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ORIGINAL ARTICLE

Influence of Clinical Features on the Health Status of Patients With Limited Cutaneous Systemic Sclerosis

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Objective. **To determine the effect of limited cutaneous systemic sclerosis (lcSSc) on patients' health status, and to identify the contributions to health status of different manifestations of lcSSc.**

Methods. **The Short Form 36 questionnaire was completed by 213 patients with lcSSc or Raynaud's syndrome and an antinuclear antibody typical of lcSSc as part of the baseline visit of the Quinapril in Scleroderma trial. Results were analyzed after correcting for age and sex using the Welsh Health Survey. Patients' results were related to their clinical characteristics.**

Results. **The mean physical component score (PCS) was 44.0 (95% confidence interval [95% CI] 42.5, 45.5), which was lower than the population norm of 50, and the median mental component score (MCS) was 52.2 (95% CI 48.5, 54.3). Raynaud's disease visual analog scale (VAS) scores, lung function, the number of organ systems affected, and skin score were significantly correlated with PCS. The total score (TDS) of an SSc severity scale showed the highest correlation. The effect of lcSSc on PCS was worse in younger patients. Multiple regression including age demonstrated that Raynaud's disease severity could predict a reduction in PCS beyond that predicted by TDS. Raynaud's disease severity and duration of lcSSc were linked to low MCS. Arthritis reduced PCS and esophageal involvement reduced PCS and MCS.**

Conclusion. **Physical health status of patients with lcSSc was reduced, with 30% of the variation predicted by TDS, age, and severity of Raynaud's disease VAS. Mental health status was not reduced in this population.**

KEY WORDS. Health status; Systemic sclerosis; Short-Form 36.

INTRODUCTION

Systemic sclerosis (SSc) is an autoimmune rheumatic disease of unknown etiology characterized by microvascular injury; excessive fibrosis of the skin; distinctive visceral involvement including the lungs, heart, kidneys, and gastrointestinal tract; and progressive macrovascular pathology. SSc is, however, a heterogeneous disorder in which distinctive clinical subsets have been recognized that differ in disease pattern and outcome. The most widely accepted scheme for clinical classification involves 2 subsets, limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc), based on the amount of cutaneous involvement that reflects to some extent the degree of visceral disease (1).

The majority of patients (>60%) fall into the category of lcSSc. In these patients compared with those with dcSSc, visceral involvement is late, occurring 10–30 years after the onset of Raynaud's phenomenon, which is usually the first event. Consequently, lcSSc has been considered to be a more benign form of the disease. However, this can be misleading because progressive vascular involvement can lead to features such as painful digital ischemia and ulceration; severe gastrointestinal disease, mostly esophageal; and significant macrovascular disease including pulmonary hypertension. These cause considerable morbidity and potentially impact greatly on health status (health-related quality of life); however, to date health status has not been formally assessed in a large group of patients with

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Table 1. Demographic and clinical data of QUINS trial patients with lcSSc and Raynaud's plus ANA diagnoses*

Variable	lcSSc (n = 187)	Raynaud's + ANA (n = 26)
Female sex, %	86	85
Age, mean ± SD years	55 ± 11.8	47.5 ± 14.5
Raynaud's disease duration, median (IQR) years	10.4 (4.8–22.2)	6.5 (2.6–16.8)
lcSSc disease duration, median (IQR) years	3.9 (1.2–8.0)	NA
TDS score, mean ± SD	4.7 ± 2.5	1.8 ± 1.0
Skin score, median (IQR)	5.0 (2–9)	0.0 (0.0–0)
Digital ulcers, %	25.1	11.5
Number of digital ulcers, mean (range)	0.70 (0–12)	0.23 (0–3)
Current/past/never smokers, %	19/33/48	15/23/62

* QUINS = Quinapril in Scleroderma; lcSSc = limited cutaneous systemic sclerosis; ANA = antinuclear antibody; IQR = interquartile range; NA = not applicable; TDS = total disease severity.

lcSSc. This study was therefore designed to assess the impact of disease on physical and psychological health as well as social functioning in a large cohort of patients with lcSSc using the Medical Outcomes Study Short Form 36 questionnaire (SF-36; SF-36 Health Survey license number R3-082102-11646 from QualityMetric Inc.) (2).

