Evaluation of Functional Disability Using the Health Assessment Questionnaire in Japanese Patients with Systemic Sclerosis

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ABSTRACT. ***Objective.*** To assess whether the functional disability in Japanese patients with systemic sclerosis (SSc) can be adequately evaluated by the Health Assessment Questionnaire (HAQ) developed in the United States.

Methods. The HAQ was completed by 121 Japanese patients with SSc, in whom SSc-specific physical examinations and laboratory tests were performed at the same time. Clinical findings associated with the disability index (DI) and individual components of the HAQ were examined using Student's t tests and Pearson's correlation tests. Logistic regression analysis was used to identify clinical findings that independently contributed to the increase in the HAQ-DI score.

Results. Japanese patients with SSc had significant functional disability, especially in the categories of eating and gripping, but the degree of disability was much less than was reported in previous studies carried out in the US. The increase in the HAQ-DI score was strongly correlated with increased total skin score, reduced oral aperture, reduced hand extension, increased finger flexion, subcutaneous calcinosis, flexion contractures, increased erythrocyte sedimentation rates, decreased percent vital capacity, and vascular involvement ($p < 0.001$ for all correlations). Multivariate logistic regression analysis showed that hand extension was the most important and an independent correlate of the HAQ-DI.

Conclusion. Our multicenter, cross-sectional study has demonstrated that the self-administered HAQ is a valuable assessment tool of functional disability in Japanese SSc patients, who have social customs different from Americans, but functional disability measured by the HAQ is potentially influenced by ethnic variability. (J Rheumatol 2003;30:1253–8)

Key Indexing Terms:
FUNCTIONAL DISABILITY HAND EXTENSION SYSTEMIC SCLEROSIS
HEALTH ASSESSMENT QUESTIONNAIRE TOTAL SKIN SCORE

Systemic sclerosis (scleroderma; SSc) is a multisystem connective tissue disorder that affects a wide variety of organs, including the skin, vasculature, lung, and gastrointestinal tract[1]. Since the clinical presentation and outcomes of SSc patients are highly variable, it is necessary to evaluate the severity and activity of the disease in individual patients. In this regard, a skin scoring method has proved useful in evaluating the disease status in SSc patients, and has been validated for use in clinical trials for assessing the efficacy of possible disease modifying drugs for SSc[2-4].

The Health Assessment Questionnaire (HAQ) is a patient self-administered instrument that has been commonly used to quantify functional capacity in patients with rheumatoid arthritis (RA)[5]. Since SSc is also a potentially disabling disease, assessing the degree of functional impairment is important. Poole and Steen first adapted the HAQ for use in SSc patients, and found they have a relatively high degree of functional impairment as measured by the HAQ[6]. An increase in the disability index of the HAQ (HAQ-DI) was

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Supported in part by grants from the Keio University Medical Science Fund and the Japanese Ministry of Education, Science, Sports, and Culture.

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Submitted September 6, 2002; revision accepted November 26, 2002.

associated with diffuse cutaneous involvement, high total skin score, poor hand mobility, tendon friction rubs, and joint pain. This research group later reported longitudinal changes in the HAQ scores and provided convincing evidence that the HAQ is an accurate tool for measuring disease status changes in SSc patients[7]. These findings were further confirmed by studies carried out in conjunction with a randomized, controlled trial of high versus low dose D-penicillamine in patients with early diffuse cutaneous SSc (dSSc)[8,9]. Based on these results, the HAQ is now widely accepted as an essential outcome measure for SSc patients in regular clinical practice as well as in clinical trials[4]. However, all previous studies validating the HAQ for the evaluation of SSc patients were conducted in the US[6-12]. Functional impairment is potentially different among nations with various social customs, but no information showing the usefulness of the HAQ in evaluating non-American patients with SSc is available to date. Moreover, it has been suggested that SSc is manifested differently by patients of various ethnic origins, even in the relatively homogeneous subset defined by the presence of anti-topoisomerase I antibody[13]. Therefore, functional disability in non-American patients with SSc may not be adequately assessed by the HAQ, because it was developed on the basis of social activities in the US. To answer this question, we have conducted a multicenter, cross-sectional study to evaluate functional disability using the HAQ in Japanese SSc patients, whose genetic backgrounds and social customs are distinct from those of most patients in the US.

