

Impact of coping strategies on patient and physician perceptions of disease severity and disability in systemic sclerosis

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Running title: Coping Strategies in SSc

Abstract.

Objective. Systemic sclerosis (SSc) results in impaired function, disability, and reduced health-related quality of life (HRQL). We investigated the impact of coping strategies on the patient global assessment of health (PtGA) and Health Assessment Questionnaire Disability Index (HAQ-DI), after controlling for clinical characteristics and disease activity. We also explored the relationship between coping strategies and correlation between PtGA and physician global health assessments (PhysGA) in SSc.

Methods. We undertook post-hoc analyses using baseline data obtained from the Raynaud's Symptom Study (RSS). The PtGA, coping strategies questionnaire (CSQ), pain catastrophizing scale (PCS), and scleroderma health assessment questionnaires (SHAQ) were collected alongside the PhysGA, clinical characteristics and patient demographics. Multivariable linear regression models and correlations were used to evaluate the relationship between coping strategies with the PtGA, HAQ-DI, and PhysGA, respectively.

Results. Of the 107 SSc patients enrolled to the RSS, there was sufficient data available for analysis of 91 participants. The mean (SD) PtGA was 40/100 (27) and the mean HAQ-DI was 0.87/3.0 (0.73). After controlling for clinical and patient demographics, pain catastrophizing and maladaptive coping skills were significantly associated with the PtGA and HAQ-DI scores ($p < 0.05$ for both), but not the PhysGA.

Conclusions. The impact of coping strategies on PtGA and HAQ-DI (but not the PhysGA in SSc) could influence the result of composite measures incorporating these outcome measures. Interventions to improve patient coping skills may support increased resilience and improve patient-perceived functional status and PtGA in SSc.

Introduction.

Systemic sclerosis (SSc) is a complex rheumatologic disease characterized by vascular dysfunction, immunological derangements and fibrosis (1). SSc is associated with increased morbidity, including chronic pain, which has significant impacts on both function and health-related quality of life (HRQL) (2,3). Previous analyses suggest that the patient global assessment of overall health (PtGA) is greatly influenced by the degree of pain, skin fibrosis (skin scores), and breathlessness (4). Furthermore, survey and longitudinal evaluations of patients with SSc suggest that perceptions of physical health greatly impacts HRQL and pain trajectories over time (5). The PtGA, Health Assessment Questionnaire-Disability Index and physician global assessment (PhysGA) are important components of the American College of Rheumatology Composite Response Index in diffuse cutaneous SSc (ACR CRISS) (6). Previous reports have identified discordance between the PtGA and PhysGA in SSc (ICC 0.377) but the reasons for this have yet to be elucidated (7). Similar discordance has been observed in other rheumatic disease populations such as Rheumatoid Arthritis (RA) (8) and Systemic Lupus Erythematosus (SLE) (9).

Coping is defined as a management strategy for distress which may be behavioral, affective, or cognitive in nature (10). In general, coping strategies include active approaches, or behaviors used to control pain or function, and passive approaches, or behaviors that involve withdrawing and surrendering control over pain. Active coping strategies include coping self-statements, diverting attention, ignoring pain sensations, increasing activity level, and reinterpreting pain sensations (11). Passive coping strategies include praying/hoping, and catastrophizing.

Generally, active coping strategies have been associated with positive adaptation with respect to pain including decreased depression and better psychological adjustment (12). Passive coping

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strategies are typically characterized as maladaptive and associated with increased pain and negative emotion. Specifically, pain catastrophizing is a cognitive response to pain that leads to magnification of pain sensations and has been associated with worse pain-related outcomes including anxiety and depression (13). We sought to further evaluate the influence of coping strategies on the PtGA and Health Assessment Questionnaire Disability Index (HAQ-DI) in SSc having hypothesized that maladaptive coping strategies would be associated with worse ratings on the PtGA and HAQ-DI. We also explored the impact of coping strategies on the correlation between the PtGA and PhysGA, to better understand the influence of factors such as coping on discordance between physician and patient assessment of global health severity in SSc.

Methods.

We undertook post-hoc analysis using baseline data from the previously reported Raynaud Symptom Study (RSS): a multicenter study designed to assess the features and determinants of Raynaud's phenomenon (RP) symptoms in SSc. The RSS was an exploratory research study comprising a convenience sample of SSc patients attending routine clinic reviews in 2 centers. Methods for data collection and survey have been described elsewhere (14,15). Briefly, patients fulfilling the 2013 American College of Rheumatology/European League Against Rheumatism classification criteria for SSc were enrolled at routine clinical care visits from specialty care clinics in Bath, UK, and Salt Lake City (SLC), USA, between April 2015 and January 2017. The study received ethical approval at each site (Bath REC 15/LO/1521 and Utah Institutional Review Board #80665) and participants provided informed written consent (including for post-hoc data analyses). Patient demographics and clinical characteristics were collected including

age, gender, ethnicity, disease duration based on time since first non-RP symptom, smoking history, clinical phenotype, SSc autoantibody status, gastroesophageal reflux disease symptoms, puffy fingers, sclerodactyly, digital ulcers (DU), digital pitting, telangiectasia, pulmonary arterial hypertension, and interstitial lung disease. Relevant patient comorbidities and medications were also collected, alongside local weather data (which may affect SSc symptoms).

