# Nailfold Videocapillaroscopy Alterations in Dermatomyositis and Systemic Sclerosis: Toward Identification of a Specific Pattern

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***ABSTRACT.*** ***Objective.*** The term *scleroderma pattern* typically defines capillary abnormalities of scleroderma spectrum disorders, mainly systemic sclerosis (SSc) and dermatomyositis (DM). Our study aimed to investigate differences in nailfold videocapillaroscopy (NVC) between DM and SSc, with a cross-sectional and longitudinal evaluation.

***Methods.*** NVC features of 29 consecutive patients with DM were compared with 90 patients with SSc categorized into the 3 subsets of scleroderma pattern: early, active, and late. Twenty patients with DM and all with SSc were also longitudinally reevaluated after 30 months of followup.

***Results.*** At baseline, all SSc groups showed giant capillaries, with significant differences with DM only for early and active pattern. Ramified capillaries were significantly more frequent and severe in DM than in early and active patterns, while DM showed an opposite trend compared with late pattern. Capillary loss was lower in early pattern and higher in active and late, compared with DM. Finally, giant-ramified capillaries were almost exclusive of DM. During followup, NVC showed a different evolution in DM and SSc. In DM we recorded a reduction of giant capillaries, while ramified capillaries increased both in DM and in early and active SSc pattern. The number of capillaries recovered in DM; conversely, capillary loss slightly worsened in all SSc patterns. Giant-ramified capillaries significantly decreased in patients with DM, remaining rare in patients with SSc.

***Conclusion.*** Our study strengthens the specificity of DM and SSc microangiopathy and points out the need for large prospective studies to confirm our results and possibly to revise current terminology by distinguishing between "scleroderma" and "dermatomyositis" patterns. (First Release June 15 2016; J Rheumatol 2016;43:1575–80; doi:10.3899/jrheum.160122)

*Key Indexing Terms:*
SYSTEMIC SCLEROSIS DERMATOMYOSITIS MICROANGIOPATHY
VIDEOCAPILLAROSCOPY SCLERODERMA PATTERN

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*Accepted for publication April 19, 2016.*

The term *scleroderma pattern* was first used by Brown and O'Leary in 1925 to define capillary abnormalities in the course of systemic sclerosis (SSc)[1]. It is represented by the association of typical capillaroscopic microvascular alterations, namely giant capillaries, microhemorrhages, ramified capillaries, microvascular array disorganization, and capillary loss or avascular areas[2,3,4]. It has since been observed that scleroderma pattern is not specific to SSc, but potentially associated with scleroderma spectrum disorders, including (with some variations according to different authors) SSc, myositis, systemic lupus erythematosus, mixed connective tissue disease, and undifferentiated connective disease[5]. SSc and dermatomyositis (DM) are more frequently associated with this typical microvascular derangement[6].

In the course of SSc, the vascular morphological changes in the nailfold occur very early and they have been widely investigated[5]. In 2000, Cutolo, *et al* proposed a reclassification of scleroderma pattern into 3 different subgroups: early, active, and late pattern, characterized by prevalent

presence of different capillaroscopic abnormalities, showing a correlation with disease duration, skin involvement, and autoantibodies[7]. Further studies suggested that scleroderma pattern observed in patients with SSc is subject to variations in the course of the disease[8,9,10], and changes in the capillaroscopic patterns were also found in relation to disease activity[4,7,11].

Capillaroscopic alterations detectable in the course of DM have been less extensively investigated. Several studies describe the association between abnormalities in nailfold microvascular array and idiopathic myopathies (IM), often considering together polymyositis (PM) and DM[12,13,14]. Recently, we analyzed capillaroscopic alterations in IM and clearly differentiated PM and DM, detecting typical scleroderma pattern exclusively in patients with DM[15]. Moreover, as well as for SSc, high variability of DM-associated microangiopathy by nailfold videocapillaroscopy (NVC) has been described[10,16].

