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Determinants of Work Disability in Patients with Systemic Sclerosis: A Longitudinal Study of the GENISOS Cohort

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Abstract

Objectives—To determine the prevalence, correlates, and predictors of work disability (WD) in the **Genetics versus ENvironment In Scleroderma Outcome Study** (GENISOS). We hypothesized that WD in systemic sclerosis (SSc) is a function of demographic, clinical, and psychosocial factors.

Methods—Patients enrolled in the GENISOS cohort were subdivided in 3 groups: work disabled, working, and retired or homemakers. The latter group ($n=29$) was excluded from further analysis. We used logistic regression analysis with a forward hierarchical variable selection strategy to investigate the independent correlates of WD at enrollment. Cox regression proportional Hazard's model with a similar variable selection strategy was utilized to determine the predictors of WD in those working at enrollment.

Results—Overall, 284 patients with mean age of 48.7 years and disease duration of 2.5 (± 1.6) years were enrolled into the GENISOS cohort, consisting of 83.5% female, 46.8% Caucasian, 28.9% Hispanic, and 20.4% African American. Patients were longitudinally followed for 3.9 (± 3.6) years in 1438 study visits. At enrollment, 124 patients (43.7%) were work disabled whereas 131 (46.1%) were working. Lower education ($p<0.001$), higher Medsger Lung Severity Index

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($p=0.012$), higher Fatigue Severity Score (FSS) ($p=0.008$), and less social support ($p<0.001$) correlated independently with WD. Of those working at baseline, 35 (26.7%) eventually developed WD. Non-Caucasian ethnicity ($p=0.038$), lower DLCO %predicted value ($p=0.038$), and higher FSS ($p=0.009$) at enrollment independently predicted WD on follow-up visits.

Conclusion—Demographic, clinical, and psychosocial factors correlate with WD cross-sectionally and predict WD longitudinally in the patients with SSc.

Keywords

Work disability; Systemic Sclerosis; Medsger Lung Severity Index; ISEL; SF-36; Fatigue

INTRODUCTION

Systemic sclerosis (SSc, scleroderma) is a chronic, multisystem, connective tissue disease of unknown etiology characterized by inflammation, vasculopathy, and widespread fibrosis of skin and internal organs (1). It is associated with substantial morbidity and mortality (2;3). Advances in diagnosis and treatment have improved the prognosis of SSc in recent years (4;5). Nevertheless, this disease continues to have a detrimental impact on patients' personal and professional lives (6–12).

Previous studies by the National Arthritis Data Work Group and other investigators have shown a substantial increase in the economic impact of musculoskeletal and rheumatic conditions over the last decades in the United States. This has increased from \$4 billion in 1963 (13) to \$353 billion in 2005 (14), with a major proportion attributable to indirect costs of work disability and wage loss (13;14). Work disability (WD) continues to be a major burden on individuals affected from rheumatic conditions. This may become even more prominent in the future, as the working years and productivity lost due to WD will increase with the expected increase in the retirement age (15).

Work disability has been extensively studied in other rheumatic conditions such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and ankylosing spondylitis (AS) (16–20). Although a few studies have addressed WD and its correlates in patients with SSc in other countries (7–11;21), there are no studies investigating this issue in the United States. Moreover, there are no published prospective studies reports investigating the long-term predictors of WD in SSc patients.

In the current study, we hypothesized that WD in SSc is a function of demographic, clinical, and psychosocial factors. We investigated the prevalence of work disability in a multiethnic cohort of early SSc patients and assessed the factors associated with WD, at early stages of disease. Then, we longitudinally examined the predictors of WD in the patients who were working at enrollment.

METHODS

The **Genetics versus ENvironment In Scleroderma Outcome Study** (GENISOS) is a multicenter prospective study of early SSc patients. It is conducted at three sites: the University of Texas Health Science Center at Houston (UTHSC-H), the University of Texas Medical Branch at Galveston (UTMB), and the University of Texas Health Science Center at San Antonio (UTHSC-SA). Study recruitment started in January 1998 and is ongoing.

Study subjects

Details of patient selection and recruitment have been previously described (3;22–25). Patients who fulfilled the following inclusion criteria were enrolled: 1) age ≥ 18 years; 2) diagnosis according to the American College of Rheumatology (formerly the American Rheumatism Association) criteria for SSc (26); 3) disease onset (defined as onset of the first non-Raynaud symptom) within five years of enrollment; and 4) defined ethnicity with all four grandparents from the same ethnic group. Patients who had SSc-like illnesses associated with environmental, ingested, or injected agents were excluded from the study. All the 284 patients enrolled at the time of analysis were included in this study. The institutional review boards of all participating sites approved the study and written informed consent was obtained from all subjects.

