Improving the sensitivity of the American College of Rheumatology classification criteria for systemic sclerosis

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ABSTRACT

Objective. *A large proportion of patients with limited systemic sclerosis (SSc) do not meet the current American College of Rheumatology (ACR) classification criteria for SSc. We undertook this study to determine whether the addition of easily available clinical variables, namely nailfold capillary abnormalities identified using a dermatoscope and visible telangiectasias, could improve the sensitivity of the current ACR classification criteria for patients with limited SSc.*

Methods. *Patients in the Canadian Scleroderma Research Group Registry with skin involvement distal to the metacarpophalangeal joints were identified and divided into two groups according to whether they fulfilled the current ACR classification criteria for SSc or not. Sensitivity of the criteria was calculated. Regression tree analysis was performed to determine whether the addition of nailfold capillary abnormalities identified using a dermatoscope and visible telangiectasias could improve the sensitivity of the criteria.*

Results. *One hundred and one (101) patients were included, in majority women with a mean age of 59 (± 13). Of these, 68 (67%) met the ACR classification criteria. The sensitivity of the criteria increased from 67% to 99% with the addition of nailfold capillary abnormalities identified using a dermatoscope and visible telangiectasias.*

Conclusions. *The SSc research community would benefit from having better classification criteria to identify patients with limited SSc. The current classification criteria for SSc may be significantly improved by the inclusion of easily identified clinical variables including nailfold capillary abnormalities using a dermatoscope.*

Introduction

Systemic sclerosis (SSc) is an extremely heterogeneous disease and presents a great deal of variability in the extent and severity of skin and visceral organ involvement (1). Thus, fundamental to the study of SSc, is the ability to classify disease. The current classification criteria for SSc are preliminary criteria developed by the American College of Rheumatology (ACR) in 1980 (2). However, experienced clinicians have noted that these criteria lack sensitivity especially for patients with limited skin involvement (3, 4). Some have found that as many as two thirds of patients with limited SSc may not meet the ACR criteria (5, 6).

Nailfold capillary abnormalities (7) and telangiectasias (8) are common in patients with limited SSc. As the criteria tend to exclude patients with limited disease in particular, there have been suggestions to revise them by including these abnormalities (5). Indeed, in a study of 152 patients with limited SSc, only 51 patients fulfilled the current ACR criteria. However, two thirds had significant nailfold capillary abnormalities and one third had clinically visible telangiectasias. Adding these two variables to the criteria improved the sensitivity for patients with limited disease from 34% to 89% (5). However, the capillary abnormalities in that study were identified using a widefield stereomicroscope. Most rheumatologists do not have easy access to this technology.

The Canadian Scleroderma Research Group (CSRG) is a unique consortium of experienced clinical and basic science researchers working together to further research in SSc. We have now established a common central database of patients from sites across Canada and are collecting extensive clinical and laboratory information on each patient. In particular, nailfold capillary abnormalities are being recorded using a dermatoscope (9). It is a handheld device used by dermatologists as an aid in the differential diagnosis of pigmented skin lesions. It does not require oil or water on the nailfold nor extensive training. It is thus quick and easy to use in the clinic and has been proposed as a tool for capillaroscopy (9).

Using the data collected on patients in the CSRG registry, we undertook to determine whether the addition of easily available clinical variables, namely nailfold capillary abnormalities identified using the dermatoscope and visible telangiectasias, could improve the sensitivity of the current ACR classification criteria for

patients with limited skin involvement, the subset of SSc in which the current criteria appear to lack sensitivity.

Methods
Patients
The patients consisted of those enrolled in the Canadian Scleroderma Research Group (CSRG) Registry. These patients undergo an extensive standardized evaluation including a history, physical evaluation and laboratory tests. The physical examination is performed by a rheumatologist and includes a detailed skin examination (10) to determine the extent of skin involvement. Among other things, the presence of sclerodactyly, digital pitting scars or loss of substance of the distal finger pad and bibasilar pulmonary fibrosis is also recorded. The purpose of this study was to determine whether we could improve the sensitivity of the current ACR criteria. We therefore included only patients with skin involvement distal to the metacarpophalangeal (MCP) joints (with or without face involvement) (4) because, by definition, those with skin invovlement proximal to the MCPs all meet the major criterion for SSc (2) and the sensitivity of the criteria is already 100% in that group.

