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Discordance between Patient and Physician Assessments of Disease Severity in Systemic Sclerosis

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Abstract

Background To describe the magnitude and correlates of discordance between patient and physician assessments of disease severity in patients with SSc.

Methods Subjects were patients enrolled in the Canadian Scleroderma Research Group Registry. The outcomes of interest were patient and physician global assessments of disease severity (scales ranging from 0-10). Predictors of disease severity represented the spectrum of disease in SSc (skin involvement; severity of Raynaud's phenomenon, shortness of breath, gastrointestinal symptoms and pain; number of fingertip ulcers, and tender and swollen joints; creatinine; and fatigue). The results of the analysis were validated in an independent sample of patients from the United States (US). **Results** Patients perceived greater disease severity than physicians (mean difference 0.78 ± 2.65). The agreement between patient and physician assessments of disease severity was, at best, modest (intraclass correlation 0.3774; weighted Kappa 0.3771). Although both patients and physicians were influenced by skin scores, breathlessness and pain, the relative importance of these predictors differed. Patients were also influenced by other subjective symptoms whereas physicians were also influenced by disease duration and creatinine. The predictors explained 56% of the deviance in the patient global assessments and 29% in the physician assessments. These findings were confirmed in the US dataset.

Conclusions Patients and physicians rate SSc disease severity differently in magnitude and are influenced by different factors. Patient and physician assessed measures of severity should be considered as complementary and used together in future studies of SSc.

Introduction

Discordance of assessments between patients and physicians occurs when patients and physicians assign different values to a health trait¹. Discordance between patient and physician assessments of disease activity has been described in several rheumatic diseases, including rheumatoid arthritis^{2, 3}, systemic lupus erythematosus^{1, 4, 5}, and ankylosing spondylitis⁶. In those studies, patient assessments were more strongly associated with subjective symptoms, such as pain, psychological well-being and function, when rating disease activity whereas physician assessments were more strongly associated with objective findings, including laboratory tests. Discordance has the potential to negatively impact patient care, in so far as patients may fail to comply with medical instructions if they are poorly informed of their condition or if physicians fail to appreciate the full impact of disease on their patients.

Little is known on the presence and magnitude of possible discordance in the assessment of disease activity in systemic sclerosis (SSc) in part probably because measuring disease activity in SSc is particularly difficult. Unlike systemic lupus erythematosus and rheumatoid arthritis, SSc is not characterized by episodes of acute inflammation, manifested by synovitis, pleuritis, dermatitis and nephritis, that can be easily differentiated from quiescent phases. Instead, the clinical features of SSc are attributable to vascular and connective tissue fibrosis that is more difficult to appreciate and

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quantify than inflammation and, when it becomes measurable, has often progressed to permanent damage. Many patients, especially those with limited skin involvement, have an indolent course without clear signs of inflammation. Furthermore, elevated acute phase proteins are inconsistently associated with early SSc, leading some to argue that patients with SSc may have an impaired acute phase response^{7, 8}.

Given the difficulty of measuring disease activity in SSc and of separating it from disease damage, disease severity has been proposed as an appropriate measure of disease status in SSc. Indeed, Medsger defines disease severity in SSc as the total effect of disease on organ function at a given point in time, including both reversible (activity) and irreversible components (damage)⁹ and, given the difficulties in defining disease activity, this is likely to be a better measure of disease status and possible discordance in SSc.

Thus, we undertook this study first, to identify the extent to which patient and physician assessments of disease severity differed and second, to identify and compare the predictors of patient and physician assessments of disease severity in patients with SSc.

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Methods

Design. Cross-sectional study of a Canadian sample of SSc patients and confirmation of the results using a sample of SSc patients from the United States (US).

Study subjects The Canadian subjects were patients enrolled in the Canadian Scleroderma Research Group Registry. Patients in this Registry are recruited from the practices of rheumatologists across Canada. They must have a diagnosis of SSc made by the referring rheumatologist, be \geq 18 years of age, be fluent in English or French, and likely to be compliant with study procedures and visits. The patients included in this study were those whose baseline visit was between September 2004 and 2008. The US patients were recruited from the University of Michigan Scleroderma Program between December 2005 and April 2006. A total of 105 sequential ambulatory SSc patients were recruited and consented to participate in a study on hand functioning. Four subjects did not complete the study.