MATERIALS AND METHODS

Patients. One hundred and twenty-one Japanese patients with SSc were enrolled in this study. These patients were recruited from 8 medical centers and selected based on the following criteria: (1) they satisfied the American College of Rheumatology (formerly the American Rheumatism Association) preliminary classification criteria for SSc[14]; (2) their SSc was diagnosed within 10 years; and (3) they did not satisfy the diagnostic criteria for additional rheumatic diseases, including systemic lupus erythematosus, polymyositis/dermatomyositis, or RA[15-17]. The mean age at examination was 55.4 ± 13.0 years and the mean disease duration was 7.3 ± 4.8 years. Eighty-eight percent were female, and 67% had dSSc. Sixteen patients (13%) were classified as having early dSSc (disease duration < 3 years)[7]. All patients gave their written informed consent, approved by the individual Institutional Review Board.

Clinical evaluation. All patients completed the HAQ and underwent a systematic evaluation for clinical and laboratory findings. One question in the HAQ was modified when translated into Japanese: a question in the eating component: are you able to cut your meat? was changed to: are you able to eat with chopsticks? The HAQ information was summed to determine the HAQ-DI. The demographic features recorded included age at examination and sex. SSc patients were classified as having diffuse (dSSc) or limited cutaneous SSc (lSSc), according to the published guidelines[18]. Skin thickness was quantified using the modified Rodnan skin score technique, in which skin thickness is assessed clinically in each of 17 body surface areas on a 0-3 scale, with a maximum score of 51[2]. Hand extension and finger flexion were measured as indices for hand mobility, and the interlabial distance with the maximally opened mouth was measured as the oral aperture, as described[2]. Other SSc-specific physical examinations included tendon friction rubs, shortening of the frenulum linguae, subcutaneous calcinosis, and flexion contractures. The definitions used to describe organ involvement (joint, vasculature, esophagus, heart, kidney, lung, and pulmonary artery) were as described[19].

The laboratory tests performed included complete blood count, erythrocyte sedimentation rate (ESR) at 1 h, serum creatinine level, and urinalysis. Rheumatoid factor was measured with a commercially available latex fixation test. Anti-topoisomerase I and anti-U1 ribonucleoprotein (RNP) antibodies were detected by double immunodiffusion or enzyme-linked immunosorbent assay using commercially available kits (MBL, Nagano or SRL, Tokyo, Japan), while anticentromere antibody was detected by indirect immunofluorescence using commercially prepared slides of monolayer HEp-2 cells (MBL). Pulmonary function tests were performed using standardized spirometric techniques, and the percent predicted vital capacity (% VC) and percent carbon monoxide diffusing capacity (% DLCO) were recorded as a proxy for the severity of lung involvement.

Statistical analysis. All continuous data are shown as the mean ± standard deviation (SD). A total of 26 clinical findings were evaluated for their relationship with the HAQ scores; these variables included demographic features (age at examination and sex), physical findings (total skin score, oral aperture, hand extension, finger flexion, tendon friction rubs, subcutaneous calcinosis, flexion contractures, and shortening of the frenulum linguae), laboratory findings (ESR, hemoglobin, platelet count, rheumatoid factor, anti-topoisomerase I antibody, anticentromere antibody, anti-U1 RNP antibody, % VC, and % DLCO), and organ involvement (joint, vasculature, esophagus, heart, kidney, lung, and pulmonary artery). Clinical subsets were developed based on dichotomous variables, and the HAQ scores in 2 subsets were compared using unpaired Student's t tests. Continuous variables were made dichotomous by division above or below the median or a cut-off value previously reported[8]. Moreover, Pearson's correlation coefficients were calculated with the HAQ scores as a continuous outcome variable. For the correlation analysis, each clinical variable was regarded as a continuous or dichotomous variable. Only significant variables were selected for further analysis by stepwise multiple regression analysis. An adjusted r^2 was calculated as part of the logistic procedure. p values of < 0.05 were considered significant. All statistical procedures were performed using the StatView software (SAS Institute, Cary, NC, USA).

