NAILFOLD CAPILLAROSCOPY ABNORMALITIES CORRELATE WITH CUTANEOUS AND VISCERAL INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS

Lucy T Sato,* Cristiane Kayser,* Luís E C Andrade*

Abstract

Objective: The aim of this study was to correlate quantitative and semiquantitative nailfold capillaroscopy (NFC) parameters with the extent of cutaneous and visceral involvement in systemic sclerosis (SSc) patients.
Methods: The presence of clinical and serological alterations was evaluated retrospectively and correlated with NFC findings (number of capillary loops/mm, vascular deletion score and number of enlarged and giant capillary loops). For evaluation of disease extension five manifestations were analyzed: finger pad lesions, skin involvement, esophageal involvement, interstitial lung disease, and pulmonary hypertension.
Results: There were 105 NFC examinations in 92 patients, 13 of whom were evaluated at two different time points. Patients with diffuse cutaneous SSc had a higher vascular deletion score than patients with limited cutaneous SSc, *sine scleroderma* SSc, and overlap syndrome (1.67±0.91 vs 0.99±0.82; p=0.0005). Modified Rodnan's skin score correlated positively with capillary deletion, evaluated by the vascular deletion score and the number of capillary loops/mm (p<0.001 and p=0.012; respectively). Patients with three or more involved tracts presented lower number of capillary loops/mm (8.00±1.69 vs 9.23±1.31 capillary loops/mm; p=0.025) and a higher vascular deletion score (1.41±0.95 vs 0.73±0.76; p=0.027) when compared to patients with less than three affected tracts. Vascular deletion score was significantly higher in patients with anti-Scl-70 antibodies that in patients without anti-Scl-70 antibodies (p=0.02).
Conclusions: NFC abnormalities correlated positively with the diffuse form of SSc, the degree of cutaneous involvement, the number of affected tracts, and the presence of anti-Scl-70 antibodies.

*Rheumatology Division, Universidade Federal de São Paulo, São Paulo, Brazil

Keywords: Microcirculation; Nailfold capillaroscopy; Raynaud's phenomenon; Systemic sclerosis.

Resumo

Objectivo: Correlacionar parâmetros quantitativos e semiquantitativos da capilaroscopia perinungueal (CPU) com a extensão do acometimento cutâneo, envolvimento visceral e alterações sorológicas em pacientes com esclerose sistêmica (ES).
Métodos: A presença de alterações clínicas e sorológicas foi avaliada retrospectivamente e correlacionada com os achados capilaroscópicos (número de capilares/mm, *score* de deleção vascular e número de capilares ectasiados e megacapilares). Para avaliação da extensão da doença, cinco manifestações foram analisadas: lesões em polpa digital, acometimento cutâneo, envolvimento esofagiano, doença pulmonar intersticial e hipertensão pulmonar.
Resultados: Foram avaliadas 105 CPUs realizadas em 92 pacientes, 13 dos quais foram avaliados em dois tempos diferentes. Pacientes com ES forma cutânea difusa apresentaram maior *score* de deleção vascular do que pacientes com ES forma cutânea limitada, ES *sine scleroderma* SSc e em superposição (1,67±0,91 *vs* 0,99±0,82; p=0,0005). O *score* cutâneo de Rodnan modificado se correlacionou positivamente com desvascularização capilar, avaliado pelo *score* de deleção vascular e pelo número de capilares/mm (p<0,001, p=0,012; respectivamente). Pacientes com três ou mais órgãos acometidos apresentaram menor número de capilares/mm (8,00±1,69 *vs* 9,23±1,31 capilares/mm; p=0,025) e maior *score* de deleção vascular (1,41±0,95 *vs* 0,73±0,76; p=0,027) em comparação com pacientes com menos de três órgãos acometidos. O *score* de deleção vascular foi significativa-

mente maior nos pacientes com anticorpos anti-Scl-70 quando comparados com pacientes com ausência destes anticorpos (p=0,02).
Conclusões: Alterações na CPU se correlacionaram positivamente com a forma cutânea difusa da ES, o grau de acometimento cutâneo, o número de órgãos envolvidos e a presença de anticorpos anti-Scl-70.