Data collection and questionnaires

As previously described (3;22–25), the demographic, clinical, laboratory tests, chest radiographs, pulmonary function tests, autoantibody profile, patient-reported clinical outcomes as well as behavioral, psychosocial and functional data were obtained at the baseline visit and then on subsequent semi-annual visits.

Outcome variable—The primary outcome was the occupational status. We have annually gathered this information in a questionnaire designed according to the definitions in the Dictionary of Occupational Titles by the United States Department of Commerce (27;28). The questionnaire collected the employment status (working full-time or part-time, unemployed, retired, disabled, student, or homemaker), job description, and the reason of the current job status if anything other than working full-time. We categorized the patients into three groups (figure 1). Group A included patients working full-time, part-time for any reasons other than health problems, and full-time students. Full-time work was defined as working ≥ 40 hours per week. Group B were work-disabled individuals, including those who were early retired, unemployed, or part-time workers because of health problems. Furthermore, the third group of patients (Group C) consisted of homemakers, retired and unemployed individuals for reasons other than health problems. We excluded Group C from further analysis as we could not determine whether their occupational status was attributable to SSc.

Independent variables—Independent variables from the following domains were investigated: demographic, clinical, patient-reported clinical and psychosocial variables.

Demographic information: Age at enrollment, gender, ethnicity, marital status, educational level, and smoking status were recorded. Marital status data were dichotomized as being married or in a marriage-like relationship versus being single, divorced, separated, or never married. We also dichotomized the educational level as holding an associate degree and above versus high school diploma and below.

Clinical manifestations: All patients were examined by the study investigators at the three study sites. Disease characteristics included disease type based on the extent of skin involvement (29), duration, and antibody profile. We calculated the disease duration with two different methods: from the first non-Raynaud's phenomenon symptom attributable to SSc and from the first symptom attributable to SSc (Raynaud's or non-Raynaud's phenomenon symptoms). History and physical examination findings, Modified Rodnan Skin Score (MRSS) (30), Medsger Severity Index (SI) (31), and history of corticosteroid and cyclophosphamide use were recorded. Presence of digital ulcers was determined based on the investigators' clinical assessment. SSc cardiac involvement was defined as having clinically significant arrhythmia or ejection fraction $\leq 40\%$.

As previously described (22), all pulmonary function tests were reviewed by a pulmonologist and studies that did not fulfill the American Thoracic Society/European Respiratory Society (ATS/ERS) were excluded (32;33). Myositis was diagnosed if the patient had proximal muscle weakness with at least one of the following: elevated levels of muscle enzymes, myopathic changes on electromyography, and/or a characteristic muscle biopsy. A decrease in range of motion > 25% in at least one joint axis was defined as joint contracture. Small joint contracture was determined based on involvement of metacarpophalangeal and/or proximal interphalangeal finger joints while large joint contracture was defined as involvement of elbow and/or knee joints. Arthritis was defined as presence of joint swelling and tenderness on physical examination not attributable to osteoarthritis, crystalline arthropathy, or trauma. Abnormal renal function was defined as serum creatinine ≥ 1.5 mg/dl. Furthermore, we calculated the number of co-morbid conditions in each patient based on the patients' history of cardiovascular disease, hypertension, diabetes mellitus, stroke, lung disease, malignancy, kidney disease, SLE, RA, thyroid disease, osteoarthritis, fibromyalgia, peptic ulcer disease, obesity (body mass index ≥ 30), depression, and other neuropsychiatric disorders.

Patient-reported clinical outcomes: pain and shortness of breath (SOB) was captured on a visual analogue scale ranging from zero to ten. Higher numbers indicated more severe pain and dyspnea.

