The relationship between changes in self-reported disability (measured by the Health Assessment Questionnaire – HAQ) in scleroderma and improvement of disease status in clinical practice

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ABSTRACT

Objectives. *To determine if a low Health Assessment Questionnaire Disability Index (HAQ-DI) score predicts subsequent improvement over the next one to two years in clinical practice and if a low HAQ is predictive of improvement in early, late, diffuse and limited SSc subsets.*

Methods. *HAQs collected at one site annually were used to determine serial relationships in low baseline HAQ and improvement in overall status over the following one to two years. Data were divided into early (≤3 years) and late, and then further into limited and diffuse SSc subgroups. We verified our results in the Canadian Scleroderma Research Group (CSRG) database.*

Results. *120 SSc patients had a baseline HAQ-DI of 0.97±0.07 (SEM). Low HAQs predicted improvement in overall HAQ at one and two years, but was not statistically significant in predicting physician improvement rating. However, improving HAQs were associated with improvement in physician assessment (better vs. same vs. worse) for overall SSc (p=0.005), early diffuse SSc (p=0.008), overall limited SSc (p=0.02) and late limited SSc (p=0.03) at 1 year (but not at 2 years). The relationship was similar for severity of disease where changes in damage were related to changes in HAQ only over the first year for all 4 subgroups.*

Conclusion. *The HAQ is a useful 'marker' of change in status in clinical practice, where an improved HAQ is associated with improved physician global assessment. The relationship is only helpful for an interval of one year. Low HAQ did not predict subsequent improvement by physician rating in SSc patients.*

Introduction

Scleroderma or systemic sclerosis is a rare connective tissue disease with no standardized treatment guidelines. Currently, most treatments target specific complications such as renal crisis, Raynaud's phenomenon (RP) and pulmonary hypertension (1). SSc is characterized by vascular damage, fibrosis and autoimmunity. It occurs in approximately 2/10,000 and is more common in women than men, often beginning in the 40s and 50s (2). The disease course is variable where some patients stabilize or improve and others can rapidly progress. In rapidly progressive diffuse SSc, the mortality rate is between 30-60% over the next 5 years (3). The two subtypes of SSc are limited and diffuse, defined by the amount of involvement in the skin. Patients with limited scleroderma have skin thickening distal to the elbows and knees but may also involve skin on the face and neck. In comparison, a patient with diffuse scleroderma will have both proximal and distal involvement (4). The mortality of the latter is increased due to increased internal organ involvement.

The HAQ is used to measure patient function and is a generic outcome measurement tool developed for use in rheumatologic diseases to measure the impact of disease on functional status (5). The HAQ consists of eight areas and is scored from 0 to 3; a HAQ of >1.0 is considered high. There is consensus in the literature that high HAQ scores are associated with increased morbidity and mortality in scleroderma (6, 7). There are known predictors of doing poorly in SSc such as rapidly progressive skin involvement, early severe internal organ involvement and high disability (8). The HAQ-DI was

one of the best predictors of survival in the Pittsburg database (8). Surprisingly, other than the absence of these signs, there are currently no adequate predictors of which patients with SSc will improve over time. Many trials examining improving scleroderma skin and overall disease modification have studied patients with diffuse scleroderma early after disease onset. Sultan et al performed an analysis where individual patient data from two randomized controlled trials were combined (9). These data showed that the best predictor of improvement in skin or overall global status after one year was having low self reported disability as reported by the Health Assessment Questionnaire Disability Index (HAQ) (10). This demonstrates that a low HAQ score at baseline predicted improvement in skin involvement over the next 1 to 2 years. One assumes that SSc patients with a lower HAQ will have less morbidity, but a low baseline HAQ predicting subsequent *improvement* in disease status is not as intuitive.

The objectives of this study were to determine if: 1) a low HAQ score in SSc predicted subsequent improvement in a clinical practice as measured by physician global assessment; 2) an improvement in HAQ predicted physician global assessment of "improved" over the next 1 to 2 years with year 1, year 2 and baseline stratified by limited and diffuse disease and then further divided into early (≤3 years) and late (>3 years) SSc; and, 3) HAQ changes over 1 to 2 years were associated with other outcomes (MD global assessments of damage and severity) overall and within subgroups.