RESULTS

HAQ-DI and individual component scores in SSc patients. The mean HAQ-DI, as calculated from the 8 different components of the HAQ in all 121 patients with SSc, was 0.46 ± 0.63, which was much lower than the previously reported score in SSc patients in the US[6-8]. Only 18 patients (15%) had a HAQ-DI ≥ 1.0, which represented moderate-to-severe functional impairment[5]. As shown in Table 1, the HAQ components showing the highest functional impairment were eating and gripping, while those with the least functional impairment were arising, walking, and hygiene. The mean HAQ-DI scores for patients with dSSc and lSSc were 0.56 ± 0.69 and 0.20 ± 0.32, respectively, and the mean HAQ-DI for 16 patients with early dSSc was 0.52 ± 0.82. When individual component scores for the 81 patients with dSSc were compared with those for the 40 patients with lSSc, all component scores were significantly higher in the patients with dSSc. The greatest difference was detected in the components reflecting hand function (dressing and gripping), whereas the scores for the components requiring lower extremity strength (arising, walking, and hygiene) as well as the reaching component showed little difference. Patients with lSSc generally had little functional disability,

Table 1. The HAQ-DI and component scores for 121 patients with SSc (results are shown as mean ± SD).

	All SSc Patients (n = 121)	Diffuse Cutaneous SSc (n = 81)	Limited Cutaneous SSc (n = 40)	Diffuse vs Limited Cutaneous SSc p
HAQ Component				
Dressing	0.40 ± 0.74	0.55 ± 0.84	0.08 ± 0.27	< 0.001
Arising	0.28 ± 0.52	0.41 ± 0.65	0.15 ± 0.48	0.03
Eating	0.74 ± 0.90	0.81 ± 0.91	0.41 ± 0.67	0.01
Walking	0.27 ± 0.61	0.35 ± 0.69	0.10 ± 0.30	0.03
Hygiene	0.26 ± 0.63	0.36 ± 0.77	0.10 ± 0.38	0.04
Reaching	0.59 ± 0.84	0.70 ± 0.93	0.36 ± 0.62	0.04
Gripping	0.69 ± 0.89	0.84 ± 0.99	0.33 ± 0.53	0.003
Activities	0.45 ± 0.83	0.57 ± 0.89	0.17 ± 0.43	0.008
HAQ-DI	0.46 ± 0.63	0.56 ± 0.69	0.20 ± 0.32	0.002

as measured by the HAQ, but had significant disability in actions that mainly required using the hands and fingers, such as eating, reaching, and gripping.

Clinical features associated with the HAQ-DI. The SSc patients were divided into clinical subsets based on 26 variables of demographic, physical, and laboratory features, and the HAQ-DI scores were compared between the 2 groups using Student's t tests. In addition, Pearson's correlation coefficients were calculated between the HAQ-DI scores and these same clinical variables. Thirteen features summarized in Table 2 were extracted as variables that were significantly related to the HAQ-DI scores by both statistical methods. From the physical findings, the total skin score, oral aperture, calcinosis, and variables reflecting structural involvement of the joints, such as hand extension and finger flexion, had a strong correlation with the HAQ-DI scores,

Table 2. Clinical variables associated with the HAQ-DI scores in 121 SSc patients.

Variable	Patients, n	HAQ-DI in various clinical subsets HAQ-DI Score mean ± SD	p	Correlations* Correlation Coefficient	p
Demographic features					
Age > 55 yrs	68	0.57 ± 0.63	0.02	0.20	0.02
Age ≤ 55 yrs	53	0.31 ± 0.58			
Physical findings					
Total skin score ≥ 20	27	0.85 ± 0.69	< 0.001	0.47	< 0.001
Total skin score < 20	94	0.34 ± 0.63			
Oral aperture < 43 mm	56	0.64 ± 0.78	0.005	–0.30	< 0.001
Oral aperture ≥ 43 mm	63	0.28 ± 0.59			
Hand extension < 175 mm	56	0.68 ± 1.19	0.006	–0.51	< 0.001
Hand extension ≥ 175 mm	63	0.24 ± 0.34			
Finger flexion ≥ 5 mm	34	0.69 ± 0.74	0.008	0.35	< 0.001
Finger flexion < 5 mm	85	0.36 ± 0.54			
Tendon friction rubs	21	0.70 ± 0.81	0.04	0.22	0.02
No tendon friction rubs	94	0.39 ± 0.58			
Calcinosis	14	0.97 ± 0.83	< 0.001	0.37	< 0.001
No calcinosis	92	0.35 ± 0.54			
Flexion contractures	60	0.65 ± 0.75	< 0.001	0.34	< 0.001
No flexion contractures	59	0.24 ± 0.37			
Laboratory findings					
ESR ≥ 40 mm	16	0.88 ± 0.78	0.002	0.34	< 0.001
ESR < 40 mm	88	0.37 ± 0.54			
% VC < 80%	22	0.73 ± 0.85	0.004	–0.39	< 0.001
% VC ≥ 80%	66	0.32 ± 0.42			
Organ involvement					
Vascular involvement	59	0.66 ± 0.75	< 0.001	0.33	0.001
No vascular involvement	62	0.26 ± 0.40			
Joint involvement	39	0.70 ± 0.74	0.002	0.28	0.002
No joint involvement	81	0.33 ± 0.53			
Heart involvement	14	0.94 ± 0.91	0.003	0.24	0.007
No heart involvement	107	0.40 ± 0.57			

