The association of sociodemographic and disease variables with hand function: a Scleroderma Patient-centered Intervention Network cohort study

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ABSTRACT

Objective. *Impaired hand function in systemic sclerosis (SSc) is a primary cause of disability and contributes diminished health-related quality of life. The objective of the present study was to evaluate sociodemographic, lifestyle, and disease-related factors independently associated with hand function in SSc.*

Methods. *Patients enrolled in the Scleroderma Patient-centered Intervention Network Cohort who completed baseline study questionnaires between March 2014 and September 2017 were included. Hand function was measured using the Cochin Hand Function Scale (CHFS). Multiple linear regression analysis was used to identify independent correlates of impaired hand function.*

Results. *Among 1193 participants (88% female), the mean CHFS score was 13.3 (SD=16.1). Female sex (standardised regression coefficient, beta (β)=.05), current smoking (β=.07), higher BMI (β=.06), diffuse SSc (β=0.14), more severe Raynaud's scores (β=.23), more severe finger ulcer scores (β=.23), moderate (β=0.19) or severe small joint contractures (β=.20), rheumatoid arthritis (β=0.07), and idiopathic inflammatory myositis (β=0.06) were significantly associated with higher CHFS scores (more impaired hand function). Consumption of 1–7 alcoholic drinks per week (β=-0.07) was associated with lower CHFS scores (less impaired hand function) compared to no drinking.*

Conclusion. *Multiple factors are associated with hand function in SSc. The presence of moderate or severe small joint contractures, the presence of digital ulcers, and severity of Raynaud's phenomenon had the largest associations. Effective interventions are needed to improve the management of hand function in patients with SSc.*

Introduction

Systemic sclerosis (SSc, or scleroderma) is a rare autoimmune disease characterised by vascular injury, immune dysfunction and an abnormal fibrotic process that can affect multiple organ systems including the skin, lungs, gastrointestinal tract and cardiovascular system (1, 2). SSc is notable for significant disruptions to activities of daily living, high levels of disability, and poor health-related quality of life (HRQL) (1-5) even compared to patients with other rheumatic diseases (4, 5). Impaired hand functioning in SSc is a primary cause of disability and contributes to lower HRQL, limitations in daily activities, and increased need for home care (6-8).

Across studies, patients with SSc consistently rank concerns related to hand function at the top of their list of problems with the greatest impact on their daily lives (8, 9). Contractures and deformities of the hand, consisting of decreased flexion and limited extension as well as reduced thumb abduction, are present in approximately 90% of patients with SSc (8, 9). Other disease manifestations that may be linked to reduced hand function include Raynaud's phenomenon, digital ulcers, skin thickening, calcinosis, synovitis, and tendon friction rubs (6-14). However, only two studies (n=190 and n=213) have used multivariable analyses to examine factors associated with hand function in SSc (13, 14). Those studies reported that digital ulcers were significantly associated with reduced hand function, as measured by the Cochin Hand Function Scale (CHFS) (8, 15), but neither

study reported multivariable results for other factors that may contribute to poor hand function. There is a need to better understand factors contributing to functional impairments of the hands in SSc in order to identify potential targets for education, prevention and treatment. Thus, the objective of the present study was to evaluate sociodemographic, lifestyle, and disease-related factors that may influence hand functioning in SSc.

Patients and methods

Patients and procedure

The study sample consisted of patients enrolled in the Scleroderma Patient-centered Intervention Network (SPIN) Cohort who completed study questionnaires from March 2014 through September 2017 (16). Patients in the SPIN Cohort were enrolled at 37 centres in Canada, the USA, the UK, France, and Spain. To be eligible for the SPIN Cohort, patients must be classified by a SPIN physician as having SSc according to the 2013 ACR/EULAR classification criteria (17); be at least 18 years of age; have the ability to give informed consent; be fluent in English, French or Spanish; and have access and be able to respond to questionnaires via the internet. The SPIN sample is a convenience sample. Eligible patients are invited by the attending physician or a supervised nurse coordinator to participate in the SPIN Cohort, and written informed consent is obtained. The local SPIN physician or supervised nurse coordinator then completes a medical data form that is submitted online to initiate patient registration in the SPIN Cohort. After completion of online registration, an automated welcoming email is sent to participants with instructions on how to activate their SPIN online account and how to complete the SPIN Cohort patient measures online. Participants complete outcome measures upon enrolment and subsequently every 3 months. Patients who completed all study variables at baseline were included in this study. The SPIN Cohort study was approved by the Research Ethics Committee of the Jewish General Hospital, Montreal, Canada and by the Institutional Reviews Boards of each participating centre.