Palavras-Chave: Microcirculação; Capilaroscopia Periungueal; Fenômeno de Raynaud; Esclerose Sistêmica.

Introduction

Systemic Sclerosis (SSc) is an autoimmune rheumatic disease of unknown etiology characterized by vascular alterations and tissue fibrosis of multiple organs. It affects mostly the skin, musculoskeletal system, heart, kidneys, lungs and gastrointestinal tract.[1] Vascular structural alterations and lesions are detected early and seem to play an important role in SSc pathogenesis. Dysfunction of vascular tone control, endothelial activation/lesion, and myointimal cell proliferation of small blood vessels and capillaries result in progressive reduction of vessel lumen, decreased blood flow, and a state of chronic hypoxia.[2,3] In the periphery, microvascular damage is characterized by enlargement and distortion of capillary loops, micro-haemorrhages and progressive devascularization.[4,5]

Peripheral microangiopathy can be easily recognized by widefield nailfold capillaroscopy (NFC), a noninvasive and safe method, that is well established in the investigation of patients with Raynaud's phenomenon and SSc.[5,6] Patients with SSc exhibit a typical pattern at NFC, designated "SD pattern" by Maricq et al., and characterized by enlargement of capillary loops, loss of capillaries, disruption of the orderly appearance of the capillary bed and distortion of capillaries.[7] Maricq et al., defined also two major nailfold capillary patterns, namely the "active" (extensive loss of capillaries and minimal capillary enlargement) and the "slow" (capillary enlargement and/or extremely enlarged capillaries with no or minimal capillary loss) pattern.[5] Recently, Cutolo et al., have reclassified the scleroderma microangiopathy into 3 different patterns: "early", "active" and "late" pattern.[8] The early pattern is characterized by few enlarged/giant capillaries, few hemorrhages, relatively well-preserved capillary distribution and no evident loss of capillaries; in the "active" pattern there are frequent giant capillaries and hemorrhages, moderate loss of capillaries, mild disorganization of the capillary architecture, absence or mild ramified capillaries, and presence of edema; the "late" pattern is characterized by irregular enlargement of the capillaries, few or no giant capillaries and hemorrhages, severe loss of capillaries with extensive avascular areas, disorganization of the normal capillary array, and presence of ramified/bushy capillaries.[8] The SD pattern has been observed in 84-97% of SSc patients but is not strictly limited to patients with SSc and can also be found in dermatomyositis, mixed connective tissue disease, and overlap syndromes with SSc.[4,5,9,10] Several studies have addressed a possible relationship between NFC alterations and the extent of skin and visceral involvement in SSc.[11-15] The apparently controversial findings of some of these studies are possibly due to small and heterogeneous samples of patients and also to heterogeneous methodology in the interpretation of NFC findings.

Our group has previously reported on a reproducible NFC method, comprehending several microangiopathic parameters assessed in quantitative and semiquantitative manner, evaluating all 10 fingers of the hands.[6] The aim of the present study was to report the morphological alterations in the peripheral microcirculation, evaluated by panoramic nailfold capillaroscopy (NFC) using the method proposed by Andrade et al.,[6] and to correlate these microvascular abnormalities with cutaneous and visceral involvement, in a large sample of patients with SSc.

Patients and Methods

Patients

This was a retrospective study which included all SSc patients seen in a two-year interval (2003-2004) at the Scleroderma Spectrum Outpatient Clinic at Federal University of São Paulo (UNIFESP) Medical School Hospital. All patients with at least one NFC exam performed in the last 15 years were included in the study. SSc diagnosis was based on the American College of Rheumatology (ACR) criteria.[16] Disease subtype was classified as follows: diffuse cutaneous SSc (skin thickening on the trunk, face, in addition to proximal and distal extremities), limited cutaneous SSc (skin thickening localized to the face and neck, and distal to the elbows

and knees), *sine* scleroderma SSc, and in overlap syndromes.[17,18] For further clinical, serological and capillaroscopic analysis patients were divided into two groups: diffuse SSc and non-diffuse SSc. The latter category comprised patients with limited cutaneous SSc, *sine* scleroderma SSc and patients with overlap syndromes.