Outcome Measures The patient and physician global assessments of disease severity in the Canadian patients were assessed using numerical rating scales (NRS) ranging from 0-10. The NRS scale is simple to complete and score and has been shown to be as reliable and responsive as visual analogue scales (VAS) to measure disease activity and function in ankylosing spondylitis¹⁰ and more reliable to assess pain in patients with rheumatoid arthritis¹¹. Physicians were asked to "rate the patient's overall health for the past week" and the NRS was anchored by the descriptors "no disease" and "very severe disease". Patients were ask to "rate your disease in the past week" and the NRS was anchored by "no disease" and "very severe limitation". The patient and physician global assessments of disease severity in the US patients were assessed using a VAS ranging from 0-100 mm, anchored by the descriptors "no severity" and "extremely severe". The scores on the VAS of 0-100 were divided by 10 to be comparable to the NRS ratings ranging from 0-10. Although the wording of the anchors on the global assessments differed slightly, the scores ranging from 0-10 were assumed to be equivalent.

Predictor variables Potential predictors of disease severity were chosen to represent the spectrum of disease in SSc, and included severity of Raynaud's phenomenon, skin involvement, fingertip ulcers, shortness of breath, joint symptoms, gastrointestinal symptoms, kidney involvement, pain and fatigue. In both samples, the methods for data collection were similar. The extent of skin involvement was recorded using the modified Rodnan skin score. Similarly, the number of fingertip ulcers and a simplified 28 swollen and tender joint count¹² were recorded by physical examination by a well-trained

health professional using standardized definitions. Creatinine was documented by laboratory testing.

Data on Raynaud's phenomenon, gastrointestinal symptoms, shortness of breath and pain was assessed using a self-report measure, the Scleroderma-Health Assessment Questionnaire (S-HAQ)¹³. The S-HAQ consists of the Disability Index of the HAQ (HAQ-DI) and items to measure symptoms specific for SSc using VAS scales. The HAQ-DI is a self-administered measure intended to assess functional ability in arthritis¹⁴. The disease specific questions in the S-HAQ relate to the severity of various symptoms, including Raynaud's phenomenon, gastrointestinal symptoms, shortness of breath and pain in the past week. Each item is anchored by the adjectives "does not interfere" and "very severe limitation" and scored separately. The Canadian patients answered the disease specific questions on the S-HAQ using an 11-point NRS, whereas a 0-100 mm VAS was used by the US patients.

Finally, fatigue was measured using the Vitality subscale of the Medical Outcomes Study Short Form 36 (SF 36)^{15, 16}. The SF-36 Vitality subscale includes 4 Likert items with 5 response options each (*all of the time* to *none of the time*) that assess patients' level of fatigue during the previous 4 weeks. Scores are normalized with a mean of 50 and standard deviation of 10. Scores below 50 represent worse and above 50 less fatigue. The SF-36 Vitality subscale has been used to measure fatigue in general population samples and in patients with medical illness and injury. A recent systematic review concluded that the SF-36 Vitality subscale has good evidence for validity, reliability, sensitivity to change, and feasibility in rheumatoid arthritis¹⁷.

Statistical Analysis The initial analyses were done using the Canadian data. The standard measure of agreement for quantitative measures is the intra-class correlation coefficient (ICC) and for ordered categorical variables the weighted Kappa statistic. Using the disease severity scores ranging from 0-10 in turn as continuous or ordinal variables, we calculated the ICC and the weighted Kappa statistic. We also fit a linear mixed model that isolated heterogeneity due to the physicians from overall disagreement to determine whether physician heterogeneity was responsible for disagreement between patient and physician assessments.

We undertook subsequent analyses to identify the predictors of patient and physician global assessments of disease severity, separately, using generalized linear models (in particular, normal, Poisson, and negative binomial regression models). We fit three separate sets of models for each of the patient and physician global assessments of disease severity: models that included all aspects of severity, models that included only the physicianrecorded aspects of severity, and models that included only the patientreported aspects of severity. In all regression models, we adjusted for demographic variables (age, gender, ethnicity, education) as well as disease duration. In multivariate analyses using generalized linear models, we found that a negative binomial regression model fit the data well for four of the six regression models. We observed under-dispersion rather than over-dispersion in the two other models (both of which used the patient reported symptom variables), so the results between the negative binomial and Poisson models yielded very similar results. Model fit was assessed using percentage deviance explained, which is analogous to R^2 in standard linear regression models. Finally, since we identified differences in predictors of patient and physician global assessments of disease severity, we undertook a regression analysis to identify the predictors of the differences. We used normal linear regression for the difference model to predict the difference between patient and physician severity scores, as there was no reason (using either model selection criteria or diagnostics) that suggested a normal assumption was inappropriate.