Study measures
Nailfold capillary abnormalities were defined as the presence or absence of any dilated loops (definitely enlarged capillary loops, generally 4 to 6-fold the normal size), giant capillary loops (loops > 10 fold the normal size) and/or avascular areas (any confluent area free of capillary loops) for each digit. No scoring was done. In case of uncertainty, assessors were specifically instructed to report no abnormality. Any clinically visible mat-like telangiectasias on the face, limbs, chest or abdomen were recorded by a rheumatologist. Assessors were asked to record the presence of macular or dot telangiectasias, excluding those in normal sun exposed areas. One lesion was sufficient to be scored. Nailfold capillary abnormalities were recorded by a rheumatologist using a Dermlite® DL100 dermatoscope (3gen, LLC, Dana Point, CA, USA). This model provides fixed cross-polarization

Table I. Baseline characteristics of 101 patients with systemic sclerosis and skin involvement distal to the metacarpophalangeal joints enrolled in the Canadian Scleroderma Research Group Registry.

	Patients who do not fulfill the ACR criteria n = 33	Patients who fulfill the ACR criteria n = 68
Women (%)	94	92
Mean age (SD)	60 (12)	59 (13)
Mean disease duration in years (SD)		
Since onset of Raynaud's	16 (14)	16 (12)
Since onset of first non-Raynaud's manifestation of SSc	9 (7)	12 (10)
Disease variables		
Skin score*		
Mean (SD)	2.2 (1.0)	3.2 (1.7) [†]
Median (IQR)	2 (2, 2)	3 (2, 4) [††]
Minimum-maximum	0-4	0-6
Patients with facial involvement (%)	0	23 (34) [†]
Sclerodactyly (%)	33 (100)	67 (99)
Patients with pitting scars or loss of digital pulp (%)	0	38 (60) [†]
Patients with bilateral basilar pulmonary fibrosis (%)	0	43 (63) [†]
Nailfold capillary abnormalities (%)		
Dilated loops	22 (67)	46 (68)
Giant loops	8 (24)	21 (31)
Avascular areas	17 (52)	38 (56)
Any dilated, giant or avascular abnormalities	24 (73)	51 (75)
Any dilated or giant loops only	22 (67)	46 (68)
Telangiectasias (%)	25 (76)	56 (82)

ACR: American College of Rheumatology; SD: standard deviation
*Scored using the modified Rodnan skin score (10), ranging from 0 to 51.
[†] $p \leq 0.001$, [††] $p \leq 0.002$.

allowing oil-free ("dry") epiluminesence. It employs a 15mm 10x hastings triplet lens and diode lighting from 8 LEDs. No oil or water on the finger is required. Observations for nailfold abnormalities were made at the edge of the nailfold of the 3rd and 4th fingertips of the each hand.

Reliability of the dermatoscope
In a separate study, we assessed reliability of the dermatoscope. Kappa coefficients were 0.63, 0.40 and 0.20 for dilated capillaries, giant capillaries and avascular areas, respectively, for interobserver reliability and 0.71, 0.55 and 0.40 for dilated capillaries, giant capillaries and avascular areas, respectively, for intra-observer reliability (11).

Statistical analysis
A regression tree analysis was performed in the following manner. Patients were divided into those who met and those who did not meet the current ACR classification criteria for SSc. Of those who did not meet the criteria, pa-

tients were divided into those with and without nailfold capillary abnormalities. Finally, of those who did not meet the ACR criteria and did not have nailfold capillary abnormalities, patients were divided into those with and without clinically visible telangiectasias. Sensitivity was defined as the number of patients classified as having SSc divided by the total number of patients and was calculated at every step. The regression tree analysis is equivalent to building successive contingency tables and examining the increase in positively identified patients for each additional dimension of the table. We repeated this process on 1000 re-sampled datasets to obtain boostrap confidence interval estimates (12). Given the limited reliability to detect avascular areas using the dermatoscope, we performed a sensitivity analyses by re-defining nailfold capillary abnormailites as dilated loops and/or giant capillary loops only.

Ethical consideration
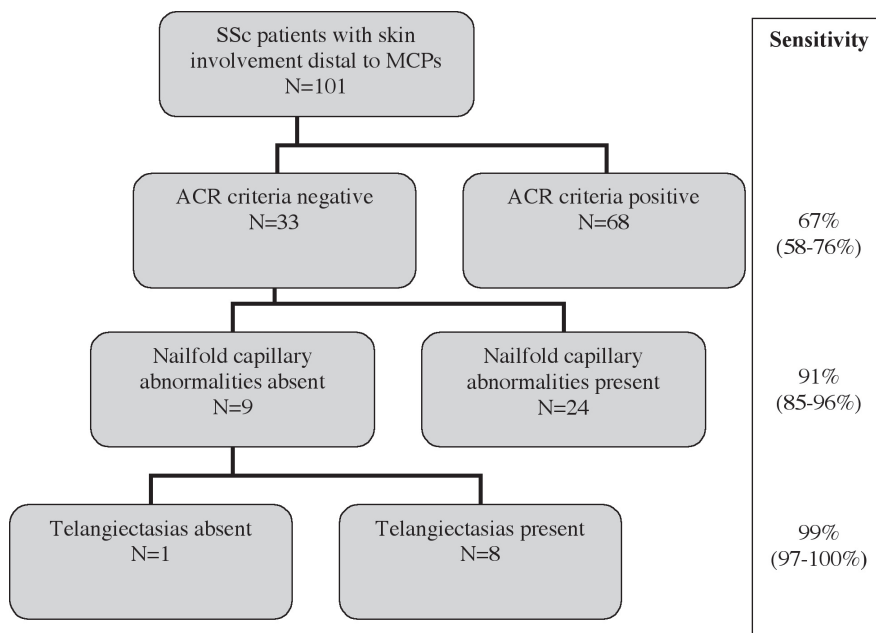Ethics committee approval for this study