Nailfold capillaroscopy

All NFCs were performed in a stereomicroscope (Olympus - SZ40) under 10-20 x magnification according to the protocol proposed by Andrade et al.[6] All the ten digits of the hands were examined, except when prevented by extremely poor visibility or amputation. The following parameters were analyzed: (1) number of capillary loops/mm, (2) vascular deletion score, (3) number of enlarged loops (about four times the normal afferent, transition, and efferent limbs width), and (4) number of giant capillary loops (10 or more times the normal width of capillary limbs). Enlarged and giant loops were counted together. The vascular deletion score was assessed according to Lee's method,[19] in which a deletion area is defined as the absence of two or more consecutive loops. Each finger was rated from 0 to 3: grade 0 – no deletion area; 1 – one or two discrete deletion areas; 2 – more than two discrete deletion areas; 3 – extensive and confluent deletion areas. For each patient the NFC parameters were calculated as the average obtained in all analyzed digits.

During the 15-year period NFCs were performed by three investigators with similar NFC training. All exams were performed according to the same NFC protocol, and examiners had no information about the patient's clinical condition. Reproducibility of the NFC examination was tested as previously described.[6]

Clinical and laboratory evaluation

All clinical and laboratory data were collected retrospectively from medical charts according to a standardized protocol routinely filled out at each visit to the Scleroderma Spectrum Outpatient Clinic during the period of 1989 to 2004.

The presence and extent of cutaneous involvement was assessed by the modified Rodnan's skin score.[20] Finger pad lesions were defined as the presence of active digital ulcerations, digital pitting scars, resorption and/or digital amputations. Esophageal involvement was evaluated by the presence of esophageal dismotility on barium contrast roentgenographic study of the upper gastrointestinal tract. The presence of lung interstitial disease was defined by forced vital capacity (FVC) < 75% of the predicted values and/or bibasal interstitial pulmonary infiltrate on chest radiogram and/or high resolution computed tomography (HRCT) showing ground-glass opacities, reticular or honeycombing pattern. Pulmonary hypertension was defined by pulmonary systolic arterial pressure (PSAP) >35mmHg, estimated on Doppler echocardiography. Finally, renal scleroderma crisis was defined by the presence of malignant hypertension and renal failure.

For evaluation of disease extension five manifestations were analyzed: (1) finger pad lesions, (2) presence of skin thickness, (3) presence of esophageal dismotility on barium study, (4) interstitial lung disease, and (5) presence of pulmonary hypertension. Only patients with available information on these five manifestations were included.

Antinuclear antibodies (ANA) were determined by indirect immunofluorescence using HEp-2 cell as substrate. Anticentromere antibodies were identified by the typical pattern on the indirect immunofluorescence HEp-2 cell assay and anti-topoisomerase I (anti-Scl-70) antibodies were determined by the double immunodiffusion method against rabbit thymus extract.

For all included patients, the clinical-laboratory evaluation was not more than 12 months apart the NFC evaluation. Patients with more than one NFC made more than 12 months apart were handled in two alternative ways. If the NFCs conclusions were different (normal NFC or nonspecific capillary alterations on the first exam and presence of SD pattern on the second, or the contrary), the clinical and laboratorial findings were analyzed at each time and compared to the relevant NFC exam. Alternatively, if the NFCs conclusions were similar in both occasions, only the NFC with closest available clinical-laboratory evaluation was taken into consideration. However, if the interval between NFCs was higher than three years each NFC/clinical/laboratory set was individually analyzed. Patients with no NFC record were excluded from the study.

Statistical analysis

Results are presented as mean and standard deviation. Correlations between NFC, clinical and laboratory parameters were evaluated by Pearson's or Spearman's correlation analysis. Associations

between qualitative parameters were analyzed by the Chi square test. Mann-Whitney's test was used to compare quantitative variables. $p<0.05$ was considered significant.