PATIENTS AND METHODS

The study group comprised 213 participants who had been recruited from 20 different centers across England and Wales to take part in a trial funded by the Arthritis Research Campaign (3). Inclusion criteria for this study were a minimum age of 18 years and a diagnosis of either lcSSc or Raynaud's disease with an SSc-specific antinuclear antibody (ANA). Patients were excluded if they had previously responded adversely to angiotensin-converting enzyme (ACE) inhibitors; needed ACE inhibition for heart problems; were women not using reliable contraception; had histories of angioedema, severe renal disease, hepatic disease, or obstructive heart disease; or were unable to speak English or Welsh. Patients were recruited between March 2001 and February 2004, and the study will close on February 1, 2006. A total of 187 patients satisfied the criteria for lcSSc (1), and 26 had Raynaud's phenomenon without skin involvement but with the presence of SSc-associated autoantibodies (including anticentromere and anti–topoisomerase I antibodies). Clinical and health status data from the baseline assessment of these patients were used in the study.

Clinical information was obtained by interviews, physical examination, medical record reviews, and questionnaires. Skin involvement was assessed using the validated modified Rodnan skin score (4). The percentage of expected forced vital capacity (FVC) and diffusing capacity of carbon monoxide were used as measures of pulmonary function and creatinine clearance for renal function. A disease severity score that has been validated for patients with SSc (5) was used, with severity scales for 9 organ systems scored from 0 (no involvement) to 4 (end-stage disease). The 9 scores were added, without any attempt to weight them, to give a total score with a theoretical range of 0–36. This score (TDS) was used as an indicator of overall disease severity.

Self-completed SF-36 standard form questionnaires, version 1 (2,6), were used to assess health status. Data were corrected for age and sex by comparison with a large data set from Wales (7) to compute norm-based T scores for individuals (6). Physical and mental component summary scores (PCS and MCS, respectively) were obtained by aggregation of the 8 domains to reduce error and allow for more straightforward comparisons between populations in different countries and between clinical conditions (6).

The mean T scores for Quinapril in Scleroderma (QUINS) trial patients were compared with the standard Welsh population by 1-sample *t*-tests. Correlations between the SF-36 scores and various clinical and laboratory measures, including the TDS, were investigated. Logistic regression was used to assess the effect of documented arthritis, pulmonary fibrosis, and involvement of gut regions on PCS and MCS. The significance level for all tests was $P < 0.01$ to compensate for multiple analyses. Multiple regression analysis using factors that were significantly correlated with PCS and MCS demonstrated the relative contributions of different clinical parameters to health status in these patients.

RESULTS

Demographic and clinical data are shown in Table 1. Patients consisted of 183 women and 30 men with a mean age of 54 years (range 19–82 years), median duration of Raynaud's symptoms of 9.9 years (range 0.2–64.6 years), and median time since lcSSc diagnosis of 3.9 years (range 0.1–41.2 years). Thirty-three percent of these patients had arthritis. Eleven percent showed symptoms of overlap with connective tissue disorders or other autoimmune conditions; 16 patients had dry eyes/dry mouth from Sjögren's syndrome, 9 had myositis, and 8 had hypothyroid function. Patients with Raynaud's disease plus ANA were considered to represent one end of the spectrum of lcSSc. Comparisons with patients with SSc who were not enrolled in the trial were limited because most patients did not consent to data collection. Of 167 patients who