* Determined by Pearson's correlation tests in which the exploratory variables are binary or continuous as appropriate.

suggesting that they contributed to functional impairment in SSc patients. In particular, the total skin score and hand extension showed the highest correlation coefficient (Figure 1). An increase in ESR and a decrease in % VC were correlated with the increased HAQ-DI score, but the presence or absence of rheumatoid factor or SSc-related antinuclear antibodies, including anti-topoisomerase I, anticentromere, and anti-U1 RNP antibodies, were not. Of SSc-related organ involvement, the presence of vascular, joint, or heart involvement was associated with the increased HAQ-DI score. In contrast, no relationship was found between the HAQ-DI and esophagus, lung, kidney, or pulmonary artery involvement.

Relationship between clinical features and individual HAQ component scores. Clinical features associated with the HAQ-DI scores were further analyzed for their relationship with each component of the HAQ (Table 3). The exposure variables were significantly correlated with nearly all components, but the degrees of the correlations were different for each clinical finding. For example, the total skin score was strongly correlated with the dressing, reaching, and gripping components, whereas hand extension and finger flexion, which were indicators of dysfunction of the hands and fingers, showed the strongest correlation with eating, suggesting that skin thickness and impaired hand function cause disability in different categories. Either the total skin score or hand extension represented the highest correlation coefficient with all categories except activities. The highest correlation coefficient with disability of activities was detected in association with calcinosis. It is interesting to note that eating was not disturbed by the decreased oral aperture, which is a variable reflecting skin thickness. Vascular involvement affected dressing and gripping components that involve finger function, whereas SSc patients with heart involvement experienced problems with dressing, walking, hygiene, and activities that require large physical movements. ESR and % VC showed the greatest correlation coefficient with activities.

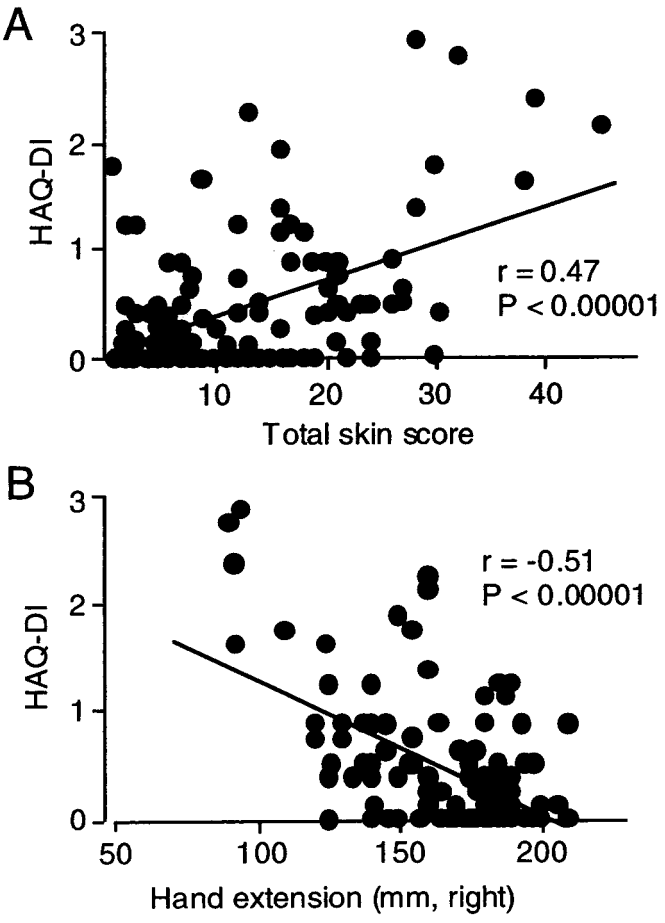

Figure 1. Correlations of the HAQ-DI scores with total skin score (A) and hand extension (B). Pearson's correlation coefficients were calculated with the HAQ-DI as a continuous variable.