Results

One hundred and five NFCs were evaluated in 92 patients, 13 of whom were evaluated at two different moments within a time interval varying from 2.5 to 12 years. The mean age of patients (79 women and 13 men) at each NFC evaluation was 47.4 years (ranging from 19 to 71) and the mean age at disease onset was 40.1 ± 13.9 years (ranging from 11 to 68). Thirty-two patients (35%) had diffuse cutaneous SSc and 60 (65%) had non-diffuse SSc, comprising 42 (45.65%) with limited cutaneous SSc, 8 (8.7%) with SSc *sine* scleroderma, and 10 (10.9%) with SSc in the context of overlap syndrome (one with rheumatoid arthritis, five with polymyositis and four with systemic lupus erythematosus) and with cutaneous involvement limited to the face and distal extremities. Among the 105 evaluations, 35 were in patients with diffuse cutaneous SSc, and 70 in patients with non-diffuse SSc. The clinical and laboratory characteristics of the patients in each evaluation are depicted in Table I. The duration of RP at time of the NFC evaluation was significantly longer in patients with non-diffuse SSc as compared with those with diffuse cutaneous disease (p=0.008). The mean modified Rodnan's skin score was 20.86 ± 11.64 in patients with diffuse SSc and 6.81 ± 6.45 in patients with non-diffuse SSc.

SD pattern was found in 84% of the NFCs. The mean number of capillary loops/mm was 8.06 ± 1.72. The mean number of enlarged and giant capillary loops in each digit was 3.38 ± 2.92 capillaries, and the mean vascular deletion score was 1.22 ± 0.91.

Patients with diffuse cutaneous SSc showed hi-

Table I. Clinical and laboratory characteristics of Systemic Sclerosis (SSc) patients

Clinical and laboratorial characteristics	Diffuse cutaneous SSc (n=35)	Non-diffuse SSc (n=70)	Total of Evaluations (n=105)	P (Diffuse vs Non-diffuse SSc)
Disease duration (years)	5.29 ± 4.10	8.61 ± 7.78	7.37 ± 6.92	P= 0.03
Vascular				
Raynaud's phenomenon (RP)	34/35 (97%)	66/69 (96%)	100/104 (96%)	NS
Duration of RP (years)	4.29 ± 3.40	8.40 ± 8.13	7.06 ± 7.24	P= 0.008
Alterations of digital pad	26/31 (84%)	29/45 (64%)	55/76 (72%)	NS
Skin thickness	33/34 (97%)	58/69 (84%)	91/103 (88%)	NS
Telangiectases	9/24 (37.5%)	28/41 (68%)	37/65 (57%)	P= 0.016
Calcinoses	2/21 (9.5%)	2/22 (9%)	4/43 (9%)	NS
Esophageal involvement				
Disfagia	18/34 (53%)	37/65 (57%)	55/99 (55%)	NS
Esophageal hypomotility	15/26 (58%)	33/50 (66%)	48/76 (63%)	NS
Interstitial lung disease				
FVC < 75%	16/29 (55%)	22/64 (34%)	38/93 (40%)	NS
Bibasal interstitial pulmonary infiltrate on chest radiogram	8/15 (53%)	17/37 (46%)	25/52 (48%)	NS
HRCT with ground-glass opacities, reticular patters or honeycombing	15/20 (75%)	21/27 (78%)	36/47 (77%)	NS
Pulmonary hypertension	3/29 (10%)	7/52 (13%)	10/81 (12%)	NS
Renal scleroderma crisis	0/10 (0%)	0/32 (0%)	0/42 (0%)	NS
Antinuclear antibodies	28/34 (82%)	62/69 (90%)	90/103 (87%)	NS
Anticentromere	0/30 (0%)	22/62 (35%)	22/92 (24%)	P<0.0001
Anti-Scl70	6/18 (33%)	4/22 (18%)	10/40 (25%)	NS

FVC: forced vital capacity; HRCT: high resolution computed tomography; NS: not significant .