Psychosocial variables: Six psychosocial variables were measured: fatigue, social support, illness behavior, learned helplessness, self-perceived physical and mental health, as well as, functional status. Fatigue was assessed with Fatigue Severity Scale (FSS), a validated 29-item questionnaire (34). Answers to each question were rated from one to seven (no fatigue to very severe fatigue impaired function). Higher scores indicated more fatigue. Social support was evaluated by using the Interpersonal Support Evaluation List (ISEL) (35). ISEL is a 40-item validated instrument comprised of four scales ranging from zero to 3 on each question and a summary measure. Higher scores indicated better social support. Coping with illness was assessed with the Illness Behavior Questionnaire (IBQ) (36). IBQ is a 62-item instrument comprised of seven scales measuring generalized hypochondriasis, disease conviction, denial, affective disturbance, affective inhibition, psychosocial versus somatic, and irritability plus a summary measure with a range of 0–35. Higher IBQ scores indicate more inappropriate illness behaviors. Learned helplessness was ascertained with the Arthritis Helplessness Index (AHI), a 15-item standardized questionnaire used in other chronic illnesses (37). Higher AHI scores indicate more perceived helplessness concerning the ability of the patient to impact on their illness. We used the medical outcome Study Short Form-36 (SF-36) to assess self-perceived mental and physical functioning (38–40). The SF-36 comprised of eight health related quality of life measures: physical functioning, role-physical, bodily pain, general health perceptions, vitality, social functioning, and role limitations due to emotional problems and mental health were individually scored. These scores were then summarized into the mental component (MCS) and physical component (PCS) summary scores, utilizing norm-based scoring based on a general population sample (mean of 50 and standard deviation of 10). All scores are rated so that higher values indicate higher levels of perceived functioning (range 0–100). The SF-36 has been previously validated in studies with SSc patients (39;40). In addition, the modified Health Assessment Questionnaire Disability Index (HAQ) was used for assessing functional status of the patients (41). Questions were graded from 0–3, based on self-perceived ability to “perform in a normal manner” to being “unable to perform”. The higher HAQ score indicated more physical disability.

Similar to our previous study (24), all psychosocial instruments demonstrated adequate internal consistency reliability. Social support measured by the ISEL questionnaire had the

Cronbach's Alphas of 0.87. IBQ and AHI showed the Cronbach's Alphas of 0.85 and 0.70. SF-36 had the Cronbach's Alphas of 0.91 and 0.88 for physical and mental components, respectively. The Cronbach's Alphas of HAQ and fatigue scores were also adequate at 0.91 and 0.90, respectively.

Statistical analysis

Patients who were homemakers, retired, or unemployed for reasons other than health problems at baseline (Group C) were excluded from analysis ($n=29$). In the cross-sectional analysis, we examined the association of the independent variables with disability status at the baseline visit (Group A versus Group B). The univariate analysis was conducted with Student's t tests for continuous and the χ^2 test for categorical variables.

We next conducted a hierarchical modeling with successive conceptual blocks to evaluate our hypothesis that demographic, clinical and psychosocial variables independently contribute to WD in SSc. The independent variables with a $p<0.1$ in the univariate analysis were added into the analysis in the following successive conceptual blocks: demographic information, clinical manifestations, self-reported clinical outcomes (pain and dyspnea), and psychosocial variables. The model fit was assessed after addition of each block by using Bayesian Information Criterion (BIC). Lower BIC values indicate better model fit. BIC values are interpreted as a weak evidence for better fit with a difference of 0–2, a positive evidence with a difference of 2–6, a strong evidence with a difference of 6–10, and very strong evidence for better fit with a difference of >10 . This approach tested the proposition that each conceptual block contributes independently to WD and is not merely a mediator of previous variables. HAQ is a direct measure of disability (41) and can mediate the effect of other factors on WD. In addition, SF-36 PCS as a measure of overall perceived physical health has overlap with clinical and patient-reported clinical outcomes and it might be partially an effect mediator of the clinical domain. Therefore, we exclude HAQ and SF-36 PCS in the blockwise hierarchical modeling and final multivariate models.

The final multivariate model at the cross-sectional level was computed utilizing a forward hierarchical variable selection strategy. This approach was chosen to decrease the effect of multi-collinearity in our analysis. We initially entered all variables that showed an association with $p<0.1$ in the univariate analysis. Subsequently, the number of independent variables was reduced to those variables that changed the R square of the entire model by 1%. We did not include income level and medical insurance as independent variables in our models because they were a consequence rather than a risk factor for WD.

We next included all patients who were working or full-time students at enrollment (Group A) in the longitudinal study. For this component, time to event (occurrence of disability) analysis was conducted utilizing a Cox proportional hazards regression model. The date of enrollment into the study was used as the starting point. An initial univariate analysis examining the relationship of independent variables with occurrence of disability after enrollment was conducted. The final multivariate model was computed using the hierarchical forward variable selection strategy as described above. All the statistical analyses were performed with NCSS 2007 (NCSS, Kaysville, UT) and STATA 11 (StataCorp, College Station, TX). The hypothesis testing was 2-sided with a $p \leq 0.05$ significance level.

RESULTS

Population characteristics and prevalence of WD at baseline visit

All 284 patients in the GENISOS were included in the study. Patients were followed for a mean ($\pm$ SD) time of 3.9 (3.6); up to 12 years, in 1438 visits. The mean age of patients at

enrollment was 48.7 (± 13.2) years and 237 (83.5%) of cohort were female. The patients were from the following ethnic groups: 133 (46.8%) Caucasian, 83 (28.9%) Hispanic, 58 (20.4%) African American, and 10 (3.5%) from other ethnic background. Diffuse skin involvement was reported in 162 (57.0%) of patients. Average disease duration at enrollment was 2.5 (± 1.6) years (table 1).