The frequent observation of scleroderma pattern in both SSc and DM reflects some pathogenetic similarities, mainly detectable in early microangiopathy[17,18]; otherwise, many differences in both pathogenesis and clinical course clearly differentiate the 2 diseases[17,18], suggesting significant peculiarities in capillaroscopic findings of SSc and DM. These data have never been well defined, to our knowledge.

The aim of our study was to investigate possible differences in nailfold capillaroscopic features of patients with DM or SSc, with a cross-sectional and a longitudinal evaluation.

## MATERIALS AND METHODS

In the first phase of the study, capillaroscopic features of 29 unselected, consecutive patients with DM were compared (female/male ratio 4.83/1, mean age 53.9 ± 17.6 yrs; Table 1) in a cross-sectional study of 90 patients with SSc (female/male ratio 44.5/1, mean age 56.35 ± 12.3 yrs) consecutively enrolled according to the type of scleroderma pattern (early, active, or late) as proposed by Cutolo, *et al*[7] (30 consecutive patients for each pattern). Patients all satisfied the Bohan and Peter criteria[19,20,21].

Early, active, and late patterns were defined as follows (Figure 1)[7]:

- Early: few enlarged/giant capillaries, few capillary hemorrhages, relatively well-preserved capillary distribution, no evident loss of capillaries.
- Active: frequent giant capillaries, frequent capillary hemorrhages, moderate loss of capillaries, mild disorganization of the capillary architecture, absent or mild ramified capillaries.
- Late: irregular enlargement of the capillaries, few or absent giant capillaries and hemorrhages, severe loss of capillaries with large avascular areas, disorganization of the normal capillary array and ramified/bushy capillaries.

*Table 1*. Demographic, clinical, and serological features of 29 patients with dermatomyositis. Data are percent unless otherwise indicated.

| Features | Values |
|---|---|
| Mean age, yrs ± SD | 53.9 ± 17.6 |
| Female/male ratio | 4.83/1 |
| Mean disease duration, mos ± SD*, range | 27.0 ± 48.4 (0–112) |
| Raynaud phenomenon | 24.1 |
| Heliotropic rash | 58.6 |
| Gottron papules | 68.9 |
| CK basal, U/l, mean ± SD | 2725.6 ± 3591.5 |
| Antinuclear antibodies | 93.1 |
| Anti-Jo1 | 3.4 |
| Anti-SSA | 13.8 |

* At enrollment. CK: creatine kinase.

All patients with DM had undergone treatment with steroids and/or immunosuppressive drugs (methotrexate, cyclophosphamide, azathioprine, or mycophenolate mofetil), while all patients with SSc were treated with conventional vasoactive (calcium channel blockers, bosentan, iloprost) and/or immunosuppressive drugs, according to the clinical picture. In patients with DM, baseline NVC was performed before any treatment in 12 cases and within 6 months in 4 patients.

For all patients with DM, occult malignancies had been excluded.

In the second phase of the study, 20 of the 29 patients with DM and all the patients with SSc were longitudinally reevaluated after 30 months of followup; 3 patients with DM died and 6 patients with DM were lost to followup. For the longitudinal evaluation, only patients with both NVC examination (baseline and end of followup) were counted.

*Collection of NVC images*. NVC was performed using a videocapillaroscope (Videocap software 3.0; DS Medica) equipped with a 200× optical probe, after patients had been in a 22°-25°C room for 20 min[22].

A drop of immersion oil was applied to the nailfold to maximize the translucency of the keratin layer, and the second through the fifth fingers of both hands were examined[22]. Two images of the middle of the nailfold were saved per finger, and then recorded, coded, stored, and independently analyzed by an expert operator (MS) blinded to patients' clinical data.