Self-administered Questionnaires:

Clinicians completed a 100-mm VAS PhysGA of disease severity (“In the past week, how would you rate this patient’s overall health?”). Patients completed the Scleroderma Health Assessment Questionnaire [SHAQ, comprising the HAQ-DI and SSc-specific 150-mm VAS subscales], the Coping Strategies Questionnaire (CSQ), the Pain Catastrophizing Scale (PCS), and separate 100-mm VAS assessments for PtGA of disease severity (“In the past week, how would you rate your overall health?”). Note, higher scores indicate worse global assessments.

The CSQ is scored using a 7-point numerical rating scale (0–6, ranging from “never do” to “always do that”) and evaluates the following domains: diverting attention, reinterpreting pain sensations, catastrophizing, ignoring sensations, praying and hoping, coping self-statements, and increasing behavioral activities (16).

The PCS instrument is scored using a 5-point NRS (0–4, ranging from “not at all” to “all the time”) and a composite score (0–52) is calculated (17). Higher scores indicate more of the trait being measured. Sub-domains of the PCS include rumination, magnification, and helplessness.

Statistical analysis.

Descriptive statistics were calculated for demographic and SSc characteristics. Multivariable regression models were used to evaluate predictors of the PtGA, the HAQ-DI, and the PhysGA. Regressions were constructed separately for the PtGA and HAQ-DI using the best combination of patient characteristics and physician scores according to adjusted R² (18). This criterion was used to balance the variability of PtGA and HAQ-DI explained prior to accounting for coping against model complexity: a predictor is included in the model only if it increases fit more than would be expected by chance. The core model for the PtGA consisted of the following variables: age, gender, telangiectasia, and the physician's overall health VAS. The core model for the HAQ-DI consisted of the following variables: gender, clinical diagnosis (limited vs diffuse cutaneous involvement), disease duration, digital ulcers, pulmonary arterial hypertension, and the physician's overall health VAS. Patients were dichotomized for each domain according to low coping strategies (score 0–2) and high coping strategies (score 3–6), as well as the PCS domains and composite score were each added to the core model one at a time to discern effects on the PtGA and HAQ-DI, respectively, controlling for the variables in the core models.

For both the PtGA and HAQ-DI, a sensitivity analysis using an expanded core model considering all non-coping patient-reported outcomes (PROs) was performed. For the PtGA, the expanded model included additional baseline patient characteristics and PROs including presence of digital ulcers, patient VAS-digital ulcers, SHAQ-pain, SHAQ-breathing, SHAQ-digital ulcers, SHAQ-patient global assessment of health, mean daily RCS, mean daily total duration of RP attacks, and mean daily number of RP attacks. Similarly, for the HAQ-DI, the expanded core model for sensitivity analysis included interstitial lung disease, physician VAS-

digital ulcers, patient VAS-digital ulcers, SHAQ-pain, SHAQ-breathing, SHAQ-digital ulcers, SHAQ-patient global assessment of health, mean daily RCS, and mean daily number of attacks. Concordance between PtGA and PhysGA was assessed using intraclass correlation coefficients (ICC). The impact of coping strategies on discordance between PtGA and PhysGA was assessed by comparing CSQ scores for patients whose PtGA and PhysGA differed by ≥ 20 points (in each direction). Discordance was defined by a difference between the PtGA and PhysGA ≥ 20 points based on previous literature in SSc and RA (7,19).

Results.

Study population

The RSS enrolled 107 patients with SSc (57 patients in Bath, UK; 50 patients from Salt Lake City, USA). Sufficient data was available for 91 patients who had completed the CSQ or PCS. The excluded patients were mostly from Bath (15 vs 1) but otherwise had similar distributions for the characteristics and physician scores used in the multivariate regression analysis. Patients were mostly female (88%), white (93%), never smokers (67%), with a mean (SD) age of 61 (12) years and mean (SD) disease duration of 10 (9) years. The majority of patients had limited cutaneous SSc (85%) with a smaller subset having diffuse cutaneous disease (15%). Across clinical care sites, patients had similar demographic and clinical characteristics including history of digital ulcers, sclerodactyly, telangiectasias, pulmonary arterial hypertension, interstitial lung disease, and antibody profile status. A full description of patient characteristics has been reported previously (14).