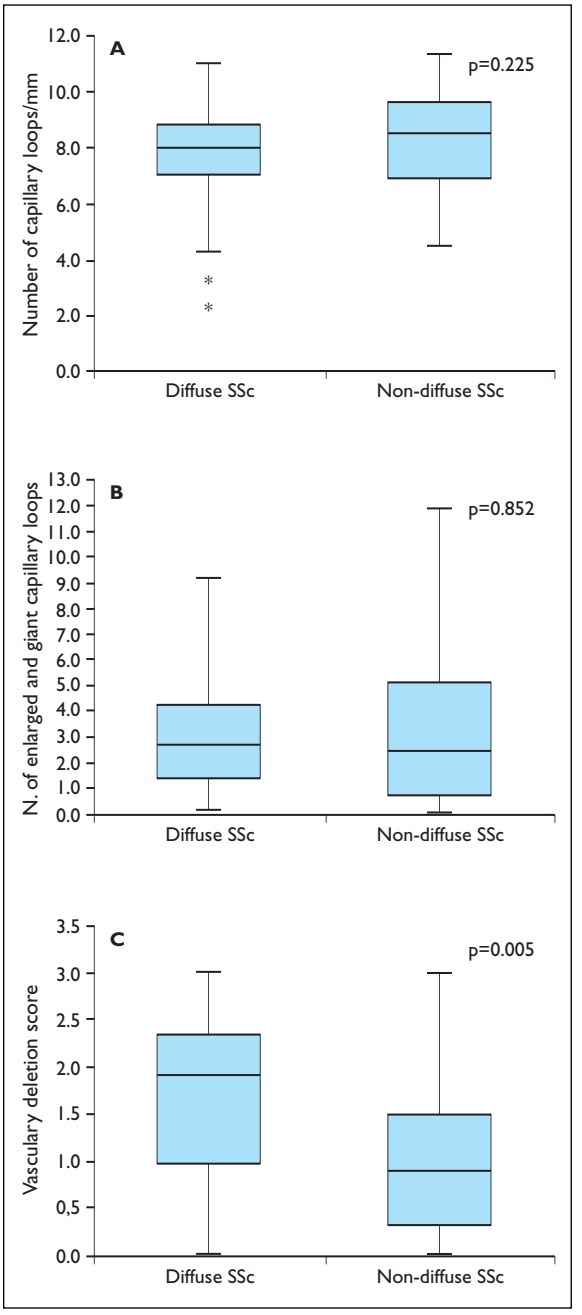

Figure 1. Distribution of the number of capillary loops/mm (**a**), number of enlarged and giant capillary loops (**b**) and, vascular deletion score (**c**) on nailfold capillaroscopy in patients with diffuse systemic sclerosis (SSc) and non-diffuse SSc.

Box-Plot graph: Rectangles depict 50% of the sample; thick horizontal bar corresponds to median; upper and lower horizontal bars represent highest and lowest figures. The symbol (*) represents outliers. N: number.

gher vascular deletion scores than those with non-diffuse disease (1.67±0.91 *vs* 0.99±0.82; p=0.0005). In contrast, no statistically significant difference was found between patients with diffuse cutaneous SSc and those with non-diffuse disease concerning the number of capillary loops/mm (7.75±1.80 *vs* 8.21±1.67 loops/mm; p=0.225) and the number of enlarged and giant capillary loops (3.19±2.37 *vs* 3.46±3.17; p=0.852) (Figure 1). Modified Rodnan's skin score showed a moderate positive correlation with vascular deletion score (r= 0.52; p<0.001) and a modest negative correlation with the number of capillary loops/mm (r = -0.26; p=0.012).

Patients with presence of finger pad lesions showed higher vascular deletion scores and decreased number of capillary loops/mm than those with absence of finger pad lesions (1.49 ± 0.90 *vs* 0.86 ± 0.82, p=0.01; 7.71 ± 1.79 *vs* 8.64 ± 1.15, p=0.03, respectively) (Table II). Among patients with esophageal dismotility, we found higher number of enlarged and giant capillary loops than those with absence of esophageal dismotility (4.28 ± 3.27 *vs* 2.82 ± 2.42, p=0.04). No difference was detected in the three NFC parameters analyzed between patients with pulmonary hypertension or interstitial lung disease and patients without these manifestations (Table II).