According to previous definitions[9,23], the following capillaroscopic variations were evaluated: tortuosities (single or multiple crossovers); enlarged loops (irregular or homogeneous increase of capillary diameter ≥ 20 μm and < 50 μm); giant capillaries (normally-shaped, homogeneously-enlarged capillary with a limb diameter ≥ 50 μm); microhemorrhages (presence of 1 or more dark red masses characterized by hemosiderin deposits due to capillary injury or thrombosis); ramified capillaries (branching, bushy, interconnected capillaries, originating from a single capillary); ramified-giant capillaries (ramified capillaries with a diameter ≥ 50 μm); disorganization of the vascular array; capillary loss (reduction of the normal number of capillaries, usually 7-10 per linear mm); and avascular area (intercapillaries distance > 500 μm). Moreover, a scleroderma pattern, defined as an alteration of the nailfold microvascular network, characterized by enlarged and giant loops, microhemorrhages, capillary loss, neovascularization, and architectural disorganization[8,15], was recorded as present or absent.

Total number of capillaries, enlarged and giant capillaries, microhemorrhages, and ramified capillaries were each scored by a semiquantitative rating scale (0: no changes, 1: < 33% of capillary alterations/reduction, 2: 33%–66% of capillary alterations/reduction, 3: > 66% of capillary alterations/reduction, per linear mm), obtaining a mean score value for each capillaroscopic measure; the disorganization of the vascular array and the avascular areas were scored as presence/absence[8,14]. Finally, the capillary loss was scored as 0 (≥ 7 capillaries/mm), 1 (4-6 capillaries/mm), or 2 (≤ 3 capillaries/mm).

*Statistical analysis*. Data were expressed as mean ± SD unless otherwise noted. Categorical variables were analyzed by chi-squared test or Fisher's exact test as appropriate; Wilcoxon test was used to compare repeated measurements in paired groups, while differences between the means were determined using Mann-Whitney U test for unpaired samples. P values ≤ 0.05 were considered statistically significant[24].

## RESULTS

*Cross-sectional study*. NVC findings at baseline for SSc versus DM are reported in Table 2.

Giant capillaries were significantly more frequent in SSc than in DM (93.4% and 58.6%, respectively, p ≤ 0.001), while higher frequency (55.2% and 34.1%; p = 0.043) and