Fig. 1. Sensitivity (95% confidence intervals) to identify SSc patients with skin involvement distal to the metacarpophalangeal (MCP) joints when clinical abnormalities are added to the current American College of Rheumatology (ACR) classification criteria.

was obtained at each CSRG site and each patient provided informed written consent to participate in this study.

Role of the funding sources
The funding sources had no role in the design of the study, analysis of the data, preparation of the manuscript and decision to submit for publication.

Results
In this study, we included 101 patients with skin involvement distal to the metacarpo-phalangeal joints only and complete clinical data. The baseline characteristics of the patients included in the study are presented in Table I. Among the 101 patients studied, only 68 met the current ACR criteria for SSc. There were no significant differences in terms of gender, age, disease duration and frequency of sclerodactyly between those who did and those who did not fulfill the ACR criteria. However, as could be expected, those who did not fulfill the criteria had significantly less skin involvement, digital pitting scars or loss of digital pulp and bilateral basilar pulmonary fibrosis.
The sensitivity of the ACR criteria was only 67% in this subset of patients with limited disease (Fig. 1). Addition of nailfold capillary abnormalities and

clinically visible telangiectasias improved the sensitivity to 99%.
In sensitivity analysis, similar results were obtained when nailfold capillary abnormalities were defined as dilated and/or giant loops only (data not shown).

Discussion
In this cohort of patients with SSc, we have shown that the addition of easily obtained clinical information to the current ACR criteria for SSc significantly improves the sensitivity to identify a subset of patients with limited disease. The significance of our findings is threefold. First, the fact that only 67% of our patients with disease distal to the MCPs meet the current ACR classification criteria for SSc underscores the poor sensitivity of these criteria for this subset of patients with limited disease and supports the need to review them. Second, the addition of easily available clinical data results in remarkable improvement in the sensitivity of the current ACR classification criteria and supports the use of such variables in ongoing efforts to update the criteria. Third, although Lonzetti *et al.* also reported that the sensitivity of the ACR criteria to identify patients with limited disease improved with the addition of nailfold capillary abnormalities and vis-

ible telangiectasias (from 34% to 89%) (5), nailfold capillary abnormalities in that study were identified using a wide-field stereomicroscope. That technique is not easily accessible to most rheumatologists. Our study documented nailfold capillary abnormalities using a handheld dermatoscope, an easy-to-use and accessible instrument that requires little formal training. Since our results parallel those of the Lonzetti study, our findings support the validity of our capillaroscopy technique using the dermatoscope.
Although we showed a significant improvement in sensitivity with the addition of the clinical abnormalities described, this study does not allow us to assess specificity. This would require a comparison group of patients without SSc. Indeed, nailfold capillary abnormalities (13) and telangiectasias (14) have been described in other auto-immune diseases. Thus, it is possible that addition of these abnormalities as criteria could theoretically compromise specificity. On the other hand, a "SSc pattern" of nailfold capillary abnormalities has been described and may be useful to ensure that the specificity of classification criteria including this clinical variable is preserved (15, 16). Similarly, to our knowledge, mat-like telangiectasias have been described only in SSc and may therefore be relatively specific (17). Clearly, a large study of patients both with and without SSc will be required to define new classification criteria that have the best sensitivity without losing specificity.
A possible limitation of this study is that some patients with early diffuse disease, whose skin disease was still minimal, may have been included in our sample of patients defined as having limited disease. Nevertheless, as indicated in Table I, the mean disease duration of the patients in this study was very long. Diffuse disease, in general, progresses early and plateaus after a few years (18). Thus, although we may have included a few cases of diffuse disease in our sample, we do not think that there were many.
The main purpose of classification criteria is to standardize clinical definitions for use in research studies. Several groups in Canada, the US and Europe

now have extensive research programs in SSc. The entire research community will benefit from having better criteria to correctly identify patients with SSc. This study provides proof of concept that the sensitivity of the current classification criteria for SSc may be significantly improved by easily identified clinical variables including nailfold capillary abnormalities using a dermatoscope.

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