Visceral involvement was studied in 50 patients who had simultaneous records for the five manifestations evaluated. These patients were classified into those presenting up to two involved tracts (n=10) and those presenting three or more involved tracts (n=40). Patients with three or more involved tracts showed lower number of capillary loops/mm and higher vascular deletion score than patients with less than three involved tracts (8.00±1.69 vs 9.23±1.31 loops/mm; p=0.025; and 1.41±0.95 vs 0.73±0.76; p=0.027, respectively) (Figure 2). There was no difference in the number of enlarged and giant capillary loops between the two groups (3.39±2.94 *vs* 3.24±2.34; p=0.98) (Figure 2).

The presence of anti-Scl-70 antibodies was studied in 40 patients at the time of the NFC. The vascular deletion score was significantly higher in patients with anti-Scl-70 antibodies (1.74±0.82) as compared with patients without anti-Scl-70 antibodies (1.11±0.96) (p=0.02). No significant difference was found in the number of capillary loops/ /mm or in the number of enlarged and giant capillary loops between patients with and without anti-Scl-70 antibodies (Table III). No patient with diffuse disease had anti-centromere antibody. Therefore, the

Table II. Nailfold capillaroscopy (NFC) alterations and correlation with finger pad lesions, esophageal dismotility, pulmonary hypertension and interstitial lung disease

	Finger Pad Lesions				
NFC alterations	**Present**	**n**	**Absent**	**n**	**P**
N. of capillary loops/mm	7.71 ± 1.79	55	8.64 ± 1.15	21	0.03
N. of enlarged and giant capillary loops	3.89 ± 2.79	55	2.58 ± 2.18	21	NS
Vascular deletion score	1.49 ± 0.90	55	0.86 ± 0.82	21	0.01
Esophagel Dismotility					
N. of capillary loops/mm	7.80 ± 1.44	48	8.51 ± 1.74	28	NS
N. of enlarged and giant capillary loops	4.28 ± 3.27	48	2.82 ± 2.42	28	0.04
Vascular deletion score	1.30 ± 0.86	48	1.04 ± 0.80	28	NS
Pulmonary Hypertension					
N. of capillary loops/mm	8.93 ± 1.15	10	8.06 ± 1.69	71	NS
N. of enlarged and giant capillary loops	1.82 ± 1.91	10	3.68 ± 2.91	71	NS
Vascular deletion score	1.0 ± 0.82	10	1.31 ± 0.95	71	NS
Interstitial Lung Disease					
N. of capillary loops/mm	8.18 ± 1.69	62	8.01 ± 1.62	38	NS
N. of enlarged and giant capillary loops	3.38 ± 2.99	62	3.97 ± 3.50	38	NS
Vascular deletion score	1.28 ± 0.95	62	1.12 ± 0.84	38	NS

N: number; NS: not significant.

association between anti-centromere antibodies and NFC abnormalities was performed only for the non-diffuse SSc patients. Among patients with non-diffuse disease no significant difference in the three NFC parameters was found between the 22 patients with anti-centromere antibodies and the 40 patients without anti-centromere antibodies (Data not shown).

Discussion

The results herein obtained were derived from a large sample of SSc patients retrospectively analyzed for NFC, clinical and laboratory variables. It represents a retrospective analysis gathering the cumulated 15-year experience using the same NFC protocol in our center.[6] This NFC protocol has the advantage of gathering well-established quantitative and semiquantitative parameters, such as the number of capillary loops, the vascular deletion score, and the number of enlarged loops analyzed in all 10 fingers of the hands. The present results showed a clear-cut association between the degree of microangiopathic alterations detected by NFC and the extent of cutaneous and visceral involvement of the disease. Among the several nailfold microvascular abnormalities observed in SSc the parameters related to devascularization (vascular deletion scores and/or number of capillary loops/ /mm), but not those related to capillary enlargement, were significantly associated with more extensive skin involvement, diffuse cutaneous SSc, presence of finger pad lesions and with a more extensive visceral involvement. In addition, patients with anti-Scl-70 antibodies had also higher vascular deletion scores.

