Lack of Relationship Between Functional Ability and Skin Score in Patients with Systemic Sclerosis

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ABSTRACT. Objective. To examine the hypothesis that functional ability is related to skin score in patients with systemic sclerosis (SSc).

Methods. In 140 patients with SSc attending clinics in the northwestern region of England, functional ability (measured using a recently developed 11 item functional questionnaire) was correlated with skin score (measured using a modified Rodnan technique — 17 sites, maximum score 3 for each site).

Results. The median functional score was 6 (range 0–31) and the median skin score 7 (range 0–37). There was no correlation between functional score and total skin score ($r_s = 0.11, p = 0.19$, Spearman). Because most of the questions of the functional score related to upper limb function, separate analyses were undertaken restricting consideration of skin involvement to (1) upper limbs only and (2) digital skin only, versus the overall functional score. Again, no evidence of an association was observed.

Conclusion. Functional ability in this broad group of patients with SSc cannot be predicted from the skin score. Although skin score is useful prognostically, it is not a major determinant of a patient's ability to perform activities of everyday living. (J Rheumatol 2001;28:292–5)

Key Indexing Terms: SYSTEMIC SCLEROSIS, SCLERODERMA, FUNCTIONAL ABILITY

Systemic sclerosis (SSc) or scleroderma is a multisystem connective tissue disease associated with significant morbidity and mortality. Its clinical manifestations are a result of excessive fibrosis and ischemic atrophy. Although internal organ involvement is well recognized, much of the disability associated with SSc arises from impairment of upper limb function and muscle weakness. Upper limb function is compromised because of skin thickening, which is usually most pronounced distally and which can result in contractures, and because of severe Raynaud’s phenomenon, which can result in irreversible digital ischemia with ulceration, scarring, and sometimes even gangrene, necessitating amputation.

An index of functional ability has been derived specifically for use in patients with SSc, taking into account their particular problems with upper limb function and muscle weakness: 9 of 11 questions relate to upper limb function and 2 to muscle weakness. The index was derived to maximize face and content validity. This instrument can be either self-administered or administered by an observer trained in functional assessment, and holds promise as a measure of patient outcome that might be usefully incorporated into clinical trials of treatment, and into studies of disease progression. Also, because it can be self-administered, it can be included in routine assessment of patients with SSc attending the outpatient clinic. Traditionally, some measure of skin involvement, for example using the Rodnan skin score or some modification thereof, has been incorporated into clinical trials, often as a primary endpoint. This is because the skin score is of prognostic value: high skin scores relate to mortality.

We examined the hypothesis that functional ability, as assessed by the recently developed index, is related to skin score in patients with SSc. This hypothesis seemed likely because indirect results of skin thickening (contractures, ulceration) restrict limb function.

MATERIALS AND METHODS

Functional ability was assessed in 140 patients with SSc (114 women, 26 men, median age 52 yrs, range 25–78) attending outpatient clinics in the northwest of England using the 11 item functional questionnaire. The median disease duration from physician diagnosis was 6 years (range 0–49 yrs). One hundred six of the patients had limited cutaneous SSc (skin involvement confined to distal to elbows, knees, and neck) and 34 had diffuse cutaneous disease. Nine of the patients with diffuse cutaneous disease had “early” disease (duration < 3 years from physician diagnosis) and 25 had “late” disease (duration > 3 years from physician diagnosis).

The clinic nurse (who was not aware of the patient’s skin score) read through the questions with the patient, to ensure that all questionnaires were fully completed and that any patient queries could be addressed. At the same visit, skin score was measured by one of 2 observers using a modified Rodnan technique — 17 sites, maximum score 3 for each site, as described. The 17 sites were the face, anterior chest, abdomen, and right...
and left upper arms, forearms, dorsum of the hands, fingers, thighs, legs, and dorsum of the feet.

Analysis. Since most of the questions of the functional index relate to upper limb function, correlations (Spearman’s) were looked for between functional score and (1) total skin score (maximum possible score 51), (2) upper limb skin score (maximum possible score 24) (3) digital skin score (maximum possible score 6).