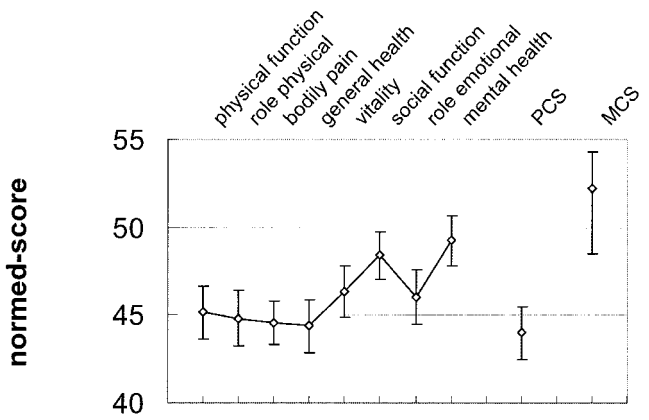

Figure 1. Results from the Short Form 36 questionnaire showing 8 domains of health status and physical component summary score (PCS; means and 95% confidence interval [95% CI]) and mental component summary score (MCS; median and 95% CI).

were eligible but did not consent to the trial, data on 78 were known from the UK scleroderma database. In comparison with patients who were eligible for the trial but did not agree to participate, QUINS trial patients were 3.5 years younger (95% confidence interval [95% CI] 1, 6) and had a disease duration 5 years shorter (95% CI 3, 6) but had no difference in the number of organ systems affected (95% CI 0, 1).

Both PCS and MCS scores were higher in patients with Raynaud's phenomenon than in those with lcSSc, but not significantly higher (mean PCS 2.76 higher, 95% CI −1.75, 7.26 and median MCS 1.44 higher, 95% CI –1.91, 5.61). Exclusion of patients with Raynaud's plus ANA from the subsequent analysis made a negligible difference, so pooled results from both groups are presented. Mean norm-based scores (related to the Welsh population mean score of 50) in the 8 SF-36 domains and PCS and MCS for the QUINS trial population are shown in Figure 1.

T scores for the 8 domains were computed and tested by a 1-sample *t*-test against the expected mean of 50. Six of the 8 domains were reduced at the $P < 0.001$ significance level; social function and mental health were not significantly reduced.

The mean PCS and median MCS of QUINS trial patients were 44.0 (95% CI 42.5, 45.5) and 52.2 (95% CI 48.5, 54.3), respectively. Correlations between clinical characteristics and PCS and MCS are shown in Table 2. Negative correlations occurred when increasing severity (e.g., TDS and visual analog scale [VAS] scores where 0 is best) was associated with decreasing health status. There were significant correlations between PCS and age, TDS, Raynaud's disease severity, number of organ systems affected, Raynaud's disease frequency, FVC, and skin score. There were fewer significant correlations with MCS, including Raynaud's disease severity, number of organ systems affected, and Raynaud's disease frequency. When the correlations were corrected for inclusion category (to differentiate patients with Raynaud's disease plus ANA from those with lcSSc), very little difference was observed, supporting our decision to pool the data.

The effect of presence or absence of disease involvement in different organ systems on health status is shown in Table 3. There was a trend toward reduction of PCS for all symptoms except the large bowel symptom, but only arthritis and esophageal involvement produced statistically significant reductions. All symptoms reduced MCS, but only esophageal involvement produced a significant reduction.

The TDS is based on disease scores of 9 organ systems without weighting. Therefore, measures of any single organ effect might add to the reduction of health status due

Table 2. Correlation of clinical features with PCS and MCS scores*

Measure	PCS		MCS	
	Correlation	*P*	Correlation	*P*
Age†	0.34	< 0.001	−0.02	0.8
TDS score	−0.33	< 0.001	−0.14	0.05
Raynaud's disease severity VAS	−0.26	< 0.001	−0.24	< 0.001
Number of organs affected†	−0.22	0.001	−0.22	0.001
Raynaud's disease frequency VAS	−0.2	0.004	−0.2	0.004
Percent expected FVC†	0.2	0.005	0.11	0.13
Skin score	−0.18	0.01	−0.11	0.13
Percent expected DLco†	0.14	0.06	0.08	0.3
Number of digital ulcers	−0.12	0.09	−0.04	0.6
Smoking history (current/past/never)	0.09	0.2	0	1
Creatinine clearance‡	−0.06	0.4	0.03	0.6
Duration of lcSSc	−0.04	0.6	−0.16	0.04
Urinary protein (24 hour urine)	−0.03	0.7	−0.09	0.2
Blood hemoglobin concentration†	0.03	0.7	0.02	0.8

* PCS = physical component summary; MCS = mental component summary; TDS = total disease severity; VAS = visual analog scale; FVC = forced vital capacity; DLco = diffusing capacity for carbon monoxide; lcSSc = limited cutaneous systemic sclerosis.
† Pearson's correlation coefficient with PCS. All other correlations are Spearman's rank correlations.
‡ 24-hour urine creatinine ratio test.