Across the whole cohort, the mean (SD) PtGA was 40 (27), the mean PhysGA was 32 (25) and the mean (SD) HAQ-DI was 0.87 (0.73), representing mild to moderate disability.

Impact of coping on patient global assessment of disease severity

In our multivariable analysis, several coping strategies were significantly associated with the PtGA after controlling for patient demographic and clinical characteristics in our core model (**Table 1**). Specifically, patients who engaged in prayer or catastrophizing (as identified by the CSQ) and rumination, magnification, or helplessness (as measured by the PCS) had higher PtGA scores on average. In a limited sensitivity analysis, even when other clinical characteristics and patient-reported outcomes were included (digital ulcers, Raynaud's phenomenon number and duration of attacks, and components of the SHAQ), PCS domains (rumination, magnification, helplessness) and PCS total score remained significantly positively associated with the PtGA, indicating that the observed link between PCS and PtGA is robust to the choice of non-coping features included in the regression model.

Impact of coping on self-administered patient assessment of disability

In multivariable analysis, multiple coping styles were also associated with the HAQ-DI, even after controlling for gender, research site, disease duration, pulmonary arterial hypertension, clinical diagnosis (limited vs diffuse), digital ulcers, and physician digital ulcer VAS (**Table 1**). Specifically, higher HAQ-DI scores were associated with patients who employed diversion, reinterpreting, catastrophizing, praying, coping self-statements, and increasing behavior activities (distraction). Consistent with sensitivity analyses for the PtGA, PCS domains (rumination, magnification, helplessness) and the PCS total score remained significantly associated with the HAQ-DI when other clinical characteristics and PROs were included. This indicates that the

association between HAQ-DI and PCS total is also robust to the choice of non-coping features included in the regression model.

Relationship between PtGA and PhysGA

There was weak/moderate positive correlation between the PhysGA and PtGA (Spearman $r=0.39$, $p<0.001$, Figure 1). Stronger positive correlations were found between the PtGA and PCS (total) ($r=0.47$, $p<0.001$, Figure 1) and between the PCS (total) and the HAQ-DI ($r=0.42$, $p<0.001$, Figure 1). The PhysGA, meanwhile, had a weak positive correlation with HAQ-DI ($r=0.24$, $p=0.03$) (**Figure 1**) and the PCS ($r=0.06$, $p=0.60$). The overall concordance between the PhysGA and PtGA was low (ICC 0.387). Patients whose PtGA was ≥ 20 units higher than PhysGA ($n=33$, 36%) had significantly higher CSQ scores than patients whose PtGA was ≥ 20 lower than PhysGA ($n=15$, 16%), particularly in terms of catastrophizing (18 vs 2 patients in high catastrophizing category, $p=0.011$). The same primary analysis strategy with PhysGA as the response in the multivariable model was performed, in which none of the PCS domains were associated with PhysGA (**Table 1**). The strongest factors influencing PhysGA were age, gender, pulmonary arterial hypertension, interstitial lung disease, telangiectasia, and physician RP VAS.

Discussion.

The findings of this multi-site, cross-sectional study of patients with SSc indicate an important association between coping strategies and patient perceptions of disability and overall health status. Patient-perceived disease severity may not be dependent on SSc disease severity alone and influenced by other important (and potentially modifiable) factors such as coping skills. This study builds upon an earlier analysis in which we reported a strong relationship between

catastrophizing (according to both CSQ and PCS) and SSc-RP symptom severity (14). Pain catastrophizing has similarly been associated with patient-reported severity of pain, disability, and poor treatment outcomes in other rheumatic diseases (20,21). A limited number of studies have examined coping strategies utilized by people living with SSc. Qualitative studies have indicated that patients with SSc utilize similar coping strategies as patients with other rheumatic disease but lack access to support services that could help improve self-esteem, resilience and self-efficacy (22,23). As expected, we found that passive coping strategies (catastrophizing, praying) are most strongly associated with the PtGA. However, 'active' coping strategies (generally labeled as adaptive), were more strongly associated with patient-reported assessment of functional impairment measured using the HAQ-DI. Additional work is required to better understand the role of specific coping strategies (and interventions that might favorably modify these) on patient perceptions of global health and functional impairment.