Lastly, we sought to confirm our findings by running the results of our our models in the US data. We used the estimated regression coefficients from the Canadian data to calculate predicted physician and patient severity assessments for the US data and estimated the association between the predicted assessments and the observed assessments using simple linear regression. At the time of analysis, the CSRG had 936 patients entered in their registry, of which 742 had complete data for the variables of interest in this study. The US sample had 101 subjects, of whom 61 had complete data. Data between patients included and excluded from the analyses were compared and there were no systematic differences. Therefore, only patients with complete data were included in the analyses. All statistical analyses were performed with SPSS v. 13 and the R statistical package¹⁸.

Ethical considerations Each patient provided informed written consent to participate in the data collection process and ethics committee approval for this study was obtained at each site.

Role of the funding sources The 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.

Results

There were 803 patients included in this study, of which 742 were Canadian and 61 from the US (Table 1). In the Canadian sample, 87% were women, mean age was 55.5 (\pm 12.4) years, and mean disease duration since the onset of the first non-Raynaud's disease manifestation was 10.7 (+9.0)years. In the US sample, 86% were women, mean age was $51.4 (\pm 11.4)$ years, and mean disease duration since the onset of the first non-Raynaud's disease manifestation was 7.5 (\pm 8.4) years. On a scale ranging from 0 to 10, with 0 being the lowest and 10 being the greatest disease severity, the mean patient and physician global assessments of disease severity were 3.63 (+ 2.54) and 2.85 (\pm 2.27), respectively, in the Canadian sample and 4.25 (\pm 2.59) and 2.04 (\pm 1.78), respectively, in the US sample. The mean difference between patient and physician assessment was 0.78 (\pm 2.65) in the Canadian sample and 2.21 (\pm 2.65) in the US sample. The positive values suggest that, on average, patients perceived greater disease severity than physicians. Of note, the difference in patient and physician ratings of disease severity in diffuse patients was 0.53 (95% confidence interval (CI) 0.23, 0.84) and in limited patients 0.92 (95% CI 0.66, 1.17). This was not statistically significant.

Agreement between patient and physician global assessments of disease severity in the Canadian data Using the disease severity scores ranging from 0-10 either as continuous or ordinal variables, we observed very similar ICC and weighted Kappa statistics (0.3774 and 0.3771, respectively). The values for these statistics indicate at best only fair agreement between patient and physician assessments of disease severity. We observed a slight difference in the extent of agreement in the two disease subsets (ICC of 0.29 (95% CI 0.19, 0.39) in the limited subset and ICC of 0.41 (95% CI 0.31, 0.50) in the diffuse subset), although this was not statistical significance.

A linear mixed model was used to assess the extent to which interphysician variability was responsible for the lack of agreement between the patient and physician severity scores. We did observe statistically significant variability between physicians in their assessments (Bayesian Iinformation Criterion (BIC) of 3202 for a model that accounted for physician heterogeneity vs. 3215 for a model that did not). A difference of 6-10 in the value of the BIC indicates strong evidence against the null hypothesis and a difference of more than 10 indicates very strong evidence¹⁹. Thus, a difference of 13 suggests very strong evidence against the model assuming no between physician heterogeneity in assessments of disease severity. Nevertheless, only approximately 5% of the overall variability in patient severity scores could be explained by the differences amongst the physicians themselves. Thus, based on these analyses, we concluded that agreement between patient and physician assessments of disease severity was, at best, modest. Inter-physician variability in assessments accounted for only a small part of the differences in assessments.

Predictors of patient and physician global assessments of disease severity in the Canadian sample

We identified similarities and differences in the predictors of patient and physician global assessments of disease severity (Table 2). The odds ratios (OR) reported in Table 2 represent the relative increase in the response (ie. the patient or physician assessments of severity) for a one unit increase in the covariate of interest (eg. skin score, shortness of breath, etc.). Thus, although skin scores, shortness of breath and pain were significant predictors of *both* patient and physician global assessments of disease severity when all covariates were included in the models, their relative impacts on physicians and patients differed. Thus, an increase of 1 unit in skin score was associated with approximately a 3% increase in the physician assessment of severity, controlling for all other variables (ie. an approximate 15% increase for a 5 unit increase in skin score). In contrast, we estimated only a corresponding 0.9% increase in patient severity assessment for a one unit increase in skin score (again controlling for all other variables) or a 4.5% increase in mean patient assessment for a 5 unit increase in skin score. The OR estimates for

shortness of breath were fairly similar in the models predicting patient (1.062) and physician (1.094) assessments of severity separately. However, pain had a larger effect in the model predicting patient assessed severity (1.121), compared to its effect in the model predicting physician assessed severity (1.032).