Methods

Multiple data are collected routinely on all outpatients at the St. Joseph's Hospital rheumatology clinic. At each clinic visit patients undergo a physical examination and are asked to complete the HAQ-DI (0-3) and visual analogue scales (VAS) for pain, fatigue, sleep and global status, which range from 0 (none) to 100 mm (very severe). Patients also complete a 5-point Likert scale of change that asks "How would you describe your overall status since the last visit?" on a scale labelled: *much better, better, the same, worse, much worse*.

All current SSc patients seen by one rheumatologist (JP) were identified from hospital billing codes and a chart review was performed. Eligible patients met the criteria for scleroderma as measured by the Preliminary ARA Criteria or had a diagnosis of scleroderma as per the investigator (11), and were seen for at least one year, had completed the aforementioned questionnaires (including those of interest: the HAQ and 5-point Likert scale) from at least two clinic visits, and were physically examined at these two visits (n=120). Data were divided into limited SSc (lcSSc) and diffuse SSc (dcSSc) and subdivided into early SSc (defined as ≤3 years since diagnosis) and late SSc (>3 years since diagnosis) creating four possible subgroups for comparison.

We calculated the mean, median and change in HAQ for the limited and diffuse scleroderma groups at their initial and follow-up visits and compared this to the changes in patient and physician assessments of overall status. Patient assessment of overall change in status was determined from the 5-point Likert scale asking "How would you describe your overall status since the last visit?" on a scale labelled: *much better, better, the same, worse, much worse,* filled out on the same dates as the HAQ. Physician assessment of overall change in status was based on expert opinion on physical examination of skin manifestations as *worse, stable* or *improved*. We divided the data into high and low baseline HAQ scores comparing the cut-off of HAQ ≤1.0 *vs.* >1.0 for each group (overall, limited, diffuse, early and late). The main data of interest were the correlation coefficients between baseline HAQ scores and the changes in overall status at one year. Data from two years were also explored. HAQ changes at year 1 from year 0 at entry were HAQ-DI ($Y_1 - Y_0$), where a positive value indicates improvement in HAQ-DI. A *p*-value of 0.05 was considered significant. Multiple comparisons were not adjusted for as we had determined the primary outcome measurements in advance and considered the subset analyses to be exploratory and possibly underpowered (such as the subset of early diffuse scleroderma).

In order to determine if our results were site-specific we repeated these methods using data from the Canadian Scleroderma Research Group (CSRG) Registry database. The CSRG is a group of Canadian rheumatologists enrolling SSc patients from 14 centers across the country where consenting patients have prospective data collected. There are patient and physician forms for the baseline visit and yearly follow-up visits. The patient forms consist of 16 Sections comprised of validated standard or modified questionnaires on: 1) general contact information; 2) socio-demographic (such as language, ethnicity and lifestyle habits); 3) other health problems 4) environmental exposures; 5) family history of autoimmune diseases; 6) symptoms ['yes' or 'no' questions, such as "I have (or I have had) Raynaud's phenomenon (fingers changing white and then MAY either change blue or red in the cold)"]; 7) patient global assessment of activity and change in status using visual analogue scales from 0 (no disease) to 10 (very severe disease) and the 5-point Likert scale asking "How would you describe your overall status since the last visit?" on a scale labelled: *much better, better, the same, worse, much worse*; 8) mood (the CES-D); 9) abilities (the HAQ-DI); 10) pain (the MPQ); 11) quality of life (the SF-36 v2); 12) resource utilization (RUQ); 13) fatigue (FACIT v4); 14) the multidimensional assessment of fatigue (MAF) scale; 15) patient health assessment (PHQ-9) and 16) satisfaction with appearance.

For the physician form, the rheumatologist records the results of the physical exam including: 1) duration and history of the disease; 2) treatments; 3) physical examination, such as vital signs, interdental distance, head and neck examination, respiratory examination, telengiectasia, upper body calcinosis, active upper body non-hand ulcers, healed upper body non-hand ulcers, modified Rodnan Skin Score, other skin manifestations; 4) upper body joint exam; 5) hand examination; 6) cardiac and abdominal examination;

Table I. Baseline characteristics of scleroderma patients.