Measures

- Sociodemographic and medical data

Patients provided age, gender, marital status, years of education, number of cigarettes smoked per week, and number of alcoholic drinks per week. SPIN physicians completed a medical data form that included all items of the 2013 ACR/EULAR SSc classification criteria (17) and provided time since first non-Raynaud's phenomenon symptoms and diagnosis, SSc subtype (limited or diffuse cutaneous SSc) (18), presence of overlap syndromes (systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, idiopathic inflammatory myositis), and presence of joint contractures (no/mild (0–25%) *versus* moderate/severe (>25%) limit in range of motion).

Standard numeric rating scales were completed by patients for Raynaud's severity in the past week and severity of finger ulcers, ranging from 0 (not severe at all) to 10 (unbearable).

- Hand function

The 18-item Cochin Hand Function Scale (CHFS) was developed to measure hand function limitations among patients with rheumatoid arthritis. CHFS items assess ability to perform hand-related activities (*e.g.* kitchen, dressing oneself, hygiene, writing/typing). Items are scored on a 0-5 Likert scale (0=*without difficulty;* 5=*impossible*). The total score is obtained by adding the scores of all items (range 0-90), and higher scores indicate more difficulty in hand function. The CHFS has been validated in SSc (15).

Statistical analyses

Descriptive statistics for the sample were calculated as means and standard deviations (SDs) for continuous variables and counts and percentages for categorical variables. CHFS scores were compared across sociodemographic and clinical variables using univariate linear regression. Multiple linear regression was used to assess the independent associations of sociodemographic (sex, age, marital status, education, smoking status, alcohol consumption and BMI) and medical variables with hand function, as measured with the CHFS. Medical variables to be included in the model were defined a priori by the research team and included disease duration, disease subtype, patient-reported severity of Raynaud's and finger ulcers, presence of puffy fingers, presence of sclerodactyly, presence of skin thickening proximal to the metacorpophalangeal joints, presence of tendon friction rubs, presence of small joint contractures, presence of systemic lupus erythematosus, Sjögren's syndrome, and idiopathic inflammatory myositis.

The assumption of normal distribution of residuals in the regression model was tested using a normal probability plot. Additionally, correlations between independent variables and tolerances were calculated to check for multicollinearity. All statistical analyses were conducted using Stata (v. 13), and all statistical tests were 2-sided with a $p<0.05$ significance level.

Results

Sample characteristics

In total, 1193 participants had complete data for all variables in the regression analyses and were included. There were 146 men (12%) and 1047 women (88%; Table I). Most patients were married or living as married (73%). Mean time since first non-Raynaud's symptoms was 11.2 (SD=8.7) years; mean time since diagnosis was 9.4 (SD=7.7) years. The mean CHFS score was 13.3 (SD=16.1).

Associations with hand function

Unadjusted associations of sociodemographic and disease variables with CHFS scores are shown in Table I. In bivariate analyses, higher age (standardised regression coefficient, beta (β)=-0.10), being married (β=-0.12), more years of education (β=-0.07), drinking 1–7 and drinking 8 or more glasses of alcohol per week (relative to no alcohol, β=-0.11 and β=-0.09, respectively) were significantly associated with lower CHFS scores (less impaired hand function). Female sex (β=.07), current smoking (β=.10), diffuse disease (β=0.28), higher patient-reported severity of Raynaud's (β=0.35) and finger ulcers (β=0.42),

presence of sclerodactyly (β=0.09), thickening of the skin of the fingers (β=0.21), current tendon friction rubs (relative to never; β=0.15), tendon friction rubs in the past (relative to never; =0.15), moderate (relative to no/mild; β=0.31) or severe (relative to no/mild); β=0.29) small joint contractures, presence of rheumatoid arthritis (β=0.10), and idiopathic inflammatory myositis (β=0.09) were significantly associated with higher CHFS scores (more impaired hand function).