In addition, significant predictors of patient assessments included severity of Raynaud's, gastrointestinal symptoms, and fatigue. The coefficient less than 1 for fatigue reflects the fact that for the measurement of fatigue, lower scores represent worse fatigue, whereas for the global assessment, lower scores represent less severe disease. In turn, other significant predictors of physician assessments included disease duration, with early disease being considered worse, and creatinine. The regression models using all patient reported and clinical covariates explained 56% of the deviance in the patient global assessments and 29% in the physician assessments, respectively. As one would expect, the patient reported variables by themselves explained much more deviance in the patient assessment than the physician assessment (54% vs. 14%) and the clinical variables by themselves explained more deviance in the physician assessment than the patient assessment (18% vs. 5%). We also noted (but do not show) a significant interaction between disease duration and skin score in the models for the physician assessments (p value < 0.001) that indicated that the amount by which the physician score

would increase for high skin scores would be smaller for patients with longer disease duration.

Finally, given that we found differences in the predictors of patient and physician assessed severity, we regressed the *difference between the patient and physician assessments* in order to determine what was most associated with the discordance between the two assessments (Table 3). Pain, gastrointestinal symptoms, Raynaud's and fatigue were associated with significantly higher values for the difference (ie. contributed more to the patient assessment than the physician assessment). Increased skin score and creatinine were associated with significantly lower values for the difference (ie. contributed more to the physician assessment than the patient assessment). Furthermore, we again found a significant interaction between skin score and duration in this model that suggested that the longer the disease duration, the less an increased skin score would be associated with the difference (data not shown).

Confirmation of the models in the US sample

To confirm our findings, we used the regression coefficients obtained from the Canadian data to predict physician assessments of severity, patient assessments of severity, and the difference between patient and physician assessments in the US patients. In these analyses, we allowed for the US and Canadian data to have different overall means, so as to examine the relationship of severity with the covariates, rather than the overall population mean. We found that the regression coefficients derived from the Canadian data explained 15.7% of the variability in the physician global assessments in the US data. This can be compared to an estimated prediction R^2 of 25.1% in the Canadian data. Similarly, regression coefficients from the Canadian data explained 43.4% of the variability in the patient assessment scores in the US data, compared to a prediction R^2 of 54.8% on the Canadian patient assessments. Finally, the Canadian model for the differences in assessments explained 22.3% of the variability in the difference in assessments in the US data, compared to a prediction R^2 of 33.3% for the Canadian data. Thus, prediction in the US data using the Canadian models was reasonably good.

We also investigated whether individual variables had a different relationship with disease severity in the Canadian and US samples. We found no strong evidence that the relationship between any of the covariates and the patient or physician assessments depended on the sample (data not shown).

Discussion

In this study, we found some similarities but also important differences in how patients and physicians rate disease severity in SSc. On average, patients rated disease severity worse than physicians. Patient and physician severity ratings were both associated with physician-rated skin scores and patient-reported shortness of breath and pain in their assessments of severity, although skin was more strongly associated for physicians than patients and pain was a more robust correlate for patients than physicians. Patient severity assessments were also significantly influenced by selfreported estimates of the severity of Raynaud's phenomenon, gastrointestinal symptoms, and fatigue, whereas physician global severity ratings were influenced by disease duration and creatinine.

This report demonstrated that, using global assessments, patients and physicians rate disease severity differently in magnitude and are influenced by different factors. The implications of our findings are twofold. First, our findings suggest that traditional biomedical assessments of disease status in SSc (eg. physician assessments of skin involvement or lab tests such as creatinine) may be supplemented by patient-derived information. In other words, patient-reported severity allows for more aspects of the disease to be captured than physician-reported assessments. In fact, it is striking that the predictors of importance for patients but not physicians were indeed in relation to symptoms for which good outcome measures in SSc are currently lacking (in particular gastrointestinal symptoms and fatigue) or where patient reports are the only means of obtaining the information (in particular Raynaud's).