The microangiopathic abnormalities characterized by devascularization and capillary enlargement are specifically observed in SSc and related diseases and tend to occur at early stages of the disease, what has granted a place for NFC in the clinical investigation of SSc and in the differential diagnosis of Raynaud's phenomenon.[21,22] This is especially relevant for the evaluation of patients at early stages of the disease, in which isolated Raynaud's phenomenon may be the only clinical manifestation. In that way, NFC has been found to bee especially helpful in distinguishing primary Raynaud's phenomenon (functional, not related to disease) from secondary Raynaud's phenomenon.[23] In a meta-analysis study, it has been found that among patients with presumed primary Raynaud's phenomenon, a secondary disorder developed in 12% of patients.[24] In patients with Raynaud's phenomenon NFC can be very helpful to exclude a se-

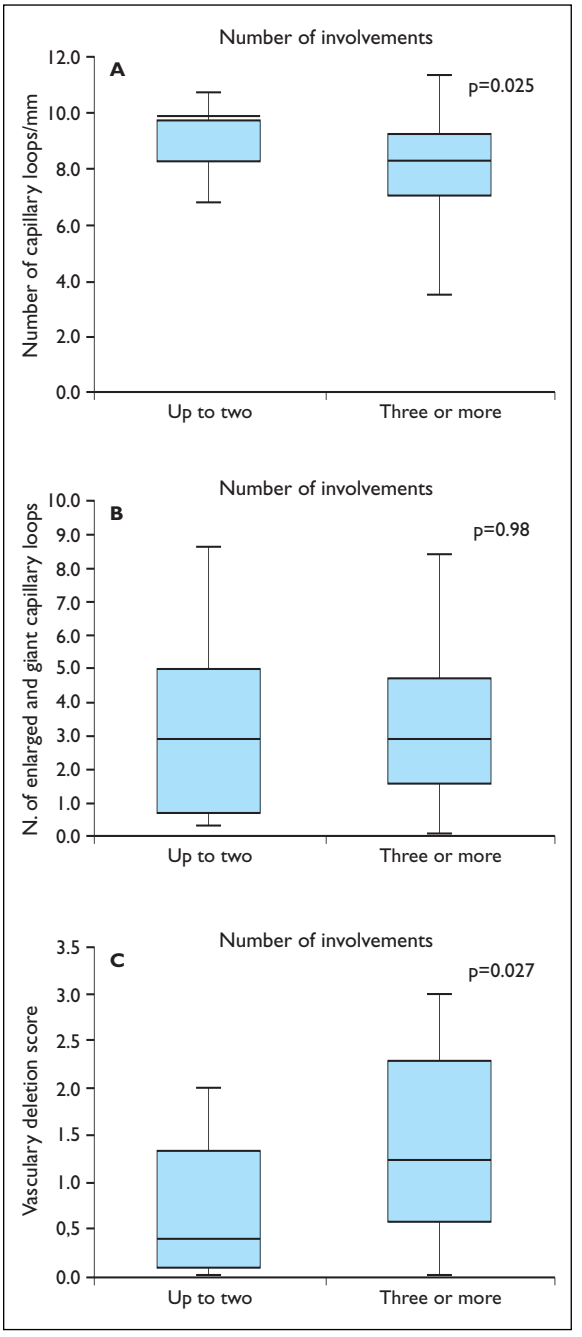

Figure 2. Distribution of patients with up to two involvements or three or more involvements according the number of capillary loops/mm (**a**), number of enlarged and giant capillary loops (**b**) and, vascular deletion score (**c**) on nailfold capillaroscopy.

Box-Plot graph: Rectangles depict 50% of the sample; thick horizontal bar corresponds to median; upper and lower horizontal bars represent highest and lowest figures. N. number.

condary disorder, since it has a high negative predictive value for the development of a connective tissue disease (>90%). On the other hand, its positive predictive value is about 50%, which is higher than any other single screening test.[23,24] The possibility that the NFC abnormalities might also correlate with the extent of cutaneous and visceral involvement in SSc is intriguing and could have implications for the understanding of the disease pathophysiology and for the clinical assessment of patients.

