-related, and job-related characteristics, and interactions between these variables, in the different studies. We can comment only insofar as our own data allow us, at least in this SSc cohort: disease characteristics and function seem to be more important predictors of work disability than demographic factors. However, this could be related to the fact that we had an older (mean age of approximately 50 years), predominantly female (83%) cohort with relatively long disease duration (about 10 years) and these specific sample characteristics may in fact have masked the impact of demographic variables on work disability in SSc.

Our study has several strengths. First, it is the first to report rates of work disability in a large, North American SSc cohort. Second, our cohort spans Canada, yielding a geographically, culturally, and linguistically diverse sample of patients. This diversity, in particular, adds to the generalizability of our findings.

The lack of an accepted definition for work disability is a limitation not only of our study, but of the field of work disability research in general, by interfering with comparability of results across studies. Nevertheless, some argue that this lack of precision does not negate that the burden of work disability associated with other rheumatic diseases remains substantial[10]. We believe that the same argument applies for SSc, although further research will be necessary to demonstrate this. Another limitation of our study includes its cross-sectional design, the concurrent assessment of both predictor and outcome variables, and the inability to control assignment of exposure variables. These study characteristics do not allow for the complete (or even formal) evaluation of causal associations. Thus, although we believe that the effects of disease severity, pain, and fatigue were, at least in part, mediated by the effect of physical function, longitudinal studies using more advanced statistical approaches are required to better understand the relationships between these variables. Finally, in our study we asked patients about only their current working status and not their working status at the onset of their SSc. We also found that co-morbidities were predictive of work disability. Thus, it is possible that individuals were disabled prior to onset of SSc due to comorbid conditions. We consider it unlikely that this can account for most cases of work disability in our sample but acknowledge that our data do not allow us to exclude this possibility completely.

Studies have shown that work-related factors, such as work type and commuting, also contribute significantly to work disability[22]. Further research will be required to explore whether work-related factors, in addition to disease characteristics and physical function, are also important determinants of work disability for patients with SSc. Clearly, identifying work-related factors would have the added advantage of providing potentially modifiable targets of intervention.

In conclusion, work disability is prevalent, occurs early and is associated with markers of disease severity and physical function in SSc. Additional research will be needed to confirm these results and to identify other, potentially modifiable, risk factors for work disability in SSc.

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