Table 3. Effect of different clinical features on the SF-36 components*

Symptom	Number of patients with symptom	Effect on PCS, mean difference (95% CI)	Effect on MCS, median difference (95% CI)
Esophageal	89	−4.6 (−7.5, −1.6)	−3.3 (−6.1, –0.8)
Arthritis	70	−4.5 (−7.6, −1.4)	−1.8 (−4.7, 0.8)
Small bowel	11	−4.1 (−10.8, 2.5)	−6.9 (−12.8, 0.4)
Large bowel	22	0.3 (−4.5, 5.2)	−2.1 (−8.5, 3.0)
Pulmonary fibrosis	22	−3.7 (−8.5, 1.2)	−1.9 (−6.8, 2.5)

* SF-36 = Short Form 36; PCS = physical component summary; MCS = mental component summary; 95% CI = 95% confidence interval.

to the TDS used in this study. This was investigated using multiple regression analysis. Factors significantly correlated with PCS, as shown in Tables 2 and 3, were considered for inclusion in the model. Lung FVC did not explain more variance when included in the model. The only factor apart from age that added more to the model to predict PCS from the TDS was the severity of Raynaud's disease VAS score. These 3 factors explained 30% of the variance of the PCS (Table 4).

MCS was largely unaffected by clinical characteristics. A similar multiple regression analysis demonstrated that only number of organs affected and severity of Raynaud's disease significantly affected MCS, explaining 10% of the variance.

DISCUSSION

The traditional outcome measure for SSc was survival time, but Bryan et al (8) have suggested 3 clinical predictors of survival (proteinuria, erythrocyte sedimentation rate, and diffusing capacity for carbon monoxide). A skin thickness test has been developed (4) and proposed as an outcome measure in SSc (9), but it may not be useful as an endpoint in the limited form of the disease. The multiorgan effects of the disease imply that many functions should be monitored, each of which will have different clinical importance for the individual patient. An overall measure of self-reported health status would be useful to assess disease effect and any changes due to treatment.

Published articles about health-related quality of life in patients with scleroderma or SSc are limited, ranging from one that included single quotations from patients and doctors about patients' quality of life after an intervention (10) to a study of patients' own assessments of a single quality-of-life item on a scale of 1 to 5 (11) to studies involving the monitoring of the physical activities of daily living including the Health Assessment Questionnaire (HAQ) and modifications (12–14). Several authors have modified the HAQ to create disease-specific questionnaires (15,16), which will be useful in assessing the effects of interventions on disease progression. However, the term "health-related quality of life" is now generally understood to include cognitive, social, and psychological attributes, and questionnaires involving these items have been developed and used in SSc (17,18) and a model of pain has been developed (19). The validity of a modified and expanded HAQ with psychological items has been tested on >600 rheumatology patients, of whom 16 had SSc (20).

It has been shown that some individuals' personal evaluation of their quality of life does not match the prediction of the SF-36 instrument, which is more precisely described as a measure of health status (21). The term "health status" has therefore been used in the present report. The internationally used SF-36, a multidimensional health status instrument, is expected to demonstrate the overall effect of SSc on the patient. It also enables comparisons between the effects of different illnesses on a patient's health status, thus contributing to the planning of health care. The SF-36 can also be used for comparisons between patients in different countries.