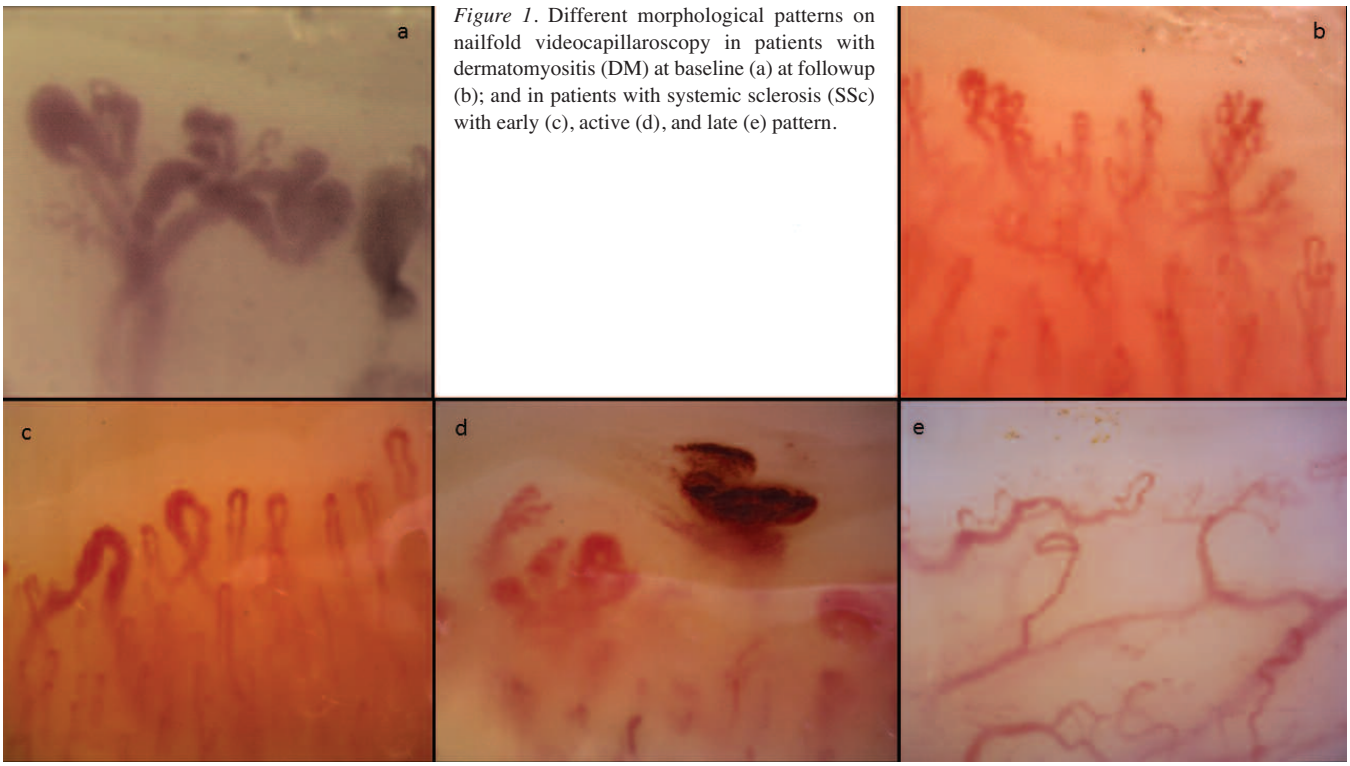



*Figure 1*. Different morphological patterns on nailfold videocapillaroscopy in patients with dermatomyositis (DM) at baseline (a) at followup (b); and in patients with systemic sclerosis (SSc) with early (c), active (d), and late (e) pattern.

*Table 2*. Capillaroscopic features at baseline.

| | DM, n = 29 | SSc, n = 90 | DM vs SSc | Early, n = 30 | DM vs E | Active, n = 30 | DM vs A | Late, n = 30 | DM vs L |
|---|---|---|---|---|---|---|---|---|---|
| Mean score (0–3), ± SD | | | | | | | | | |
| | | | p | | p | | p | | p |
| Giant capillaries | 1.2 ± 1.2 | 1.21 ± 0.6 | ns | 1.03 ± 0.3 | ns | 1.64 ± 0.7 | ns | 0.93 ± 0.6 | ns |
| Ramified capillaries | 0.83 ± 0.9 | 0.48 ± 0.8 | 0.042 | 0 ± 0 | ≤ 0.001 | 0.09 ± 0.3 | ≤ 0.001 | 1.37 ± 0.7 | 0.008 |
| Hemorrhages | 0.4 ± 0.6 | 0.47 ± 0.6 | ns | 0.3 ± 0.5 | ns | 0.93 ± 0.6 | 0.003 | 0.17 ± 0.4 | 0.034 |
| Capillary loss | 0.93 ± 0.6 | 1.26 ± 0.8 | 0.048 | 0.53 ± 0.5 | 0.018 | 1.29 ± 0.5 | 0.027 | 1.97 ± 0.6 | ≤ 0.001 |
| Frequency (%) | | | | | | | | | |
| | | | p | | p | | p | | p |
| Giant capillaries | 58.6 | 93.4 | ≤ 0.001 | 100 | ≤ 0.001 | 100 | ≤ 0.001 | 80 | ns |
| Ramified capillaries | 55.2 | 34.1 | 0.043 | 0 | ≤ 0.001 | 9.7 | ≤ 0.001 | 93.3 | 0.01 |
| Hemorrhages | 41.4 | 41.8 | ns | 30 | ns | 77.4 | 0.004 | 16.7 | 0.047 |
| Ramified + giant capillaries | 34.5 | 1.1 | ≤ 0.001 | 0 | ≤ 0.001 | 3.2 | 0.002 | 0 | ≤ 0.001 |

DM: dermatomyositis; SSc: systemic sclerosis; E: early; A: active; L: late; ns: not significant.

severity (0.83 and 0.48; p = 0.042) were observed for ramified capillaries in patients with DM than in patients with SSc. The presence of giant-ramified capillaries was typical of DM (34.5% vs 1.1%, p ≤ 0.001). Capillary loss was more severe in SSc than in DM (1.26 vs 0.93; p = 0.048).