Second, in the absence of a gold standard to measure disease severity in SSc, both patient and physician global assessments of disease severity could be used together, to better approximate "true" disease severity. Indeed, in a study of Raynaud's phenomenon in patients with SSc, both physician and patient assessments of Raynaud's phenomenon activity were found to be valid and reliable and the authors recommended that both be included in the core set of measures for use in future clinical trials in this area²⁰. Similarly, although definitive validation of patient and physician global assessments of disease severity in SSc has yet to be done, our data suggest that the two measures may provide complementary data and both should be considered as outcome measures in this highly heterogeneous disease.

There are limitations that should be considered in interpreting the results of this study. First, patients in the Canadian Scleroderma Research Group registry are a convenience sample of SSc patients. Their median disease duration since the onset of non-Raynaud's symptoms was 10 years, suggesting a sample of patients with generally stable disease. Moreover, patients with very severe SSc that were too sick to participate or that died earlier in their disease course, were not included in the present study. This may have resulted in an over-representation of healthier patients in our SSc sample (survival cohort), and results may therefore not be generalizable to the full spectrum of SSc. Despite these limitations, the demographic and clinical characteristics of Canadian Scleroderma Research Group Registry patients in this study were consistent with other outpatient SSc samples that have been reported in the research literature²¹.

Second, it is possible that the strong association between patient-assessed severity and symptoms (e.g., pain, fatigue, severity of Raynaud's) occurred because both outcome and predictors were self-reported and the relationship reflects, to some degree, characteristics of the patient that influence how distress is reported on self-report questionnaires²². As a result, the relationships between outcome and predictors may be overstated in the models for patientassessed severity reported in this study. On the other hand, there are currently no good substitutes for patient-reported symptoms such as pain, fatigue, and severity of Raynaud's, and this limitation is thus largely inevitable.

Finally, both samples of patients were composed of predominantly white, female SSc patients. Consequently, this limits the generalizability of our results in so far as SSc patients from other ethnic groups or men are concerned. The strength of our study lies in its large, multi-centre sample of Canadian patients and validation of the results in an independent sample of SSc patients.

In summary, we showed that patients and physicians rate SSc disease severity differently in magnitude and are influenced by different factors. Thus, patient and physician assessed measures of severity should be considered as complementary and should be used together in future studies of SSc.

				ubjects 64	
	Mean	SD	Mean	SD	
Age, years	55.48	12.39	51.44	11.37	
Disease duration, years	10.70	8.98	7.48	8.35	
Skin score (0-51)	10.69	9.62	8.20	7.27	
Raynaud's (0-10)	2.83	2.87	4.11	3.00	
Shortness of breath (0-10)	2.04	2.60	2.32	2.77	
Gastrointestinal symptoms (0-10)	1.80	2.60	1.87	2.52	
Pain (0-10)	3.65	2.74	4.23	2.48	
Number of fingertip ulcers	1.28	2.46	0.55	1.47	
Swollen joint count (0-28)	0.65	2.32	0.30	1.34	
Tender joint count (0-28)	1.45	3.78	0.98	2.74	
Fatigue*	48.85	21.70	42.34	22.83	
Creatinine, umol/L	83.77	53.74	79.42	35.45	
Pt assessment of severity (0-10)	3.63	2.54	4.25	2.59	
MD assessment of severity (0-10)	2.85	2.27	2.04	1.78	
	Number	Percent	Number	Percent	
Females	642	86.50%	55	85.94%	
Diffuse disease	299	40.30%	31	48.44%	
White	601	81.00%	58	90.62%	
Education > high school	355	47.84%	48	75.00%	

Table 1 Baseline characteristics of study subjects

PT – patient; MD - physician

*Fatigue was measured using the SF-36 Vitality subscale. Scores are normalized with a mean of 50 and standard deviation of 10. Scores below 50 represent worse and above 50 better quality of life.

Table 2 Negative binomial regression results to identify predictors of the physician (MD) and patient (Pt) global assessments of disease severity in the Canadian data. This table contains the estimated odds ratios with 95% confidence intervals for the six different models. Shaded cells indicate confidence intervals that do not include 1. Note that creatinine was transformed by taking the square root in order to improve model assumptions and decrease the influence of outlying points. Results are given as square root of creatinine.