Multivariate logistic regression analysis. The HAQ-DI was correlated with many variables and most of the positive correlations were thought to be inter-related. To further assess independent effects of individual clinical variables on the HAQ-DI, 13 clinical variables that were found to have statistically significant associations with the HAQ-DI were evaluated by stepwise multiple logistic regression analysis. Three clinical variables were retained in the final model, and these included hand extension ($p < 0.001$), calcinosis ($p = 0.003$), and ESR ($p = 0.03$). Hand extension was confirmed to be the greatest and an independent factor contributing to the functional disability measured by the HAQ, although the association of the total skin score with the HAQ-DI was lost after stepwise multiple regression analysis. The adjusted r^2 for this model was 0.49, but the model without hand extension had an adjusted r^2 of only 0.21, suggesting that 57% of the effect of this model on the HAQ-DI can be ascribed to dysfunction of hand distensibility.

DISCUSSION

We found that Japanese patients with SSc had functional disability as measured by the HAQ (0.46), but this score was lower than that in Japanese patients with RA (0.66)[20]. It was also noted that the mean HAQ-DI score in Japanese SSc patients was much lower than has been reported in previous studies performed in the US[6-8]. In a similar cross-sectional study by Poole and Steen, the mean HAQ-DI was 0.92 for all SSc patients, and 1.10 for dSSc and 0.67 for lSSc[6]. The patient population in their study appeared to be similar to ours: the proportion of dSSc was 56% versus 67%, and the mean disease duration was 9.2 versus 7.3 years, respectively. In another report involving 1,250 SSc patients by Steen and Medsger, the mean HAQ-DI was 1.09 in dSSc, 0.72 in lSSc, and 1.22 in early dSSc[7]. Moreover, the mean HAQ-DI score in patients with very early dSSc (disease duration < 18 months) was shown to be 1.04, and 53% of the patients had moderate-to-severe functional impairment

Table 3. The relationship between associated clinical features and specific components of the HAQ as measured by Pearson's correlation coefficients. The HAQ component showing the highest correlation coefficient in each clinical feature is underlined.

Clinical Features	HAQ-DI	Dressing	Arising	Eating	Walking	Hygiene	Reaching	Gripping	Activities
Total skin score	0.47†	0.49†	0.28**	0.39†	0.23*	0.38†	0.46†	0.44†	0.39†
Oral aperture	–0.30†	–0.38†	–0.16	–0.16	–0.27**	–0.25**	–0.32†	–0.23*	–0.24**
Hand extension	–0.51†	–0.48†	–0.39†	–0.51†	–0.33†	–0.47†	–0.44†	–0.39†	–0.41†
Finger flexion	0.35†	0.30**	0.30**	0.36†	0.21*	0.32†	0.31†	0.34†	0.22*
Calcinosis	0.37†	0.34†	0.19	0.25**	0.29**	0.33†	0.31**	0.32†	0.42†
Flexion contractures	0.34†	0.35†	0.31†	0.28**	0.19*	0.29†	0.27**	0.27**	0.30†
Vascular involvement	0.33†	0.33†	0.20*	0.28**	0.21*	0.20*	0.29**	0.35†	0.27**
Joint involvement	0.28**	0.27**	0.20*	0.25**	0.18*	0.24**	0.24**	0.25**	0.21*
Heart involvement	0.24**	0.27**	0.16	0.08	0.27**	0.27**	0.22*	0.16	0.25**
ESR	0.34†	0.26**	0.29**	0.29**	0.29**	0.25*	0.20*	0.31**	0.37†
% VC	–0.39†	–0.25*	–0.34**	–0.35†	–0.30**	–0.24*	–0.31**	–0.37†	–0.41†

* $p < 0.05$; ** $p < 0.01$; † $p < 0.001$.