		London Clinic	CSRG
No.		120	294
Diffuse (%)		41	45
Limited (%)		59	55
Mean age (SE)		58.47 ± 1.05	55.04 ± 0.72
Mean disease duration (years) (SE)		11.75 ± 0.68	10.6 ± 0.4
HAQ-DI baseline	Total SSc	0.97 ± 0.07	0.82 ± 0.04
	Limited SSc	0.87 ± 0.08	0.62 ± 0.06
	Diffuse SSc	1.12 ± 0.11	0.99 ± 0.06
HAQ - Pain baseline	Total SSc	1.28 ± 0.08	N/A
	Limited SSc	1.26 ± 0.10	N/A
	Diffuse SSc	1.31 ± 0.13	N/A
Severity score (range: 0-5)	Total SSc	--	2.46 ± 0.12
	Limited SSc	--	1.92 ± 0.16
	Diffuse SSc	--	2.89 ± 0.18
Patient-assessed disease status (%better)	Total SSc	50.8	--
	Limited SSc	56.3	--
	Diffuse SSc	42.9	--
Physician opinion at Year 1	% improved	16.7	--
	% stable	67.5	--
	% worse	13.3	--
Physician opinion at Year 2	% improved	12.5	--
	% stable	57.5	--
	% worse	15.8	

Table II. Mean change in HAQ-DI and patient-reported disease change stratified by baseline HAQ score (where ≤1.00 = low score) for patients at the London, Ontario Clinic.

	Low	High	Total	*p*
HAQ-DI (year 1 - baseline)	0.15 ± 0.04	-0.002 ± 0.06	0.09 ± 0.04	0.04
HAQ-DI (year 2 - year 1)	0.03 ± 0.05	0.017 ± 0.05	0.03 ± 0.03	0.8
HAQ-DI (year 2 - baseline)	0.17 ± 0.05	-0.05 ± 0.07	0.08 ± 0.04	0.01
Patient-reported disease change (year 1 - baseline)	0.28 ± 0.10	0.02 ± 0.12	0.17 ± 0.08	0.11
Patient-reported disease change (year 2 - year 1)	0.05 ± 0.09	-0.12 ± 0.09	-0.2 ± 0.07	0.21
Patient-reported disease change (year 2 - baseline)	0.31 ± 0.13	-0.19 ± 0.14	0.11 ± 0.10	0.01

Change in HAQ-DI = Y_1-Y_0 where positive (+) is improvement and negative (-) is worsening.
Patient-reported disease change was: "compared to last visit would you rate your overall disease as much better, better, same, worse, much worse".

7) lower body joint score; 8) neurological examination; 9) global assessment of severity, activity and damage using visual analogue scales from 0 (no disease/ no activity/ no damage) to 10 (very severe disease/ most activity/most damage) and a 6-point Likert scale of each asking (for damage) "How much damage do you think the patient has from his/her scleroderma?": *no damage, very low damage, low damage, moderate damage, high damage, very high damage*; 10) classification; and 11) hand measurements. Blood work and investigations including echocardiograms and pulmonary function tests are also collected at baseline and yearly visits. (More information can be found about the CSRG and its research activities at http://csrg-grcs.ca/.)

At the time of this study, CSRG data was available for 438 patients; 262 had completed their Year 1 follow-up and 112 patients had completed their 2-year follow-up, with completed HAQs and physician assessments. We compared the patient's HAQ-DI score at baseline and 1-year and 2-year follow-ups to the physician global assessment of disease activity and severity, as determined by the Likert scales in the physician case report form. Patients with incomplete data were included provided that they had some data on the parameters of interest and had completed at least two HAQs (at baseline and one or two years of follow-up). As patients also had a modified Rodnan Total Skin Score (MRSS) performed, which is a validated assessment of the amount of skin involvement and its severity (12), as part of their CSRG examination, we also looked at the relationship between baseline HAQ scores and skin scores in the CSRG population (n=438). However, not enough patients had skin scores performed to examine this relationship in our single-site rheumatology clinic.