	All covariates used		Only clinical covariates		Only patient reported	
	MD Assessment	Pt Assessment	MD Assessment	Pt Assessment	MD Assessment	Pt Assessment
Age	1.000 (0.997, 1.006)	1.006 (0.997, 1.004)	1.004 (0.992, 1.009)	0.999 (0.994, 1.004)	1.000 (0.995, 1.004)	1.000 (0.996, 1.003)
Female	1.027 (0.893, 1.184)	1.042 (0.931, 1.168)	0.974 (0.838, 1.134)	0.964 (0.822, 1.130)	0.903 (0.777, 1.051)	0.996 (0.893, 1.112)
White	0.962 (0.849, 1.092)	1.046 (0.947, 1.158)	0.971 (0.851, 1.109)	1.017 (0.887, 1.165)	0.995 (0.866, 1.145)	1.061 (0.961, 1.175)
Disease duration	<mark>0.993 (0.987, 0.999)</mark>	0.997 (0.992, 1.002)	0.995 (0.989, 1.001)	1.001 (0.994, 1.007)	<mark>0.986 (0.980, 0.992)</mark>	0.996 (0.991, 1.000)
> High school	1.025 (0.928, 1.132)	1.024 (0.946, 1.108)	0.995 (0.896, 1.106)	0.943 (0.846, 1.051)	0.992 (0.889, 1.107)	1.013 (0.937, 1.096)
Shortness of breath	1.094 (1.073, 1.116)	1.062 (1.046, 1.078)	XXX	XXX	1.082 (1.058, 1.106)	1.060 (1.044, 1.075)
Pain	1.032 (1.010, 1.055)	1.121 (1.101, 1.140)	XXX	XXX	1.045 (1.021 ,1.070)	1.123 (1.103, 1.142)
GI symptoms	0.987 (0.966, 1.008)	1.018 (1.002, 1.034)	XXX	XXX	0.990 (0.967, 1.014)	1.018 (1.003, 1.033)
Fatigue*	0.999 (0.997, 1.001)	<mark>0.994 (0.992, 0.996)</mark>	XXX	XXX	0.998 (0.995, 1.001)	<mark>0.994(0.992, 0.996)</mark>
Raynaud's	0.983 (0.964, 1.002)	1.028 (1.013, 1.042)	XXX	XXX	0.984 (0.963, 1.005)	1.028 (1.014, 1.043)
Skin score	1.030 (1.025, 1.035)	1.009 (1.005, 1.013)	1.030 (1.025, 1.035)	1.012 (1.006, 1.018)	XXX	XXX
Fingertip ulcers	1.009 (0.989, 1.028)	1.008 (0.991, 1.024)	1.009 (0.988, 1.030)	1.019 (0.996, 1.042)	XXX	XXX
Swollen joints	1.004 (0.980, 1.028)	1.010 (0.992, 1.028)	0.999 (0.973, 1.024)	0.998 (0.973, 1.024)	XXX	XXX
Tender joints	0.996 (0.982, 1.009)	0.993 (0.983, 1.003)	1.005 (0.990, 1.020)	1.023 (1.008, 1.039)	XXX	XXX
Creatinine	1.036 (1.011, 1.062)	1.012 (0.991, 1.032)	1.035 (1.008, 1.063)	1.008 (0.978, 1.039)	XXX	XXX
Deviance Explained	28.9%	55.9%	17.5%	4.6%	13.8%	54.3%

*The coefficient less than 1 for fatigue reflects the fact that for the measurement of fatigue *lower* scores represent worse fatigue.

Table 3 Linear regression results to identify the predictors of the difference between patient and physician global assessments of severity in the Canadian data. Shaded cells indicate confidence intervals that do not include 0. Note that creatinine was transformed by taking the square root in order to improve model assumptions and decrease the influence of outlying points on the results. Results are given in terms of the square root of creatinine.

	Estimated coefficient (95% CI)	p-value
Age	-0.003 (-0.017, 0.011)	0.63
Female	0.015 (0-0.483,0.453)	0.95
White	0.253 (-0.145, 0.652)	0.21
Duration	0.010 (-0.008, 0.029)	0.28
> High school	-0.043 (-0.360, 0.274)	0.79
Shortness of breath	0.007 (-0.062, 0.076)	0.85
Pain	0.327 (0.256, 0.399)	<0.0001
Gastrointestinal symptoms	0.136 (0.067, 0.206)	<mark><0.0005</mark>
Fatigue	-0.015 (-0.023, -0.006)	<0.001
Raynaud's	0.164 (0.100, 0.227)	<0.0001
Skin score	<mark>-0.069 (-0.86, -0.052)</mark>	<0.0001
Fingertip ulcers	0.000 (-0.068, 0.068)	0.99
Swollen joints	0.017 (-0.058, 0.092)	0.66
Tender joints	-0.015 (-0.062, 0.032)	0.52
Creatinine	-0.102 (-0.192, -0.013)	<mark>0.025</mark>
Deviance Explained	37.95%	

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