At enrollment, 131 patients (46.1%) were in Group A, including 111 (39.1%) full-time workers, 14 (4.9%) working part-time for reasons other than health problems, and 6 full-time students (figure 1). Group B (n=124; 43.7%) consisted of 83 (29.2%) patients self-reported as work disabled and 41 (14.3%) part-time workers, unemployed, or retired earlier due to health problems. The remainder of patients were in Group C (n=29, 10.2%).

We included the patients in Group A (working at baseline) for longitudinal study. Out of 131 patient, 96 (73.3%) were still working while 35 (26.7%) became disabled after, 4.4 (± 3.8) years of follow up, in 740 visits (figure 1).

Univariate analysis of WD correlates at baseline visit

In the univariate analysis, the following demographic variables were associated with WD: older age, non-Caucasian ethnicity, being single, separated, or divorced, lower educational background (holding high school diploma or lower degrees), while there was no association with gender.

Among clinical manifestations; cardiac involvement, lung disease (FVC and DLCO % predicted values), small joint contracture, number of co-morbid conditions, and Medsger Gastrointestinal (GI) Tract and Lung Severity Indices were significant correlates of WD. However, disease duration, MRSS, digital ulcers, GI symptoms like dysphagia and diarrhea, body mass index, abnormal renal function, arthritis, large joint contracture, myositis, elevated creatinine kinase, and serologic findings were not associated with WD. Moreover, recent treatment with corticosteroid and history of ever cyclophosphamide therapy did not correlate with WD (table 2 and supplement 1). Patient-reported clinical outcomes, VAS pain and shortness of breath, were both significantly higher in those with WD.

Patients with WD had more maladaptive illness behavior (higher IBQ score), more fatigue (higher score on Fatigue Severity Scale), higher learned helplessness (higher score on AHI) and HAQ scores. Furthermore, they reported less interpersonal support (lower ISEL score) and health related quality of life (lower SF-36- mental and physical components) (table 2 and supplement 1).

Independent correlates of WD at enrollment – Successive conceptual blocks

To determine the independent correlates of work disability in the patients with SSC; we successively added the following conceptual blocks into the multivariate multiple: 1) different demographic; 2) clinical manifestations; 3) patient-reported clinical outcome; and 4) psychosocial variables into conceptual blocks. The demographic characteristics (table 3, Model 1) provided the Bayesian information criterion (BIC) of 330 ($p < 0.001$ for Model 1). In Model 2, we added the clinical manifestations to demographic variables resulting in an improved BIC of 303, which demonstrated a strong evidence for better model fit ($\Delta = 27$, $p < 0.001$ for model 2). In Model 3, the patients reported clinical outcomes (pain and dyspnea) were added to the previous two blocks. Model 3 had a BIC value of 295 which is consistent with positive evidence for better model fit to the observed data ($\Delta = 8$, $p < 0.001$ for Model 3).

In Model 4, the psychosocial factors were added to the demographic and clinical manifestation blocks. Model 4 had the lowest BIC (290) and showed a strong evidence for

better model fit compared to Model 2 (delta= 13) and positive evidence for better model fit to Model 3 (delta=5). This blockwise hierarchical modeling strategy indicated that each successive block contributed independently to WD and was not merely a mediator of previous blocks while it cannot be ruled out that the successive models (e.g.: patient-reported clinical outcomes or psychosocial factors) are partially effect mediators of previous conceptual blocks.

Independent correlates of WD at enrollment – Final model

All relevant demographic, clinical, and psychosocial variables were included in the final model (table 4). The forward hierarchical model showed that educational level below associate's degree ($p<0.001$), higher Medsger Lung Severity Index ($p=0.004$), higher Fatigue Severity Score ($p<0.001$), and less social support ($p<0.001$) were independently associated with WD, at baseline. For example, those patients who had an associate degree or above were 78% less likely to be WD at the baseline visit while with each unit decrease in the ISEL score (less social support), the patients were 2.1 times more likely to be WD.

Univariate predictors of WD on follow up visits

We next examined predictors of developing WD in patients belonging to Group A (figure 1). Small joint contractures ($p=0.001$), lower DLCO % predicted value ($p=0.017$) and Medsger's Lung Severity Index ($p=0.049$) at enrollment were the significant clinical predictors of long-term work disability. Furthermore, all six psychosocial measures were significant predictors of WD in the Cox regression univariate analysis. Higher IBQ, Learned helplessness, FSS, and HAQ scores ($p=0.001$, $p=0.041$, $p=0.006$, $p=0.002$, respectively) and lower ISEL, SF-36 PCS and MCS scores ($p=0.014$, $p=0.002$, and $p=0.041$) were predictor of WD. However, serologic findings, MRSS, abnormal renal function, cardiac involvement, number of co-morbid conditions, and history of treatment with corticosteroid or cyclophosphamide did not influence on long-term the work disability (supplement 2).