Results

One hundred and twenty SSc patients had a mean baseline HAQ-DI of 0.97±0.07 (SEM) in the London SSc Clinic, of whom 38 had less than 3 years duration at first HAQ and 49 had diffuse SSc. The mean age was 58.5±1.0 years (SEM) and 82.5% were female. Twenty of the diffuse patients had early disease and within the 71 with limited SSc, only 18 were early. Baseline characteristics are shown in Table I.

Those with a low baseline HAQ had a statistically significant mean improved HAQ at 1 year (Table II). Patient-reported change in disease status was more likely to improve in low HAQ than with a high HAQ, but was only significant over 2 years. There was no significant association between low HAQ at baseline and physician rated improvement at one and two years (data not shown). A change in HAQ was related to improvement in physician assessment at one year and less so at two years (Table IIIa, p=0.005). There were no significant findings when comparing HAQ change and improvement at 2 years (Table III).

In order to determine if these results were site specific or generalizable, data from the CSRG registry database were obtained (Tables I, IIIb and IV). Of the 438 patients, 262 patients at Year 1 and 112 patients at Year 2 had serial annual HAQs, where one-third had disease duration of ≤3 years (these numbers are not due to drop-out, but rather variable lengths of follow-up as the registry enrolls patients continuously). The

Table IIIa. Relationship between change in HAQ and Physician Global Assessment at Year 1 and Year 2: Data from the London, Ontario Clinic.

		No.	No. HAQ-DI$_1$	No. HAQ-DI$_2$	Physician assessment Year 1 *vs.* HAQ-DI$_1$ - HAQ-DI$_0$		Physician assessment Year 2 v*s.* HAQ-DI$_2$ -HAQ-DI$_1$		Physician assessment Year 2 *vs.* HAQ-DI$_2$ - HAQ-DI$_0$		Deceased (yes/no) *vs.* HAQ-DI$_0$	
					r	*p*	r	*p*	r	*p*	r	*p*
Diffuse & Limited	Early & Late	120	116	103	0.21	**0.005**	0.02	0.8	0.07	0.3	0.25	**0.05**
	Early only	38	38	34	0.33	**0.003**	0.10	0.4	0.01	0.9	0.19	0.5
	Late only	82	78	69	0.15	0.1	0.10	0.3	0.14	0.2	0.27	0.07
Diffuse only	Early & Late	49	48	44	0.14	0.2	0.09	0.40	0.02	0.8	0.16	0.4
	Early only	20	20	19	0.41	**0.008**	0.17	0.31	0.01	0.95	0.10	0.7
	Late only	29	28	25	0.15	0.3	0.04	0.8	0.00	0.98	0.21	0.4
Limited only	Early & Late	71	68	59	0.26	**0.02**	0.18	0.1	0.25	**0.03**	0.33	0.06
	Early only	18	18	15	0.24	0.2	0.13	0.6	0.17	0.8	N/A	N/A
	Late only	53	50	44	0.32	**0.03**	0.22	0.1	0.26	0.06	0.31	0.09

Early disease is defined by ≤3 years disease duration by the date of the HAQ-DI$_0$. Physician assessment is based on assessment of skin manifestations (*i.e.* worse, stable, improved). Bolded *p*-values are statistically significant.

Table IIIb. Relationship between change in HAQ and Physician Global Assessment at Year 1 and Year 2 of follow-up: Data from the CSRG.