*Early/active/late pattern versus DM*. At baseline, NVC findings in DM differed from those observed in SSc regardless of their specific patterns (early, active, and late; Table 2).

Giant capillaries were more frequently detected in early and active patterns than in DM (p ≤ 0.001 and p ≤ 0.001, respectively). Ramified capillaries were significantly more frequent and with higher score in DM than early and active patterns, while an opposite trend was observed comparing DM alterations and late SSc pattern.

The capillary loss was lower in early pattern than in DM (p = 0.018), and more severe in active and late compared with DM findings (p = 0.027 and p ≤ 0.001, respectively).

Finally, giant-ramified capillaries were almost exclusively found in patients with DM (Table 2).

*Longitudinal study*. NVC was repeated after 30 months in 20 patients with DM and in all patients with SSc (Table 3), while

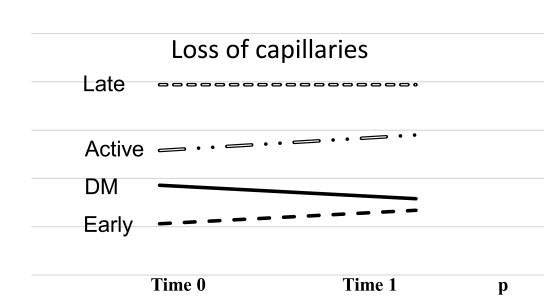
*Table 3*. Capillaroscopic features after 30 months of followup.

| | DM, n = 20 | SSc, n = 90 | DM vs SSc | Early, n = 30 | DM vs E | Active, n = 30 | DM vs A | Late, n = 30 | DM vs L |
|---|---|---|---|---|---|---|---|---|---|
| Mean score (0–3), ± SD | | | | | | | | | |
| | | | p | | p | | p | | p |
| Giant capillaries | 0.58 ± 0.9 | 1.19 ± 0.7 | 0.001 | 1.13 ± 0.5 | 0.002 | 1.61 ± 0.7 | ≤ 0.001 | 0.83 ± 0.7 | ns |
| Ramified capillaries | 1.53 ± 1.1 | 0.7 ± 0.9 | 0.002 | 0.2 ± 0.5 | ≤ 0.001 | 0.48 ± 0.8 | 0.001 | 1.5 ± 0.9 | ns |
| Hemorrhages | 0.31 ± 0.7 | 0.47 ± 0.6 | ns | 0.53 ± 0.6 | ns | 0.81 ± 0.75 | 0.009 | 0.67 ± 0.25 | ns |
| Capillary loss | 0.79 ± 0.8 | 1.36 ± 0.8 | 0.012 | 0.67 ± 0.7 | ns | 1.45 ± 0.7 | 0.007 | 1.97 ± 0.6 | ≤ 0.001 |
| Frequency (%) | | | | | | | | | |
| | | | p | | p | | p | | p |
| Giant capillaries | 36.8 | 86.8 | ≤ 0.001 | 93.3 | ≤ 0.001 | 100 | ≤ 0.001 | 66.7 | ns |
| Ramified capillaries | 78.9 | 47.3 | 0.012 | 16.7 | ≤ 0.001 | 35.5 | 0.003 | 90 | ns |
| Hemorrhages | 21.1 | 39.6 | ns | 50 | ns | 61.3 | 0.006 | 6.7 | ns |
| Ramified + giant capillaries | 15 | 7.7 | ns | 3.3 | ns | 9.7 | ns | 10 | ns |

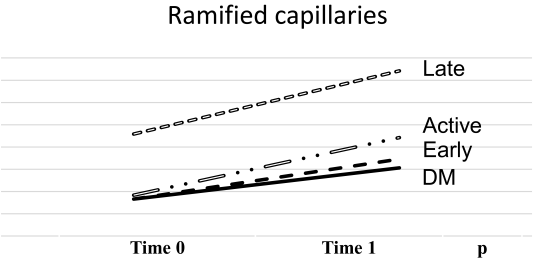
DM: dermatomyositis; SSc: systemic sclerosis; E: early; A: active; L: late; ns: not significant.