Results from the multivariable linear regression are shown in Table II. The R^2 for the model was 0.375, and adjusted R^2 was 0.362. Female sex (β=0.05, p=.035), current smoking (β=0.07, p=0.004), higher BMI (β=0.06, p=0.012), diffuse SSc (β=0.14, p<0.001), more severe Raynaud's scores (β=0.23, p<0.001), more severe finger ulcer scores (=0.23, p<.001), moderate (β=0.19, p<0.001) or severe small joint contractures (β=0.20, p<0.001), rheumatoid arthritis (β=0.07, p=0.004), and idiopathic inflammatory myositis (β=0.06, p=0.020) were significantly associated with higher CHFS scores (more impaired hand function). Consumption of 1–7 alcoholic drinks per week (β=-0.07, p=0.004), on the other hand, was associated with lower CHFS scores (less impaired hand function) compared to no drinking.

Regression diagnostics found no evidence for deviation from the assumption of normal distribution of residuals based on a normal probability plot. All tolerance values were between 0.64 and 0.96, indicating that multicollinearity was not an issue.

Discussion

The main finding of this study was that the presence of digital ulcers, the presence of moderate or severe contractures of the small joints, and patient-reported Raynaud's phenomenon severity were the most robust independent correlates of impaired hand function in patients with SSc with diffuse disease subtype also strongly associated. Additionally, female sex, current smoking, higher BMI and comorbid rheumatoid arthritis and idiopathic inflammatory myositis were significantly associated with more impaired hand function.

Raynaud's phenomenon and digital ulcers are both common clinical features in patients with SSc, and in the SPIN Cohort, 99% of patients had Raynaud's phenomenon and 34% had digital ulcers. A number of pharmacologic and non-pharmacological treatments are available to manage these symptoms. Different vasodilating drug therapies are available to reduce Raynaud's and to prevent and improve healing of digital ulcers (19-23). In addition, treatment of Raynaud's phenomenon typically involves lifestyle modification to reduce exposure to potential triggers, including avoiding exposure to cold and maintaining whole body and digital warmth, smoking cessation, avoiding medications that worsen vasoconstriction and behavioural interventions to manage stress (21, 23, 24). On the other hand, current pharmacologic and non-pharmacological treatments fail to completely control Raynaud's phenomenon and prevent digital ulcers, and they are not tolerated by many SSc subjects. Our data underscore the important impact that Raynaud's phenomenon and digital ulcers have on patients and send a strong signal that novel, effective and well-tolerated interventions are still required.

There are no well-proven treatments for hand contractures in SSc. Three RCTs have evaluated physical or occupational therapy interventions to improve hand function in SSc, but all were limited by small samples (n <20 per arm) and significant methodological shortcomings (25). An RCT (n=53) of a 12-week multidisciplinary day treatment program, which included hand exercises, reported grip strength and reduced disability compared to usual care 24 weeks post-randomisation (26). More recently, another RCT tested a one-month general SSc home-based exercise therapy program, which included hand exercises (n=218) (27). The program improved hand function significantly at 6-months follow-up, but gains were no longer statistically significant at 12-months post-randomisation, possibly because the program did not focus specifically on hand function and that the one-month program did not provide resources to support ongoing patient adherence. One concern is that, while referral to hand therapists with experience in the treatment of SSc is often suggested to improve joint mobility, access to these services is difficult for many patients (16). The SPIN-HAND trial, which is currently underway, will evaluate the effectiveness of an online, self-guided program of hand exercises designed to improve hand function (28). Alternatively, given the important contribution of contractures to functional limitations, future efforts should also be directed to prevention of contractures since reversibility remains a significant challenge.