Independent predictors of WD in the multivariate model

In the multivariate model following a forward hierarchical variable selection strategy, non-Caucasian ethnicity ($p=0.038$), lower DLCO ($p=0.038$), and higher score on Fatigue Severity Scale ($p=0.009$) at baseline were the only independent predictors of WD on follow up visits (table 5). Caucasians had 54 % less chance of becoming work disabled compared to non-Caucasians ($p=0.038$). Similarly, patients with higher DLco% predicted at the baseline visit were less likely to develop WD on follow-up visits. Moreover, for each point increase in FSS score at the baseline visit, the patient had 96% higher risk of developing WD ($p=0.009$). This final model supports our initial hypothesis that demographic, clinical and psychosocial factors contribute to WD in SSc.

DISCUSSION

Professional life plays a crucial role in patients' overall quality of life. Herein, we demonstrate that demographic, clinical, and psychosocial factors contribute to SSc-WD. To our knowledge, this is the first report on impact of SSc on the employment status in the United States. Moreover, it is the first longitudinal study examining the predictors of WD in patients with early SSc.

In addition to comprehensive demographic and clinical data, we also investigated the cross sectional and longitudinal influence of social support (ISEL), learned helplessness (AHI), coping skills (IBQ), and other previously reported psychometric correlates of WD in SSc (fatigue, HAQ and SF-36) (7–11;21). We hypothesized that demographic, clinical, patient-

reported outcomes, and psychosocial factors determine the occupational status in an individual with SSc.

Confirming previous studies (7–11), we showed a high prevalence of WD in early SSc. However, the observed prevalence was higher than reports from the well-characterized Canadian Scleroderma Registry Group (46% versus 21%) (7). This discrepancy could be explained by differences in the investigated study populations. Our patients had a higher frequency of diffuse cutaneous involvement (57% versus 48%). Furthermore, GENISOS was an incident cohort with mean disease duration of 2.5 years at enrollment, which is more likely to include patients with severe disease than a prevalent cohort. Moreover, the majority of the study population was Caucasian (90%) in the Canadian Scleroderma Registry whereas GENISOS included 53 % Non-Caucasian patients; Non-Caucasians had a higher mortality rate (3) and were more likely to be disabled (table 2). On the other hand, the prevalence of WD in GENISOS was lower than another study of 72 SSc patients in France (8). Same group later reported a WD prevalence of 41% among patients with digital ulcers (9). Differing health care policies of the investigated countries might also contribute to the observed variations in prevalence rate of WD (16). Nevertheless, the prevalence of work disability in SSc is substantially higher than other common rheumatic conditions (10;16–20).

In agreement with previous studies, demographic variables, specifically lower educational level (7;11), lung involvement (9;11), fatigue severity (7;11), and social support were independent correlates of WD at the cross sectional level in our study. Patients with lower educational level are more likely to hold occupations that are physically demanding. Therefore, its correlation with WD is not surprising. Similar demographic variables were correlates of WD in patients with early RA (42) and SLE (43). Fatigue also correlated with WD in previous studies of patients with SSc (21).

Confirming a recent report by Sandqvist *et al.*, social support was an independent correlate of WD in the GENISOS cohort (21). Previous studies have shown the impact of social support on disease activity, self-perceived quality of life, and occupational status in the patients with SLE (17;44;45). Furthermore, a national longitudinal study of the overall population in the United States demonstrated that social support is an independent predictor of overall functional health (46). These further emphasize on the pivotal role of high quality social relationships with family and friends on the patient's work ability. Because of its modifiable nature, the independent correlation between social support and WD suggests the necessity of multifaceted psychosocial interventions to enhance the working abilities among the patients with SSc.

After follow up of 4.4 years, almost one in four patients working at enrollment (Group A) became work disabled. Using Cox proportional hazards regression model, non-Caucasian ethnicity, lung involvement (DLCO % predicted), and higher score on Fatigue Severity Scale at baseline were the independent predictors of WD in the longitudinal study.

We have previously shown that non-Caucasian patients have higher mortality in the GENISOS cohort (3), indicating an overall less favorable prognosis (3;47;48). The predictive significance of non-Caucasian ethnicity for development of WD might be secondary to unmeasured demographic, clinical, and psychosocial factors. Health care factors leading to disparities in access to care might also be important (49). Non-Caucasian ethnicity was also predictive of WD development in other rheumatic diseases like SLE (50).