Our findings may, in part, explain the poor concordance between the PtGA and PhysGA reported previously (7), and replicated in this work. Our analysis indicates that coping strategies, as might have been expected, do not generally influence PhysGA; which is more strongly influenced by disease related factors such as age and organ-specific manifestations of SSc. In contrast, both the PtGA and HAQ-DI were strongly influenced by catastrophizing habits (rumination, magnification, helplessness) and each had a stronger positive correlation with the PCS (total) than the PhysGA, a surrogate for disease activity. Our findings necessitate the need for larger and longitudinal study; especially as coping strategies could influence the ACR Composite Response Index for Clinical Trials in Systemic Sclerosis (CRISS) which incorporates both the PtGA, HAQ-DI and PhysGA (6). The ACR CRISS does, however, focus on change of

these patient-reported parameters over time which may be less influenced by coping and further longitudinal studies are required to evaluate the impact of coping strategies on PRO instrument change following intervention. Coping and emotional functional PROs should be considered as potentially relevant outcome measures to facilitate the design and interpretation of future SSc trials.

Given the associations we have identified between coping and patient perceptions of global disease activity and disability, we would support previous calls for patient-centered approaches to enhance self-esteem, resilience and self-efficacy to improve health and quality of life outcomes in SSc (22). These interventions have been studied in arthritis and other chronic disease patient populations including cognitive behavioral therapy (CBT), mindfulness, and other mixed method self-management approaches. Evidence is greatly lacking regarding utility of behavioral change interventions designed to modify pain catastrophizing and maladaptive coping behaviors in SSc. However, SSc focus group studies endorse patient interest for increased access to support groups and intervention (24).

This study benefits from being a relatively large study of carefully phenotyped patients from two tertiary clinical care sites, but larger studies are required to explore these associations across larger cohorts of patients. However, the patients included in this study had mild to moderate disease according to PhysGA and conclusions may not be generalizable to those with severe disease. Furthermore, an accurate measurement of SSc disease severity, such as the Medsger Severity Scale was not available to guide interpretation. While the utilization of baseline data from a study designed to evaluate impacts of RP may have resulted in selection bias, almost all

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patients with SSc have RP thus this is thought to be a representative sample of the general population. The cross-sectional approach also limits our ability to predict long-term outcomes and the natural evolution of coping strategies in established disease. This study also included predominantly white individuals and may not be generalizable to other races and ethnicities who may differ in coping strategies based on culture. Furthermore, additional study is needed to determine whether non-pharmacologic approaches (i.e., behavioral health interventions) may be utilized in a multidisciplinary fashion to improve patient-perceived global disease severity and disability in SSc.

Conclusions.

Maladaptive coping strategies, particularly catastrophizing, are associated with worse overall patient-perceived disability and PtGA after controlling for patient demographics, clinical phenotype and physician assessment of global disease severity. Coping strategies may influence the outcome of composite measures of disease severity such as the ACR CRISS. Further large-scale study and longitudinal assessment is warranted to better understand the role of coping in long-term outcomes in SSc.

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Table 1. Effect of coping skills and catastrophizing on PtGA, HAQ-DI, and PhysGA.

	PtGA		HAQ-DI		PhysGA	
	Multivariable Model*		Multivariable Model**		Multivariable Model***	
	β (SE)	p	β (SE)	p	β (SE)	p
CSQ						
Diversion	9.63 (5.73)	0.097	0.43 (0.16)	0.011	4.24 (4.88)	0.388
Reinterpreting	8.79 (5.37)	0.106	0.33 (0.16)	0.038	1.15 (4.65)	0.805
Catastrophizing	17.22 (5.51)	0.003	0.51 (0.16)	0.002	-2.19 (5.07)	0.667
Ignoring	-6.51 (5.42)	0.234	-0.22 (0.16)	0.176	-3.36 (4.68)	0.476
Praying	16.92 (5.27)	0.002	0.41 (0.16)	0.012	7.44 (4.68)	0.116
Coping	-1.70 (7.28)	0.816	0.50 (0.20)	0.012	8.99 (5.67)	0.117
Increased Behavior	2.77 (6.47)	0.670	0.43 (0.18)	0.022	4.89 (5.09)	0.340
PCS						
Total	0.90 (0.23)	<0.01	0.02 (0.006)	<0.01	0.22 (0.22)	0.326
Rumination	2.16 (0.62)	<0.01	0.04 (0.018)	0.030	0.03 (0.56)	0.954
Magnification	3.19 (0.95)	<0.01	0.07 (0.027)	0.016	1.16 (0.91)	0.204
Helplessness	2.14 (0.50)	<0.01	0.05 (0.014)	<0.01	0.90 (0.45)	0.050

*After adjusting for core model= age, gender, telangiectasia, physician's overall health VAS.

**After adjusting for core model= gender, disease duration, pulmonary hypertension, clinical diagnosis (limited vs diffuse), digital ulcers, and physician digital ulcer VAS

*** After adjusting for core model = age, gender, pulmonary hypertension, interstitial lung disease, telangiectasia, physician Raynaud's VAS

Figure 1. Correlations between a) PtGA and PhysGA, b) PtGA and PCS (total), c) HAQ-DI and PhysGA, and d) HAQ-DI vs PCS (total).