3 patients with DM died and 6 patients with DM were lost to followup.

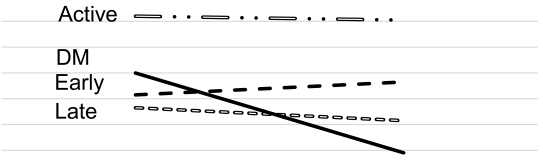
The main capillaroscopic features showed a different evolution in patients with DM and SSc (Figure 2). In particular, at the end of followup, patients with DM showed a relevant reduction of the giant capillaries and a significant increase of ramified capillaries (p = 0.058 and p = 0.022, respectively). In SSc, an increase of ramified capillaries was observed in early and active patterns (p = 0.034 and p = 0.008, respectively), while the other variables remained unchanged. Of interest, a mild improvement in the number of capillaries was observed for DM; on the contrary, in SSc a mild worsening of the capillary loss was recorded in early and active patterns, while the severe capillary loss observed



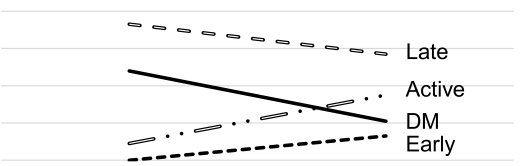

| | Time 0 | Time 1 | p |
|---|---|---|---|
| **DM** | 0.89 | 0.79 | ns |
| **Early** | 0.53 | 0.67 | ns |
| **Active** | 1.29 | 1.45 | ns |
| **Late** | 1.97 | 1.97 | ns |




| | Time 0 | Time 1 | p |
|---|---|---|---|
| **DM** | 0.74 | 1.53 | 0.022 |
| **Early** | 0 | 0.2 | 0.034 |
| **Active** | 0.09 | 0.48 | 0.008 |
| **Late** | 1.37 | 1.5 | ns |




| | Time 0 | Time 1 | p |
|---|---|---|---|
| **DM** | 1.2 | 0.58 | 0.058 |
| **Early** | 1.03 | 1.13 | ns |
| **Active** | 1.64 | 1.61 | ns |
| **Late** | 0.93 | 0.83 | ns |




| | Time 0 | Time 1 | p |
|---|---|---|---|
| **DM** | 0.48 | 0.21 | 0.018 |
| **Early** | 0 | 0.13 | ns |
| **Active** | 0.1 | 0.35 | 0.034 |
| **Late** | 0.73 | 0.57 | ns |

*Figure 2*. Different evolution over time of the main capillaroscopic variables in dermatomyositis (DM) and early, active, and late scleroderma pattern. NS: not significant.

in late pattern remained unchanged. The severity and the frequency of giant-ramified capillaries significantly decreased in patients with DM during followup (Figure 2), remaining a rare finding in patients with SSc, with the exclusion of late pattern (Figure 1).

No significant associations were observed between NVC changes and autoantibody profile, Raynaud phenomenon (RP), or calcium channel blocker therapy.

## DISCUSSION

In our study, we analyzed NVC changes of 90 patients with SSc and 29 with DM in a cross-sectional and longitudinal evaluation, and showed significant differences.

Capillaroscopy represents a fundamental tool for differential diagnosis between primary and secondary RP, as well as for the early diagnosis and clinico-prognostic assessment of patients with SSc and other scleroderma spectrum disorders[5,7,12,25,26,27]. The progressive diffusion of NVC provided the possibility to store, reelaborate, and share the images, allowing an advance in the elaboration of new semiquantitative and quantitative scoring methods[7,12,25,26,27]. Despite the recent improvements, some current definitions, including the so-called scleroderma pattern, still derive from previous observations acquired with stereomicroscope evaluation[12,26].

In the late 1970s, Maricq, *et al* suggested that microvascular alterations should be detected mainly in the setting of "scleroderma spectrum disorders" encompassing some connective tissue diseases, distinguishing between "scleroderma pattern," typical of SSc, and "scleroderma-like pattern," associated to other conditions[28].