Scleroderma pulmonary involvement, including both interstitial lung disease and pulmonary arterial hypertension, is the primary cause of SSc- related death (51). Confirming previous results, we have shown that pulmonary involvement is also a predictor of mortality in the

GENISOS cohort (3). Therefore, it is not surprising that pulmonary involvement was associated with WD at baseline and longitudinally in the current study.

In the Scleroderma Lung Study, treatment with oral cyclophosphamide led to improvement in health-related quality of life measures along with better pulmonary function (52). In the current study, treatment with cyclophosphamide had no significant relationship to WD. However, differences in baseline characteristics between treated and untreated groups might have blunted the treatment effect. Randomized controlled studies with long-term follow up are more appropriate to determine the effect of various medications on WD.

Fatigue is one of the most common and overlooked complaints in patients with SSc (53). Our results confirm previous cross-sectional studies indicating that fatigue is an important contributor to WD (21;53;54). In our study, fatigue was not only correlate (cross-sectional) but also a predictor (longitudinal) of WD. Fatigue might be partially a mediator of the effects of demographic and clinical and factors on WD. However, our analysis with successive conceptual blocks demonstrates that psychosocial factors including fatigue contribute independently to WD and are not merely mediators of demographic or clinical factors. Our findings further underscore the need for future studies focusing on pathophysiology and treatment of fatigue in SSc.

In agreement with a previous study (21), small joint contracture was associated with WD at the univariate level. However, it was neither an independent correlate nor predictor of WD in the multivariate model. It is possible that a dichotomized variable as defined in our cohort does not capture the true severity of small joint contracture.

The GENISOS cohort includes a large number of early SSc patients from different ethnic backgrounds. The current study demonstrates the first assessment of prevalence, correlates, and predictors of WD in SSc that includes a sizable Hispanic and African American population. This enhances the generalizability of our findings. Furthermore, the comprehensive array of demographic, clinical, and psychosocial variables decreases the likelihood of missing important correlates or predictors.

However, the current study had some limitations. The majority of study subjects were recruited from tertiary medical centers, which can introduce referral bias (toward more severe cases). Detailed information on job descriptions and demands was not available in the GENISOS cohort. Therefore, we could not evaluate the impact of job demands on WD. Moreover, we could not examine change in the professional level i.e. downgrading to another job due to SSc in the current study. We did not use a validated psychometric instrument to assess depression in the GENISOS cohort. However, other psychometric instruments for assessment of mental health such as SF-36 MCS were utilized in the current study.

In conclusion, work disability is a prominent problem in patients with SSc. More than 40% of patients were already work disabled at early stages of the disease. After 4.4 years, more than one forth of those working at enrollment eventually became work disabled. Work disability is a function of demographic background, clinical and psychosocial factors, cross-sectionally and longitudinally. These findings underscore the need for a multi-disciplinary approach to treatment of SSc patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
The employment status of the patients at enrollment and follow-up visits

Table 1

Socio-demographic, disease characteristics, and employment status of the patients enrolled in the GENISOS cohort

Age, mean ($\pm$ SD), yr	48.7 (13.2)
Gender; female, n (%)	237 (83.5)
Ethnicity, n (%)	
<i>Caucasian</i>	133 (46.8)
<i>African American</i>	58 (20.4)
<i>Hispanic</i>	83 (28.9)
<i>Other</i>	10 (3.5)
Marital status, married or marriage like relationship, n (%)	161 (56.7)
Educational level, associate degree and/or above, n (%)	116 (40.8)
Annual income level*, mean ($\pm$ SD)	5.1 (2.1)
Smoker, current, n (%)	50 (17.6)
Cutaneous involvement, diffuse, n (%)	162 (57.0)
Disease duration, mean ($\pm$ SD)*, yr	2.5 (1.6)
Employment Status, n (%)	
<i>Non-work disabled (Group A)</i>	131 (46.1)
<i>Work disabled (Group B)</i>	124 (43.7)
<i>Retired or homemakers (Group C)</i>	29 (10.2)

Annual income level of 5 reflects income range of \$20,000 -, \$29,999.