		No. HAQ-DI$_1$	No. HAQ-DI$_2$	Change in physician assessed disease activity from baseline to Year 1 *vs.* HAQ-DI$_1$ - HAQ-DI$_0$		Change in physician assessed disease activity from Year 1 to Year 2 *vs.* HAQ-DI$_2$ -HAQ-DI$_1$		Change in physician assessed disease activity from baseline to Year 2 *vs.* HAQ-DI$_2$ -HAQ-DI$_0$	
				r	*p*	r	*p*	r	*p*
Diffuse & Limited	Early & Late	262	112	0.17	**0.005**	0.14	0.2	0.18	0.06
	Early only	91	38	0.30	**0.004**	0.02	0.9	0.14	0.4
	Late only	171	74	0.02	0.8	0.17	0.2	0.18	0.1
Diffuse only	Early & Late	142	69	0.16	0.06	0.19	0.11	0.1	0.4
	Early only	50	24	0.30	**0.035**	0.06	0.8	-0.3	0.2
	Late only	92	45	-0.01	0.935	0.24	0.1	0.2	0.2
Limited only	Early & Late	114	40	0.18	0.058	-0.08	0.7	0.4	**0.02**
	Early only	38	14	0.32	**0.054**	-0.20	0.5	0.5	**0.04**
	Late only	76	26	0.05	0.691	-0.05	0.8	0.1	0.5

Bolded *p*-values are statistically significant (or close to significance).

physician-assessed activity at Year 1 was significantly related to a change in HAQ (Yr1 – Yr0) overall (p=0.005), in early SSc (p=0.004), in the early diffuse subset (p=0.04) and in the early limited subset (p=0.05). Future changes in physician assessment were not significantly related to HAQ changes except at Year 2 in limited SSc (overall and early). Thus, the results were similar to our single SSc clinic. There were no significant relationships between a low baseline HAQ score and improvement over the next 1 to 2 years.

Damage scales were collected in the CSRG on a 6-point Likert scale and changes in damage were related to changes in HAQ, but only over the first year, for overall and early disease, diffuse overall and early diffuse SSc (Table IV). Again the relationship was not significant in subsequent years for severity of disease.

Table V shows the relationship between change in skin scores and low HAQ scores vs. high scores in the CSRG cohort (n=438). An improvement in skin score was associated with low HAQ in limited SSc overall (p=0.02) and early limited SSc (p=0.003) at Year 1 and with a high HAQ in diffuse SSc overall (p=0.03) and late diffuse SSc (p=0.04) at Year 2. All other results were not significant.

Discussion

SSc patients with low baseline self reported disability (as measured by the HAQ-DI) do not have a better chance of improving at one year of follow up, but an improved HAQ is related to improvement in global status (MD or patient) over the next year, which is a helpful parameter in following patients.

In the past we have demonstrated that a low HAQ-DI in early diffuse SSc RCTs was associated with improvement (as measured by skin scores) in the subsequent 1 to 2 years. This until now has not been addressed in clinical practice or within limited SSc of any duration. RCTs have reported that HAQ is related

Table IV. Changes in physician opinion of disease severity (6-point Likert scale) *vs.* changes in HAQ Scores over 2 years from the CSRG.

		N	Change in Physician Assessed Disease Severity from Baseline to Year 1 vs. $HAQ\text{-}DI_1 - HAQ\text{-}DI_0$		Change in Physician Assessed Disease Severity from Year 1 to Year 2 vs. $HAQ\text{-}DI_2 - HAQ\text{-}DI_1$		Change in Physician Assessed Disease Severity from Baseline to Year 2 vs. $HAQ\text{-}DI_2 - HAQ\text{-}DI_0$	
			r	*p*	r	*p*	r	*p*
Diffuse & Limited	Early & Late	299	0.189	**0.002**	0.042	0.674	0.160	0.096
	Early only	102	0.369	**0.000**	-0.065	0.702	-0.004	0.979
	Late only	197	0.029	0.706	0.075	0.548	0.251	**0.035**
Diffuse only	Early & Late	160	0.256	**0.002**	0.084	0.502	0.188	0.128
	Early only	57	0.399	**0.004**	-0.045	0.835	-0.066	0.758
	Late only	103	0.061	0.569	0.126	0.425	0.321	**0.036**
Limited only	Early & Late	129	0.011	0.910	-0.129	0.453	0.080	0.629
	Early only	41	0.246	0.142	-0.127	0.679	0.260	0.368
	Late only	88	-0.067	0.565	-0.142	0.519	0.002	0.991

Bolded *p*-values are statistically significant (or close to significance.)