The present study has limitations that should be considered in interpreting results. First, the SPIN Cohort constitutes a convenience sample of SSc patients receiving treatment at a SPIN recruiting centre, and patients at these centres may differ from those in other settings. Additionally, SSc patients in the SPIN Cohort complete questionnaires online, which may further limit the generalisability of findings. A recent comparison between SPIN Cohort participants and the European Scleroderma Trials and Research (EUSTAR) and Canadian Scleroderma Research Group (CSRG) cohorts, however, showed that the SPIN Cohort is broadly comparable with these cohorts, increasing confidence that insights gained from the SPIN Cohort should be generalisable (29). An additional limitation of the present study relates to the nature of disease characteristics included in the analyses. Specifically, the majority of the variables included in the models consisted of fairly crude indicators of either the presence or absence of a particular disease factor, and most did not reflect severity, which may have reduced detected associations. We have included patient-reported severity of finger ulcers, but not other factors such as presence of infection, depth or area of the ulcer. Furthermore, while other factors may have been of interest (*e.g.* socioeconomic status, access to healthcare), data for these factors were not available or variables were not selected to be included in our a priori model, thus were beyond the scope of the present paper. No information was available on treat-

Table I. Sociodemographic and disease characteristics among SSc patients (n=1193) and unadjusted association with hand function as measured with the CHFS.

Variable	N (%) or Mean (SD)	Unstandardised regression coefficient (95% Confidence Interval)	Standardised regression coefficient	*p*-value
Demographic				
Female sex, n (%)	1047 (88)	3.21 (5.99, 0.43)	0.07	0.024
Age in years, mean (SD)	55.1 (12.3)	-0.14 (-0.21, -0.06)	-0.10	<0.001
Married or living as married, n (%)	865 (73)	-4.19 (-6.23, -2.16)	-0.12	<0.001
Education in years, mean (SD)	15.1 (3.5)	-0.30 (-0.56, -0.05)	-0.07	0.021
Current Smoker, n (%)	88 (7)	5.86 (2.37, 9.33)	0.10	0.001
Alcohol consumption (drinks/week), n (%)				
0	665 (56)	reference	--	--
1-7	439 (37)	-3.71 (-5.63, -1.78)	-0.11	<0.001
8+	89 (7)	-5.52 (-9.05, -1.98)	-0.09	<0.001
BMI, mean (SD)	25.6 (5.8)	-0.00 (-0.16, 0.16)	-0.00	0.978
Disease characteristics				
Time since onset first non-Raynaud's symptom in years, mean (SD)	11.2 (8.7)	0.03 (-0.08, 0.13)	0.01	0.630
Diffuse SSc, n (%)	475 (40)	9.12 (7.32, 10.91)	0.28	<0.001
Presence of Raynaud's, n (%)[a]	1171 (99)	1.64 (-6.31, 9.59)	0.01	0.686
Patient-reported severity of Raynaud's, mean (SD)	3.7 (2.8)	1.99 (1.69, 2.30)	0.35	<0.001
Presence of finger ulcers, n (%)	400 (34)	6.23 (4.32, 8.13)	0.18	<0.001
Patient-reported severity of finger ulcers, mean (SD)	1.6 (2.7)	2.54 (2.23, 2.85)	0.42	<0.001
Presence of puffy fingers, n (%)	697 (58)	1.57 (-0.29, 3.42)	0.05	0.097
Presence of sclerodactyly, n (%)	975 (82)	3.70 (1.34, 6.06)	0.09	0.002
Presence of skin thickening of the fingers proximal to the metacorpophalangeal joints, n (%)	657 (55)	6.75 (4.96, 8.55)	0.21	<0.001
Tendon friction rubs, n (%)				
Never	906 (76)	reference	--	--
Currently, with or without past	145 (12)	7.17 (4.40, 9.94)	0.15	<0.001
In the past, but not currently	142 (12)	7.31 (4.51, 10.11)	0.15	<0.001
Small joint contractures, n (%)				
No/Mild	905 (76)	reference	--	--
Moderate	208 (17)	12.96 (10.72, 15.18)	0.31	<0.001
Severe	80 (7)	18.91 (15.53, 22.29)	0.29	<0.001
Presence of systemic lupus erythematosus, n (%)	33 (3)	-0.50 (-6.07, 5.07)	-0.01	0.860
Presence of Sjögren's syndrome, n (%)	117 (10)	1.99 (-1.08, 5.07)	0.04	0.203
Presence of rheumatoid arthritis, n (%)	65 (6)	7.34 (3.34, 11.35)	0.10	<0.001
Presence of idiopathic inflammatory myositis, n (%)	68 (6)	6.34 (2.41, 10.26)	0.09	0.002
Cochin Hand Function Scale total score, mean (SD)	13.3 (16.1)	--	--	--