(HAQ-DI ≥ 1.0) in the D-penicillamine trial[8]. Thus, the functional disability measured by the HAQ in Japanese SSc patients appears to be milder than in patients in the US, independent of disease subset and disease duration. One possible explanation for this difference is milder skin thickening and hand dysfunction in Japanese SSc patients in comparison with American patients. In fact, the frequency of total skin score ≥ 20 was found in only 27 patients (22%) in our SSc patients, compared to 210 of 614 patients (34%) in the study by Steen and Medsger[7], and these frequencies were significantly different ($p = 0.01$). In contrast, total skin score of our patients with dSSc was comparable to that of patients with very early dSSc in the D-penicillamine trial[8] (19.0 ± 9.2 vs 21.0 ± 8.0, not significant).

Alternatively, it is possible that the questions in the HAQ, which was developed on the basis of an American lifestyle, were not sensitive enough to detect functional impairment in Japanese patients, and functional disability in Japanese SSc patients might be underestimated. Therefore, the inclusion of questions reflecting a Japanese lifestyle, such as sitting square on a tatami mat and taking off their shoes at the entrance hall, may be necessary to increase its sensitivity. In addition, it might be worth considering the character of the Japanese. For example, Japanese people, particularly the elderly, regard perseverance as a virtue and report their symptoms less than the actual state, leading to their having lower scores. In this regard, the mean HAQ-DI score in Japanese patients with RA was also lower than the score in RA patients in the US (0.66 vs 0.82)[5,20], suggesting that the differences in cultural values play a big role.

When the HAQ component scores in our patients were compared with those reported in the US, all the component scores except eating were much lower in the Japanese[6,8]. The relatively high eating score in Japanese patients might be explained by our modification of the question in the eating category, in that eating with chopsticks requires more delicate finger movement than cutting meat with a knife and a fork.

Thirteen clinical variables were identified as clinical features associated with the HAQ-DI by univariate analysis. The majority of these associations were not unexpected, and were in accord with those reported in previous studies with Americans[6-8], indicating that clinical findings affecting functional ability are shared between Japanese and American SSc patients in general. We further evaluated independent effects of these clinical variables on the HAQ-DI using a multivariate logistic regression model, and found that hand function assessed by the hand extension measurement was the most important contributor to functional impairment in SSc patients. In contrast, the total skin score was not retained as an independent factor contributing to functional disability. This is consistent with the study using SSc patients enrolled in the D-penicillamine trial, in which the total skin score was not retained in the final model, whereas hand extension gave the highest odds ratio by stepwise multiple regression analysis[8]. Lack of significant association of total skin score with the HAQ-DI in multivariate analysis is likely to be explained partly by a strong correlation between total skin score and hand extension ($r = 0.55$, $p < 0.001$ in our study). Thus, we should focus on physical and functional limitations, such as hand dysfunction reflected by reduced hand spread, as an important target of future therapeutic intervention, in addition to skin thickening.

Several clinical features associated with the HAQ-DI in this study were not examined or reported in previous studies. One such example is the strong correlation between the presence of subcutaneous calcinosis and the increased HAQ-DI score. Multiple regression analysis revealed that calcinosis was an independent variable affecting patients' functional ability. Calcium deposits occur mainly in the digital pads and periarticular tissues, and calcinosis is occasionally complicated by pain of motion. In addition, the calcium salts sometimes ulcerate the skin and cause recurrent episodes of local inflammation. Because calcinosis mainly affected the category of activities, it may limit move-

ment mainly in large joints due to pain. On the other hand, the study conducted in conjunction with the D-penicillamine trial failed to detect a correlation between the HAQ-DI scores and heart involvement, which was detected by the univariate analysis in our study[8]. These discrepancies might reflect differences in the patient populations studied: our subjects included SSc patients with late disease who had advanced and irreversible organ involvement, whereas patients with end-stage organ failure were excluded in the D-penicillamine trial. Since only a small number of patients had subcutaneous calcinosis or heart involvement, a role of these findings in functional disability might be underestimated in our study and others.

In summary, there is a strong link between the patients' own assessments of functional disability on the HAQ-DI and the measurements derived from physical and laboratory evaluations in Japanese SSc patients. Thus, the HAQ-DI can be used to assess functional disability in SSc patients who have ethnic backgrounds and social customs different from Americans. However, our findings strongly suggest that the functional disability measured by the HAQ is influenced by ethnic variability. A prospective study involving SSc patients analyzed in this study is ongoing to examine longitudinal changes in the HAQ and their association with outcomes.

ACKNOWLEDGMENT

We thank Dr. Mikio Kajihara for assisting in multivariate analysis, and Kyoko Kimura for managing patient databases.

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