Table V. Change in skin score in patients with low baseline HAQ scores (≤1) and high baseline HAQ scores (>1) in the CSRG (n=438) cohort at Year 1 and Year 2. A negative score represents an improvement.

SSc Type		Change in skin score (Yr 1-baseline)			Change in skin score (Yr 2 – Yr 1)		
		Low HAQ	High HAQ	*p*	Low HAQ	High HAQ	*p*
Early		0.273 ± 7.28	-0.071 ± 7.95	0.8	0.42 ± 3.89	-1.20 ± 4.54	0.1
Late		-0.70 ± 4.87	0.23 ± 5.92	0.3	0.85 ± 5.51	-1.18 ± 6.26	0.07
Limited		-0.01 ± 3.26	1.96 ± 5.51	0.02*	0.15 ± 4.03	-1.10 ± 6.66	0.3
Diffuse		-0.72 ± 7.79	-0.73 ± 6.97	1.0	1.31 ± 5.87	-1.26 ± 5.28	0.03*
Early	Limited	-0.03 ± 2.87	5.29 ± 7.52	0.003*	0.35 ± 3.44	-2.50 ± 3.99	0.09
	Diffuse	0.52 ± 9.97	-1.95 ± 7.59	0.3	0.50 ± 4.37	-0.69 ± 4.97	0.4
Late	Limited	0.00 ± 3.50	0.86 ± 4.34	0.4	0.04 ± 4.35	-0.50 ± 7.58	0.7
	Diffuse	-1.49 ± 6.04	-0.10 ± 6.64	0.3	1.80 ± 6.60	-1.56 ± 5.52	0.04*

*Statistically significant.

to other outcomes, but patients with active disease are selected to participate and most RCTs are less than or equal to 2 years in length (12). Determining relationships in clinical practice between change in HAQ and change in physician reported global status verifies that over 1 year there is concordance, but beyond that the relationships weaken. It appears that physician opinion on status change (improvement vs. same or worse) at 1 year in SSc is related to an improved HAQ, but especially in early disease and in early diffuse SSc.

We looked at the relationship in changes in skin scores and low vs. high HAQ scores in the CSRG cohort only (skin scores were not available from our single-site clinic). An improvement in skin score was associated with low HAQ score in the limited SSc overall and early limited SSc groups at one year only; however at 2 years an improvement in skin score was significantly associated with a high HAQ score in the diffuse SSc overall and late diffuse SSc groups. The results for all other subgroups were not significant, and unfortunately we cannot draw any conclusions about the relationship between low HAQ scores and skin scores from this data.

A limitation of the single site data might be the under 'powering' of some of our results. The number of patients with early disease was small, but p values were usually most significant in early disease. However, our results were similar to the larger CSRG database. Another limitation of the study are that the patient 5-point Likert scale (at our site) and the physician 6-point Likert scale (in the CSRG questionnaire) used for global assessment of severity, activity and damage, although they are commonly used, have never been formally validated (13).

The HAQ-DI is a functional measure that can reflect disease activity, damage and other patient factors (14). This has been found in rheumatoid arthritis (RA) where there is more reversibility of the HAQ in early disease (14). Comparatively, over time the HAQ is reflective of both activity and damage where the latter is irreversible. This is likely why the association is strongest with early SSc in general. It is known that SSc patients with high HAQs do poorly. An improved HAQ over 1 year is related to improved physician global assessment at 1 year. Changes in HAQ are related to activity and damage.

Perhaps the relationship does not predict improvement at greater than one year due to other factors such as irreversible damage occurring or stabilization of many patients over subsequent years. Most patients did not improve or worsen over 1 to 2 years but actually remained unchanged (in the mostly prevalent database).

It may be "best practice" to perform HAQ-DI at least annually in patients with SSc, as a change in HAQ is related to physician assessed global disease activity changes over the next year.

In conclusion, the HAQ-DI is a useful 'marker' in SSc because changes in HAQ-DI correspond to other measures of disease activity and severity in clinical practice. However, the utility of a low HAQ-DI in predicting near future improvement in SSc does not perform well in clinical practice.

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