The SF-36 was used in one small study of 44 patients with SSc, leading to the conclusion that "as expected, patients scored low on quality of life questionnaires" (22). Recently 3 other small studies, all using the SF-36 with patients with both diffuse and limited SSc, reported reduced health status but gave conflicting results in terms of correlation with clinical parameters (23–25). The SF-36 has been used as an outcome measure after sacral nerve stimulation (26). A detailed study of poor lung function in patients with SSc used the SF-36 as one method to compare these patients with those diagnosed with chronic obstructive pulmonary disease (27). Also, the SF-36,

Table 4. Multiple regression analysis predicting physical component summary score*

Variable	b	95% CI	R^2 change	*P*
Age	0.33	0.22, 0.44	0.117	< 0.001
TDS score	−1.63	−2.14, –1.13	0.146	< 0.001
Raynaud's disease severity VAS	−0.08	−0.13, –0.04	0.050	0.001

* 95% CI = 95% confidence interval; TDS = total disease severity; VAS = visual analog scale.

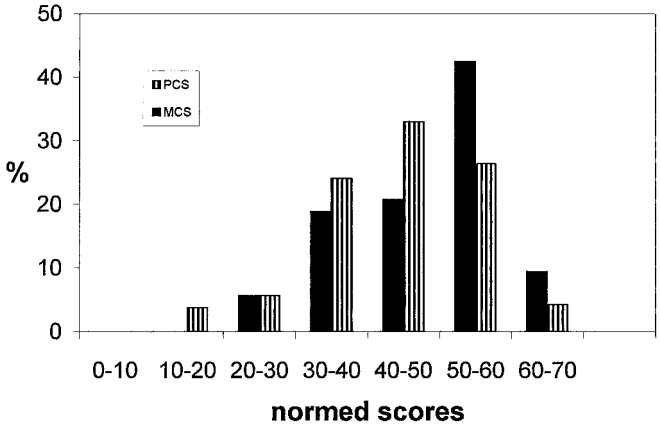

Figure 2. Distribution of physical component summary score (PCS) and mental component summary score (MCS) among patients in the QUINS trial. The mean score of PCS and MCS for the Wales population is assigned the normed value of 50 with a standard deviation of 10.

among other questionnaires, was used to compare SSc with rheumatoid arthritis (28).

In this report, we present data based on the SF-36 version 1 standard form questionnaire (2), which was self completed by 213 patients at the baseline visit when they were enrolled in the QUINS trial. The age and sex distribution of our trial patients (85% women, median age 54 years [interquartile range 45–62 years]) was different from the general adult population. Because health status estimates are lower for women and decrease with age, it was necessary to make comparisons using age- and sex-matched data. Interview methods of obtaining data tend to result in higher scores than self-completed questionnaires (29), and SF-36 forms were self completed in the QUINS trial; therefore, results were compared with normative data from a postal SF-36 survey (7). The population of Wales demonstrated a lower quality of life than that of the US; therefore, Welsh data were chosen for comparison as a conservative test. We chose not to use data sets from England because they were either interview based (30) or from self-completed SF-36 questionnaires in a single region of England (31), or they do not include individuals >64 years of age (32).

Normed mean values of the 8 domains of the SF-36 for 213 QUINS trial patients (shown in Figure 1) demonstrated that the scores of the physical domains were more reduced than the scores of those assessing mental health. The 4 mainly physical domains with vitality and role emotional were all significantly different from the Welsh population data ($P < 0.001$); social function and mental health scores were reduced, but not significantly ($P = 0.02$ and $P = 0.3$, respectively).

The mean PCS, obtained by aggregating the 8 domain scores and relating them to a population norm of 50 (6), was 44.0 (95% CI 42.5, 45.5). The median MCS was 52.2 (95% CI 48.5, 54.3). Distributions of PCS and MCS scores are shown in Figure 2. The most common PCS score of QUINS patients was between the norm and 1 standard deviation below the norm. The most common MCS score was between the norm and 1 standard deviation above the norm, but some patients scored very low. Other studies have focused on anxiety and depression in patients with SSc, but the SF-36 did not reveal lower mental health status in the QUINS trial patient group as a whole.