Patients with limited cutaneous disease tend to have lower skin scores than patients with diffuse cutaneous disease, so subgroup analyses were performed looking for correlations [Spearman’s rho (rs)] between total, upper limb, and digital skin scores and functional score in the 2 SSc subgroups.

Functional score might be related to both age and disease duration and thus correlation between these variables was also examined. As the functional score was highly negatively skewed, a negative binomial regression analysis was undertaken to adjust the effect of skin score for any influences of age and disease duration. All analyses were undertaken using Stata®

Finally, because patients with early diffuse cutaneous disease form a distinct subgroup in which function can rapidly deteriorate with disease progression, subgroup analyses were performed looking for correlations between functional score and total skin score in patients with early and late diffuse cutaneous disease.

RESULTS
The median functional score was 6 (range 0–31) and the median skin score 7 (range 0–37). There was no correlation between functional score and total skin score (rs = 0.11, p = 0.19, Spearman). Nor were there significant correlations between functional score vs upper limb skin score (rs = 0.12, p = 0.15) or digital skin score (rs = 0.12, p = 0.17).

Limited cutaneous disease subgroup. In the 106 patients with limited cutaneous disease, there was also no significant correlation between functional score and total skin score (rs = 0.14, p = 0.15). Nor were there significant correlations between functional score vs upper limb skin score (rs = 0.15, p = 0.13) or digital skin score (rs = 0.10, p = 0.30).

Diffuse cutaneous disease subgroup. In the 34 patients with diffuse cutaneous disease, there was no correlation between functional score and total skin score (rs = 0.19, p = 0.28). Nor were there significant correlations between functional score vs upper limb skin score (rs = 0.15, p = 0.41) or digital skin score (rs = 0.12, p = 0.51).

Adjustment for confounders. Skin score might be highest, in some patients, in early disease. Similarly, older patients, who are likely to have greater disability for a variety of reasons, tend to have more limited disease. Thus the negative results observed may be explained by the potential confounding due to either or both of disease duration and age. However, there was no correlation between functional score and disease duration either for the patient group as a whole: rs = 0.10, p = 0.23 or when subdivided by disease group — limited disease: rs = 0.16, p = 0.11 and diffuse disease: rs = −0.09, p = 0.64. Age, however, was weakly related to function in the group as a whole: rs = 0.17, p = 0.05. This effect was stronger in the limited subgroup: rs = 0.23, p = 0.02. The results of the negative binomial regression are shown in Table 1 and confirm the absence of influence of skin score on function after adjusting for these variables.

Early versus late diffuse cutaneous disease. There was no significant correlation between functional score and total skin score in the 9 patients with early diffuse cutaneous disease (rs = 0.36, p = 0.34) or in the 25 patients with late diffuse cutaneous disease (rs = 0.21, p = 0.31).

DISCUSSION
Our results suggest that functional ability, as assessed by the new functional instrument, is not related to skin score in patients with SSc. Some patients with high skin scores (> 20) had very little functional limitation, whereas others with very low skin scores were severely functionally disabled. Nor was functional score related to disease duration, probably reflecting how patients with a long disease duration may have very mild disease whereas others with early aggressive disease may be severely functionally impaired.

There are several possible reasons why no relationship was found between functional index and skin score:

1. Problems inherent in the functional index. The functional index used in this study concentrates on upper limb function, with several of the questions addressing fine finger movement. These functions may be less affected by skin score than by other features of disease such as digital ulceration and digital ischemia, sclerodactyly (as opposed to more widespread skin change), calcinosis, arthritis, muscle weakness, and flexion contractures. It is therefore possible that patients with low skin scores had significant digital problems and therefore performed poorly.

In this study the questionnaire strictly speaking was not “self-administered,” in that the clinic nurse asked the questions. The nurse was blind to the skin score: thus this is unlikely to have had a significant influence on results.