The results obtained in the present study confirm previous reports on a positive correlation between the degree of abnormalities at NFC and the extent of cutaneous and visceral involvement in SSc.[11,12,25-27] Maricq et al, in 1976, first studied this issue by analyzing capillary abnormalities in 28 SSc patients, 13 with Raynaud's phenomenon and 3 with dermatomyositis.[11] A positive correlation was found between the degree of microvascular abnormalities and the number of affected systems. In another study of the same group, a positive association was founded between the presence of the "active" pattern on NFC and more extensive skin involvement. They also presented a higher frequency of involvement of all organ systems than those with a "slow" pattern.[12] Recently, Ostojic and Damjanov,[25] also found more extensive capillary loss in patients with diffuse cutaneous SSc comparing to patients with limited SSc. Also in accordance with our findings, Bredemeier et al.,[15] found a positive correlation between the vascular deletion score in NFC and higher Rodnan's skin score, presence of anti-Scl-70 antibodies, signs of peripheral ischemia, esophageal dysfunction and pulmonary disease. On the other hand, some other studies could not find such association.[14,28] Heterogeneity in patient selection and NFC methodology may contribute to the lack of association observed in the latter studies.

In our study anti-Scl-70 antibodies were determined only in 40 patients at the time of the analysis due to non-availability of anti-Scl-70 at the institution. Despite this limitation we found higher vascular deletion scores in patients with anti-Scl-70 antibodies in the sera. The latter association supports a possible relationship between disease severity and NFC abnormalities since this autoantibody has been previously demonstrated to be associated with more severe and extensive disease.[29]

The analysis of the present series of patients disclosed epidemiological features similar to those

Table III. Nailfold capillaroscopy (NFC) alterations and correlation with anti-Scl 70 antibodies

	Anti-Scl 70 antibodies				
NFC alterations	**Present**	**n**	**Absent**	**n**	**P**
N. of capillary loops/mm	7.12 ± 1.58	10	8.32 ± 1.87	30	NS
N. of enlarged and giant capillary loops	3.07 ± 1.65	10	2.50 ± 2.43	30	NS
Vascular deletion score	1.74 ± 0.82	10	1.11 ± 0.96	30	P=0.02

N: number; NS: not significant.

registered in the literature in that there was female predominance, disease onset around 40 year old in average, and the predominance of the cutaneous limited disease.[17,30] As for the distribution of clinical manifestation it is noteworthy that there was no case of renal scleroderma crisis, what may be due to bias of the retrospective study.

It is relevant to point out that the present study represents a retrospective analysis of the cumulative 15-year experience with NFC uniformly performed according to the protocol proposed by Andrade et al.[6] This protocol uses established quantitative and semi quantitative techniques, allowing the concomitant determination of several parameters that are strongly associated with SSc, such as the number of capillary loops, the number of enlarged loops and the degree of avascular score. It should also be emphasized that conventional NFC is a simple and low cost method, and therefore feasible in any average Rheumatology Division. More recently studies using videocapillaroscopy has been also published with interesting results.[26,31] However it should be noticed that this is a much more expensive method and is restricted to specialist centers.

Nonetheless, the retrospective design of the study bears some intrinsic limitations. For example, not all patients followed in our hospital had the necessary records for NFC, clinical and laboratory data within a one-year interval and therefore could not be included in the study. In addition only 50 patients could be included for the analysis of correlation of NFC abnormalities and the number of involved tracts, since the other ones did not have the required simultaneous records for the five clinical involvements. On the other hand, this particular retrospective analysis is strengthened by the fact that these patients have been followed by the same standard protocol for clinical, laboratory and NFC evaluation.

Despite these limitations, the results obtained showed a clear-cut association of the degree of NFC microangiopathy with the extension of the cutaneous and visceral involvement as well as with the presence of anti-Scl-70 antibodies. Therefore, it is appropriate to consider the NFC approach for the evaluation of the extension and severity of SSc. Prospective studies with long follow-up are warranted to investigate a possible role for nailfold capillary microscopy in the prediction of disease extension and severity.

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Correspondence to

Luís E. C. Andrade
Universidade Federal de São Paulo (UNIFESP),
Rheumatology Division
Rua Botucatu 740, 3º andar
CEP 04023-062, São Paulo, SP, Brazil
E-mail: luis.andrade@unifesp.br

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