Clinical experience with SSc would suggest that the severity and frequency of Raynaud's disease attacks, the number of digital ulcers, and the number of organs affected by the condition would affect the patients' estimates of their health status. Other parameters such as lung function and hemoglobin levels might also affect patients' estimates. A disease severity scale for SSc (5) was used to generate a total score (TDS), giving equal weight to each of the 9 measures. The TDS has not been validated but might correlate with health status measurements. The severity scale was developed for patients with diffuse and limited SSc, and the QUINS population showed a maximum TDS of 12 compared with the theoretical maximum of 48. This reduced range, however, was sufficient to establish highly significant correlations with health status, suggesting that the unweighted TDS may be a useful measure of disease in lcSSc. The fact that lung FVC did not add to the variance of PCS explained by TDS suggests that weighting of the lung function item in the TDS is not necessary.

Tests of the correlation of SF-36 measures with Raynaud's symptoms were not reported in earlier studies (23–25). In this study, patients' own assessments of frequency and severity of their Raynaud's disease attacks using VAS scales were negatively correlated with both PCS and MCS and with each of the 8 domains of the SF-36. More frequent and more severe Raynaud's disease attacks were linked to lower scores. These correlations of Raynaud's disease VAS scores with PCS and MCS are compatible with the report that patients with SSc perceive Raynaud's phenomenon to be the predominant problem with their hand function (33).

The time since the onset of Raynaud's symptoms was not correlated with PCS or MCS scores. This was not surprising because Raynaud's symptoms may occur for many years, even decades, before development of other organ involvement and diagnosis of SSc. There was a trend toward increasing time since diagnosis of lcSSc associated with lower MCS, as shown in Table 2, but this association was not significant at the 0.01 level.

It was expected that patients with arthritis, pulmonary fibrosis, or involvement of the gastrointestinal tract would have reduced health status. These effects, which are a further validation of the SF-36 as a measure of health status in patients with SSc, are shown in Table 3. Involvement of the esophagus was reflected in significantly reduced MCS, as shown in Table 3. This finding was compatible with those relating gastrointestinal function to depression (34), although the SF-36 does not measure depression per se. SF-36 data from QUINS trial patients reveal better health (higher health status) than SF-36 data from patients with rheumatoid arthritis (35,36) and systemic lupus erythematosus (37).

Limited cutaneous SSc is a disease with especially variable expression, and the number of patients in the QUINS trial with certain characteristics, such as involvement of the small bowel at the start of the trial, was small. However, we believe that because the QUINS trial population

was made up of patients from district general hospitals as well as specialist centers in various geographic areas of England and Wales, these results are representative of patients with lcSSc as a whole. The trial included patients with Raynaud's symptoms plus lcSSc-specific autoantibodies; however, as Table 1 confirms, these patients were part of the lcSSc spectrum, and we believe we are justified in pooling data from these 2 groups. It is probable that patients with SSc with very severe clinical manifestations of the disease would be excluded by the exclusion criteria and/or by unwillingness to commit to a 3-year trial. We conclude that the health status results presented here probably underestimate the reduction in health status of patients with lcSSc as a whole, because severely ill patients will be excluded from this trial and patients with Raynaud's disease plus autoantibodies will be included.

This study has found that patients with lcSSc had poor physical health status compared with population norms, but that mental health status was not generally reduced. Approximately 30% of the variability of the PCS score was predicted by age, an unweighted total score of disease severity, and the patients' self assessment of severity of Raynaud's disease attacks. Ten percent of the variation in mental health status can be predicted from our data.

We suggest that the unweighted total of the SSc disease severity score (5) as well as Raynaud's disease severity VAS score can provide an overall measure of disease severity in patients with the limited form of SSc. Further studies that investigate the weighting of individual components of the disease severity scale would be useful to produce an optimal disease severity summary score. Treatments to reduce the severity of Raynaud's symptoms and to ameliorate the function of organs affected should improve patients' health status. SF-36 data will be analyzed as the health status outcome measure of treatment with quinapril.