Table 2

Univariate analysis of work disability correlates at enrollment

	Group A (n=131)	Group B (n=124)	Regression coefficient (95% CI)	P-Value
Demographic				
Age, yr, mean ($\pm$ SD)	45.3 (13.0)	50.9 (12.5)	-5.58 (-8.72, -2.43)	<0.001
Gender, Female, %	81.7	84.7	0.81 (0.39, 1.64)	0.523
Ethnicity, Caucasian, %	54.9	35.5	0.45 (0.26, 0.77)	0.002
Marital status, married, %	62.6	45.1	0.49 (0.29, 0.84)	0.005
Educational level, %	53.1	22.7	0.26 (0.15, 0.46)	<0.001
Clinical manifestations				
Cutaneous involvement, diffuse, %	55.8	58.1	0.91 (0.54, 1.54)	0.706
Disease duration, mean ($\pm$ SD), yr				
<i>first non-Raynaud's phenomenon symptom attributable to SSc</i>	2.41 (1.61)	2.71 (1.57)	-0.29 (-0.68, 0.10)	0.143
<i>first symptom attributable to SSc</i>	4.68 (6.48)	4.19 (4.11)	-0.48 (-0.85, 1.82)	0.480
MRSS, mean ($\pm$ SD)	14.9 (10.6)	16.3 (12.9)	-1.39 (-4.31, 1.52)	0.344
Cardiac involvement, %	20.8	41.3	2.67 (0.99, 70.46)	0.032
Small joint contracture, %	11.5	25.6	2.66 (1.29, 5.63)	0.003
FVC % predicted, mean ($\pm$ SD)	84.8 (19.6)	75.9 (23.5)	8.24 (2.59, 13.67)	0.003
DLCO % predicted, mean ($\pm$ SD)	72.5 (21.8)	64.3 (24.7)	6.24 (0.01, 12.37)	0.046
No of comorbidities, mean ($\pm$ SD)	1.5 (1.4)	2.0 (1.5)	-0.53 (-0.92, -0.15)	0.007
Medsger Severity Index, mean($\pm$ SD)				
<i>General</i>	0.4 (0.8)	0.6 (0.9)	-0.18 (-0.38, 0.02)	0.080
<i>Perivascular</i>	1.4 (1.0)	1.6 (1.1)	-0.23 (-0.50, 0.03)	0.085
<i>Skin</i>	1.5 (0.8)	1.6 (0.9)	-0.02 (-0.22, 0.20)	0.845
<i>Joint</i>	0.6 (1.1)	0.8 (1.3)	-0.13 (-0.46, 0.17)	0.373
<i>Muscle</i>	0.2 (0.4)	0.3 (0.4)	-0.07 (-0.17, 0.04)	0.232
<i>GI Tract</i>	0.6 (0.6)	0.8 (0.6)	-0.23 (-0.34, -0.02)	0.019
<i>Lung</i>	1.1 (1.1)	1.6 (1.1)	-0.43 (-0.72, -0.15)	0.002
<i>Heart</i>	0.2 (0.7)	0.3 (0.7)	-0.03 (-0.21, 0.14)	0.746
<i>Kidney</i>	0.1 (0.3)	0.1 (0.6)	-0.06 (-0.18, 0.06)	0.299
Autoantibody profile, %				
ANA	96.9	93.5	0.45 (0.09, 1.75)	0.195
ACA	13.9	12.2	0.86 (0.38, 1.92)	0.697
ATA	17.9	19.0	1.07 (0.54, 2.14)	0.832
<i>Pol III</i>	25.9	19.3	0.68 (0.35, 1.30)	0.213
<i>UI-RNP</i>	9.8	10.2	0.96 (0.38, 2.40)	0.938
Ro	3.1	6.6	2.17 (0.56, 10.11)	0.204
Patient-reported clinical outcome				
VAS pain score, mean ($\pm$ SD), mm	35.0 (32.5)	49.4 (33.5)	-14.4 (-22.81, -5.99)	<0.001
VAS SOB, mean ($\pm$ SD), mm	21.4 (27.9)	36.9 (32.8)	-15.5 (-23.20, -7.78)	<0.001
Psychosocial measures				
IBQ score, mean ($\pm$ SD)	15.4 (6.0)	18.1 (5.4)	-2.68 (-4.14, -1.21)	<0.001

	Group A (n=131)	Group B (n=124)	Regression coefficient (95% CI)	P-Value
AHI, mean ($\pm$ SD)	36.4 (6.9)	38.8 (6.0)	-2.35 (-4.01, -0.69)	0.006
FSS score, mean ($\pm$ SD)	4.4 (1.0)	4.9 (0.8)	-0.43 (-0.66, -0.20)	<0.001
ISEL score, mean ($\pm$ SD)	8.5 (1.3)	7.5 (1.7)	0.99 (0.59, 1.38)	<0.001
SF-36-PCS, mean ($\pm$ SD)	37.4 (10.4)	30.4 (8.9)	7.23 (4.71, 9.74)	<0.001
SF-36-MCS, mean ($\pm$ SD)	48.1 (12.2)	44.2 (10.6)	3.86 (0.92, 6.78)	0.010
HAQ score, mean ($\pm$ SD)	0.7 (0.6)	1.2 (0.7)	-0.46 (-0.64, -0.28)	<0.001