[a]Due to missing values: n=1187.

ments administered to patients in the SPIN Cohort. Finally, although the medical variables included in the model were defined a priori by the research team with expertise in hand function problems in SSc, due to the scarcity of previous studies in this area, our study was exploratory in nature.

In sum, the present study is the first to examine the independent associations of sociodemographic, lifestyle, and disease-related factors with hand functioning in a large cohort of SSc patients. Results highlight that multiple factors may contribute to hand disability in SSc, with joint contractures, patient-reported severity of Raynaud's phenomenon and digital ulcers having the largest associations. Adequately-tested prevention strategies, medical treatments, and rehabilitation programs are needed to improve the management of hand function problems in patients with SSc.

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Table II. Multiple linear regression of the relationship between sociodemographic and disease variables with hand function, as measured by the CHFS (n=1193).

Variable	Unstandardised regression coefficient (95% Confidence Interval)	Standardised regression coefficient	*p*
Demographic			
Female sex	2.46 (4.74, 0.17)	0.05	0.035
Age (years)	0.00 (-0.06, 0.06)	0.03	0.990
Married or living as married	-1.44 (-3.13, 0.25)	-0.04	0.094
Education (years)	-0.11 (-0.32, 0.11)	-0.02	0.321
Current smoker	4.16 (1.30, 7.02)	0.07	0.004
Alcohol consumption (drinks/week)			
0	reference	--	--
1-7	-2.28 (-3.85, -0.71)	-0.07	0.004
8+	-2.46 (-5.37, 0.44)	-0.04	0.097
BMI	0.16 (0.04, 0.29)	0.06	0.012
Disease characteristics			
Time since onset first non-Raynaud's symptom (years)	0.09 (-0.00, 0.18)	0.05	0.054
Diffuse SSc	4.54 (2.70, 6.39)	0.14	<0.001
Patient-reported severity of Raynaud's (0-10)	1.32 (1.04, 1.61)	0.23	<0.001
Patient-reported severity of finger ulcers (0-10)	1.41 (1.10, 1.72)	0.23	<0.001
Presence of puffy fingers	1.11 (-0.44, 2.66)	0.03	0.160
Presence of sclerodactyly	1.09 (-0.97, 3.16)	0.03	0.299
Presence of skin thickening of the fingers proximal to the metacorpophalangeal joints	0.21 (-1.61, 2.02)	0.01	0.823
Tendon friction rubs			
Never	reference	--	--
Currently, with or without past	1.05 (-1.33, 3.42)	0.02	0.387
In the past, but not currently	2.06 (-0.40, 4.52)	0.04	0.101
Small joint contractures			
No/Mild	reference	--	--
Moderate	8.20 (6.11, 10.30)	0.19	<0.001
Severe	13.04 (9.90, 16.18)	0.20	<0.001
Presence of systemic lupus erythematosus	-1.83 (-6.40, 2.73)	-0.02	0.431
Presence of Sjögren's syndrome	-0.36 (-2.95, 2.22)	-0.01	0.782
Presence of rheumatoid arthritis	4.89 (1.60, 8.19)	0.07	0.004
Presence of idiopathic inflammatory myositis	3.84 (0.60, 7.09)	0.06	0.020

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