REFERENCES

1. LeRoy EC, Black C, Fleischmajer R, Jablonska S, Krieg T, Medsger TA Jr, et al. Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. J Rheumatol 1988;15: 202–5.
2. Ware JE, Snow KK, Kosinski M. SF36 Health Survey: manual and interpretation guide. Lincoln (RI): QualityMetric Incorporated; 2000.
3. Maddison P. Prevention of vascular damage in scleroderma with angiotensin-converting enzyme (ACE) inhibition. Rheumatology (Oxford) 2002;41:965–71.
4. Brennan P, Silman A, Black C, Bernstein R, Coppock J, Maddison P, et al, and the UK Scleroderma Study Group. Reliability of skin involvement measures in scleroderma. Br J Rheumatol 1992;31:457–60.
5. Medsger TA Jr, Silman AJ, Steen VD, Black CM, Akesson A, Bacon PA, et al. A disease severity scale for systemic sclerosis: development and testing. J Rheumatol 1999;26:2159–67.
6. Ware JE, Kosinski M. SF-36 physical and mental health summary scales: a manual for users of version 1. 2nd ed. Lincoln (RI): QualityMetric Incorporated; 2001.
7. National Assembly for Wales. Welsh Health Survey. London: Her Majesty's Stationery Office; 1998.
8. Bryan C, Knight C, Black CM, Silman AJ. Prediction of five-year survival following presentation with scleroderma: development of a simple model using three disease factors at first visit. Arthritis Rheum 1999;42:2660–5.
9. Seibold JR, McCloskey DA. Skin involvement as a relevant outcome measure in clinical trials of systemic sclerosis. Curr Opin Rheumatol 1997;9:571–5.
10. Grabowski G, Grant JP. Nutritional support in patients with systemic scleroderma. JPEN J Parenter Enteral Nutr 1989;13: 147–51.
11. Tomaino MM, Goitz RJ, Medsger TA. Surgery for ischemic pain and Raynaud's phenomenon in scleroderma: a description of treatment protocol and evaluation of results. Microsurgery 2001;21:75–9.
12. Muellegger RR, Hofer A, Salmhofer W, Soyer HP, Kerl H, Wolf P. Extended extracorporeal photochemotherapy with extracorporeal administration of 8-methoxypsoralen in systemic sclerosis: an Austrian single-center study. Photodermatol Photoimmunol Photomed 2000;16:216–23.
13. Poole JL, Williams CA, Bloch DA, Hollak B, Spitz P. Concurrent validity of the Health Assessment Questionnaire Disability Index in scleroderma. Arthritis Care Res 1995;8:189–93.
14. Sultan N, Pope JE, Clements PJ, and the Scleroderma Trials Study Group. The health assessment questionnaire (HAQ) is strongly predictive of good outcome in early diffuse scleroderma: results from an analysis of two randomized controlled trials in early diffuse scleroderma. Rheumatology (Oxford) 2004;43:472–8.
15. Ruof J, Bruhlmann P, Michel BA, Stucki G. Development and validation of a self-administered systemic sclerosis questionnaire (SySQ). Rheumatology (Oxford) 1999;38:535–42.
16. Steen VD, Medsger TA Jr. The value of the Health Assessment Questionnaire and special patient-generated scales to demonstrate change in systemic sclerosis patients over time. Arthritis Rheum 1997;40:1984–91.
17. Oelzner S, Schmidt S, Looks A, Lange D, Oelzner P, Hein G, et al. Explorative study on quality of life in patients with progressive-systemic scleroderma. Aktuelle Derm 1999;25: 129–32. In German.
18. Grassegger A, Schuler G, Hessenberger G, Walder-Hantich B, Jabkowski J, MacHeiner W, et al. Interferon-gamma in the treatment of systemic sclerosis: a randomized controlled multicentre trial. Br J Dermatol 1998;139:639–48.
19. Benrud-Larson LM, Haythornthwaite JA, Heinberg LJ, Boling C, Reed J, White B, et al. The impact of pain and symptoms of depression in scleroderma. Pain 2002;95:267–75.
20. Pincus T, Swearingen C, Wolfe F. Toward a multidimensional Health Assessment Questionnaire (MDHAQ): assessment of advanced activities of daily living and psychological status in the patient-friendly health assessment questionnaire format. Arthritis Rheum 1999;42:2220–30.
21. Covinsky KE, Wu AW, Landefeld CS, Connors AF Jr, Phillips RS, Tsevat J, et al. Health status versus quality of life in older patients: does the distinction matter? Am J Med 1999;106: 435–40.
22. Enomoto DN, Mekkes JR, Bossuyt PM, Yong SL, Out TA, Hoekzema R, et al. Treatment of patients with systemic sclerosis with extracorporeal photochemotherapy (photopheresis). J Am Acad Dermatol 1999;41:915–22.
23. Georges C, Chassany O, Mouthon L, Tiev K, Marjanovic Z, Meyer O, et al. Quality of life assessment with the MOS-SF36 in patients with systemic sclerosis. Rev Med Interne 2004;25: 16–21. In French.
24. Del Rosso A, Boldrini M, D'Agostino D, Placidi GP, Scarpato A, Pignone A, et al. Health-related quality of life in systemic sclerosis as measured by the Short Form 36: relationship with clinical and biologic markers. Arthritis Rheum 2004;51:475–81.
25. Cossutta R, Zeni S, Soldi A, Colombelli P, Belotti Masserini A, Fantini F. Evaluation of quality of life in patients with systemic sclerosis by administering the SF-36 questionnaire. Reumatismo 2002;54:122–7. In Italian.
26. Kenefick NJ, Vaizey CJ, Cohen RC, Nicholls RJ, Kamm MA. Medium-term results of permanent sacral nerve stimulation for faecal incontinence. Br J Surg 2002;89:896–901.
27. Khanna D, Clements PJ, Furst DE, Chon Y, Elashoff R, Roth MD, et al. Correlation of the degree of dyspnea with health-related quality of life, functional abilities, and diffusing ca-