2. Problems inherent in the skin score. While measurement of skin score is one of the key outcome measures in patients with SSc, and as mentioned above, patients with the highest skin scores are recognized as having the highest mortality, skin score is subjective. In this study skin score in each patient was assessed by one of 2 clinicians. It is recognized that there is substantial intraobserver variability in the technique®. Intra and interobserver variability have been estimated at 12% and 25%, respectively®. This measurement

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Change in Functional Score</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>139*</td>
<td>1.02</td>
<td>1.00–1.04</td>
</tr>
<tr>
<td>Limited SSc</td>
<td>106</td>
<td>1.01</td>
<td>0.96–1.07</td>
</tr>
<tr>
<td>Diffuse SSc</td>
<td>33*</td>
<td>1.03</td>
<td>0.97–1.08</td>
</tr>
</tbody>
</table>

*Disease duration missing in one subject.

Adjusted for age at diagnosis and disease duration.
error makes any correlation between skin score and function more difficult to detect. However, despite this measurement error, others have found an association between the Health Assessment Questionnaire (HAQ) (one measurement of functional impairment) and skin score\(^8,9\).

3. Problems in relating functional index and skin score. The functional index was developed in a cohort of 47 patients, of whom 38% had diffuse cutaneous disease\(^1\). Only 24% of our cohort had diffuse disease — reflected in the median skin score of only 7 in the 140 patients studied — and only 9 of the 34 patients with diffuse disease had disease duration < 3 years. It is of interest that in our study the patient with the highest functional index of 31 had the second highest skin score of 36 — she had an aggressive pattern of diffuse disease, and it seems likely that in this subgroup with early diffuse disease, skin score may relate to functional score. While we found no correlation between disease duration and skin score even when patients with early diffuse cutaneous disease were considered as a separate subgroup, the number in this subgroup was small.

Another explanation is that there is, in fact, no relation between skin score and function — skin score has no effect on a patient’s activities of everyday living. It has to be recognized that a very large number of factors, including pain, affect function. In patients with limited cutaneous SSc vascular insufficiency rather than fibrosis is the dominant clinical feature. For example, one patient with a skin score of zero but severe painful digital ischemia had a high functional score of 25.

The lack of relationship we observed between functional index and skin score is in contrast to the findings of Steen, et al\(^5\) and Clements, et al\(^9\). Both these studies were of patient populations very different from ours: in Steen, et al 55% of patients had diffuse disease and in Clements, et al all patients had early diffuse disease — duration < 18 months since the onset of the first manifestation of SSc other than Raynaud’s phenomenon. Steen, et al reported that disability index, as assessed by modified HAQ, was related to skin involvement\(^6\), and that changes in this modified HAQ correlated with changes in skin score. Methodological differences may be relevant, and Steen, et al did not directly correlate the modified HAQ score for each patient with the total skin score for each patient, as we did. A possible weakness in our study is that we did not compare our functional index to the modified HAQ\(^8\) and we hope to do so in the future. Clements, et al also reported an association between skin score and disability as measured by the Disability Index of the HAQ\(^9\). Again, skin score and disability score were not directly correlated; rather, disability scores from patients with a skin score \(\geq 20\) were compared to those with a skin score \(< 20\) and significant differences were found\(^9\). That roughly half the patients in this study had skin scores \(\geq 20\) emphasizes the difference between this patient cohort and ours. That the median functional score in our cohort was only 6 indicates that most of our patients were only minimally functionally impaired.

An advantage of the functional index used in our study is that it is extremely quick and simple to complete, and avoids the use of visual analog scales that many patients find conceptually difficult. It was also based on patients’ reports on their predominant disabilities resulting from scleroderma. In SSc as in other rheumatic diseases, increasing attention is being paid to assessment of functional status\(^10\). Recently Ruof, et al reported another self-administered SSc questionnaire\(^11\) that included not only disability related questions but also questions about general and organ based involvement.

There is a need to develop and refine outcome measures for use in patients with SSc that accurately assess function and that are reproducible and sensitive to change, so that these can be incorporated into clinical trials\(^12\). The lack of relationship between functional index and skin score we observed does not negate the potential usefulness of this particular functional index as a measure of outcome in clinical trials in patients with SSc: it simply means that it is not a surrogate for skin score, probably because this functional index and skin score reflect different aspects of the SSc disease process. The functional index used in this study has not yet been evaluated prospectively, and so further work is required to assess its ability to detect change within an individual over time, as well as applying it in larger numbers of patients with early diffuse disease.

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REFERENCES