However, over the years the 2 terms have been considered synonymous, and only a few authors have tried to differentiate the specific microvascular alterations of SSc from those observed in other connective tissue diseases, particularly DM[29].

Although IM were often evaluated together, it has been recently demonstrated that a scleroderma pattern is not typical of PM, while it is frequently reported in DM[15].

De Angelis, *et al* observed in a small number of patients a rapid change over time of capillary morphology and architecture in DM when compared with patients with SSc, especially regarding microhemorrhages, avascular areas, neoangiogenesis, microaneurysms, and irregularly enlarged capillaries; while no significant differences were found for homogeneous enlarged capillaries, giant capillaries, and hairpin/crossed capillaries[16].

Klyscz, *et al* also observed in a case report an evolution of capillaroscopic findings in DM, with improvement of irregularly enlarged capillaries, microhemorrhages and capillary loss after disease stabilization[6].

In 2010, Mercer, *et al* performed a longitudinal evaluation of NVC features in PM and DM patients, observing marked changes in capillary morphology[12]; 1 year later Mugii, *et al* suggested that changes in nailfold capillaries might reflect disease activity in DM[14].

Moreover, significant variations of NVC features have been demonstrated also in SSc[8,10], and NVC findings seem to correlate with the disease severity[7,8] and the risk of developing some visceral involvement[25,27,30].

In our study, the comparison between SSc and DM at baseline showed a particularly higher prevalence of giant capillaries along with a more pronounced severity of capillary loss in the former and higher frequency of ramified capillaries in the latter. Interestingly, giant-ramified capillaries were almost exclusively observed in patients with DM.

To avoid bias from a potentially different evolution over time of the microangiopathy in either SSc or DM, we distinguished between SSc early, active, and late capillaroscopic patterns recorded at baseline; 3 patterns that should partially mirror SSc pattern evolution over time[7].

Patients with DM were characterized by early presence of giant ramified capillaries, a very rare finding in SSc. During followup, the giant capillaries disappeared, whereas small, irregular ramified capillaries were observed in DM, while in SSc the disappearance of giant capillaries was usually associated with the development of a late pattern with a progressive reduction of capillary density (Figure 1).

On the whole, DM microangiopathy showed more pronounced variations during followup if compared with SSc; in particular, the main signs of severity (giant capillaries and the loss of capillaries) had an opposite tendency in DM and SSc, with a reduction in DM and an increase or stability in patients with SSc.

Besides some common aspects, the pathogenesis of SSc and DM seems to be quite dissimilar, and with a different clinical course[17,18]: SSc often shows a slow but progressive evolution, while DM has, more frequently, an acute onset[31]. Our present findings suggest that NVC alterations in SSc and DM might partially reflect these differences; at baseline, a severe microangiopathy characterizes DM, with disappearance of some major morphological capillaroscopic alterations (capillary loss, giant-ramified capillaries) over time; but SSc microangiopathy usually shows an evolution through early, active, and late pattern over a long period[7].

We cannot exclude that the proper pharmacological treatment of the 2 diseases (mainly immunosuppressant for DM and vasoactive drugs for SSc) could interfere differently with the evolution of the microangiopathy, suggesting an *ad hoc* longitudinal study is needed to clarify the effect of the therapies on SSc and DM microangiopathy[32].

Results of our study further strengthened the strategic role of NVC in clinical practice and as a useful research tool. In fact, it allowed identification of a specific feature in DM microangiopathy well distinguishable from those of SSc.

Our results suggest that the presence of ramified-giant capillaries in the first phases of the disease, associated with

a normal or slightly reduced capillary density, should be helpful for differential diagnosis between SSc and DM. Large multicenter prospective studies are needed to confirm our results. If they are confirmed, we propose the revision of the current terminology, distinguishing between "sclero-derma-like" or "dermatomyositis pattern" that should be properly used in DM, and "scleroderma pattern," more specific of SSc.

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