pacity for carbon monoxide in patients with systemic sclerosis and active alveolitis: results from the Scleroderma Lung Study. Arthritis Rheum 2005;52:592–600.
28. Danieli E, Airo P, Bettoni L, Cinquini M, Antonioli CM, Cavazzana I, et al. Health-related quality of life measured by the Short Form 36 (SF-36) in systemic sclerosis: correlations with indexes of disease activity and severity, disability, and depressive symptoms. Clin Rheumatol 2005;24:48–54.
29. Bowling A. Measuring health: a review of quality of life measurement scales. Milton Keynes: Open University Press; 1991.
30. Health Survey for England in 1996. London: The Stationery Office; 1998.
31. Brazier JE, Harper R, Jones NM, O'Cathain A, Thomas KJ, Usherwood T, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. BMJ 1992;305:160–4.
32. Jenkinson C, Coulter A, Wright L. Short form 36 (SF36) health survey questionnaire: normative data for adults of working age. BMJ 1993;306:1437–40.
33. Sandqvist G, Eklund M, Akesson A, Nordenskiold U. Daily activities and hand function in women with scleroderma. Scand J Rheumatol 2004;33:102–7.
34. Nietert PJ, Mitchell HC, Bolster MB, Curran MY, Tilley BC, Silver RM. Correlates of depression, including overall and gastrointestinal functional status, among patients with systemic sclerosis. J Rheumatol 2005;32:51–7.
35. Ruta DA, Hurst NP, Kind P, Hunter M, Stubbings A. Measuring health status in British patients with rheumatoid arthritis: reliability, validity and responsiveness of the short form 36-item health survey (SF-36). Br J Rheumatol 1998;37:425–36.
36. Kosinski M, Kujawski SC, Martin R, Wanke LA, Buatti MC, Ware JE Jr, et al. Health-related quality of life in early rheumatoid arthritis: impact of disease and treatment response. Am J Manag Care 2002;8:231–40.
37. Panopalis P, Petri M, Manzi S, Isenberg DA, Gordon C, Senecal JL, et al. The systemic lupus erythematosus tri-nation study: longitudinal changes in physical and mental well-being. Rheumatology (Oxford) 2005;44:751–5.

APPENDIX A: MEMBERS OF THE QUINS TRIAL STUDY GROUP

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