SD, Standard deviation; MRSS, modified Radon Skin Score; FVC, Forced vital capacity; DLCO, Diffuse capacity of the lung for carbon monoxide; ANA, anti-nuclear antibody; ACA, anti-centromere antibody; ATA, anti-topoisomerase antibody; Pol III, anti- RNA polymerase III antibody; U1-RNP, anti-U1-ribonucleoprotein; VAS, visual analogue scale; SOB, shortness of breath; IBQ, Illness Behavior Questionnaire; AHI, Arthritis Helplessness Index; FSS, Fatigue Severity Scale; ISEL, Interpersonal Support Evaluation List; SF-36 PCS, Short form 36 physical component summary; SF-36 MCS, Short form 36 mental component summary; HAQ, Health assessment questionnaire.

Table 3

Block-wise modeling of demographic, clinical, patient-reported clinical outcomes, and psychosocial correlates of work[RS1]

	Model 1	Model 2	Model 3	Model 4
	Demographic	Demographic and clinical manifestations	Demographic, clinical, and patient-reported outcome	Demographic, clinical, and psychosocial factors
Age at enrollment	0.04 (0.02, 0.06)	0.03 (0.01, 0.06)	0.03 (0.01, 0.06)	0.03 (−0.01, 0.06)
Ethnicity	−0.66 (−1.24, −0.08)	−0.50 (−1.18, 0.17)	−0.47 (−1.18, 0.23)	−0.46 (−1.26, 0.35)
Marital status	−0.72 (−1.27, −0.17)	−0.56 (−1.19, 0.07)	−0.42 (−1.08, 0.25)	−0.24 (−0.99, 0.51)
Educational level	−1.10 (−1.69, −0.51)	−1.19 (−1.88, −0.49)	−1.19 (−1.94, −0.44)	−1.48 (−2.32, −0.64)
Cardiac involvement		1.03 (−0.01, 2.07)	1.14 (0.07, 2.20)	0.85 (−0.29, 1.98)
FVC %predicted		−0.01 (−0.02, 0.01)	−0.01 (−0.02, 0.02)	−0.01 (−0.03, 0.02)
DLCO %predicted		−0.01 (−0.02, 0.01)	0.01 (−0.02, 0.02)	0.01 (−0.02, 0.03)
Small joint contracture		0.31 (−0.55, 1.16)	0.21 (−0.68, 1.10)	0.07 (−0.95, 1.08)
Number of co-morbidities		0.06 (−0.17, 0.28)	−0.01 (−0.24, 0.24)	−0.04 (−0.31, 0.23)
Medsges GI		0.62 (0.08, 1.16)	0.73 (0.14, 1.31)	0.48 (−0.13, 1.09)
Severity Index				
Medsges Lung		0.19 (−0.24, 0.62)	0.19 (−0.26, 0.64)	0.37 (−0.15, 0.89)
Severity Index				
VAS pain			0.03 (−0.09, 0.15)	0.02 (−0.12, 0.16)
VAS SOB			0.08 (−0.58, 0.22)	0.03 (−0.13, 0.19)
FSS				0.83 (0.29, 1.36)
IBQ				−0.02 (−0.12, 0.07)
AHI				0.01 (−0.05, 0.07)
ISEL				−0.31 (−0.59, −0.01)
SF-36-MCS				0.01 (−0.03, 0.05)
Model <i>p</i> -value				< 0.001
BIC	< 0.001	< 0.001	< 0.001	289.53
	330.32	302.51	294.89	

BIC, Bayesian information criterion

Table 4

Multivariate analysis of demographic, clinical, patient-reported clinical outcomes, and psychosocial correlates of work disability at enrollment, based on forward hierarchical models

Characteristics	Odds ratio	95 % Confidence interval	<i>p-value</i>
Educational status	0.22	0.12, 0.43	<0.001
Medsker Lung Severity Index	1.50	1.14, 1.99	0.004
Fatigue Severity Scale	2.18	1.51, 3.14	<0.001
ISEL	0.66	0.54, 0.82	<0.001

Table 5

Demographic, clinical, and psychosocial predictors of work disability based on multivariate Cox regression modeling

	Hazard ratio (95% CI)	<i>P-value</i>
Ethnicity, Caucasian	0.46 (0.22, 0.96)	0.038
DLCO % predicted value	0.98 (0.97, 0.99)	0.038
Fatigue severity score	1.96 (1.19, 3.25)	0.009