# Different microvascular involvement in dermatomyositis and systemic sclerosis. A preliminary study by tight videocapillaroscopic assessment

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## ABSTRACT

**Objectives.** *To observe for changes in capillary morphology and architecture by tight sequential videocapillaroscopic (VCP) assessment in patients with dermatomyositis (DM) and systemic sclerosis (SSc).*

**Methods.** *VCP examination was performed in 6 patients with DM and 9 with SSc, at baseline and after one month for three times. Four consecutive fields were examined bilaterally for any single finger (from 2nd to 5th). The best visible image per each digit was selected and images from baseline and follow-up were analysed as a sequence, to allow the same capillaries to be tracked and re-assessed. The following abnormalities were identified: homogeneous enlarged capillaries, giant capillaries, irregularly enlarged capillaries, microhaemorrhages, microaneurysms and neoangiogenesis. Capillary density was also considered.*

**Results.** *A significant progressive change of the following abnormalities was detected in DM patients with respect to SSc patients: microhaemorrhages (p=0.009), avascular areas (p=0.024), neoangiogenesis (p=0.001), microaneurysms (0.001), and irregular enlarged capillaries (p=0.044). No significant differences were found for homogeneous enlarged capillaries (p=0.140), giant capillaries (p=1.0) and hairpin/crossed capillaries (0.516).*

**Conclusions.** *Our preliminary study demonstrated a rapid change of the capillary morphology and architecture in DM with respect to SSc patients. Additional investigations involving larger series of patients may be useful to support more strongly our observations.*

## Introduction

A characteristic disarranged microvascular pattern, named the "scleroderma pattern" has been widely demonstrated by different instruments in patients with systemic sclerosis (SSc) (1-3). It is not strictly limited to SSc, and may be observed in other connective tissue disorders, especially in dermatomyositis (DM), in which a remarkable microvascular involvement is a well-known characteristic (4-6).

In recent years the advances in imaging acquisition by the videocapillaroscopy (VCP) technique make possible a more accurate assessment of microvascular changes in SSc and related diseases (2, 3, 7). Since occasional observations lead to the consideration that the arrangement of nailfold capillaries in DM may vary rapidly (4, 8), we aimed at observing the capillary morphology and architecture over time, by "tight" sequential VCP assessment in DM patients, and compare them with a control group of patients with SSc.

## Methods

*Patients*

Six consecutive patients (1 male and 5 females) with DM (9) and 9 consecutive patients (1 male and 8 females) with SSc (10) were included in this preliminary study. All patients had RP and no concomitant diseases were reported. Current smokers were excluded.

The 6 patients with DM had a mean age of 50.8 years (SD 10.5; range 38-65), and a mean disease duration of 3.6 years (SD 3.6; range 1–10). One patient was ANA positive, 1 patient was receiving methotrexate plus glucocorticoids, 1 patient azathioprine, 2 patients cyclosporine. Disease activity was determined using the Myositis Disease Activity Assessment (MYOACT) (11). All DM patients showed a low global disease activity, except patient n. 3 (Table I).

The 9 patients with SSc included 2 patients with dcSSc and 7 with lcSSc, with a mean age of 55.1 years (SD 14.2; range 30–76), and a mean disease dura-

tion of 7.1 years (SD 5.0; range 2–15). Six patients were anti-centromere positive, while 1 was anti-Scl70 positive. Two patients were receiving nifedipine, 2 patients pentoxifylline, and 2 patients bosentan.

*Study design*

Ethical approval for the study was obtained from the local Ethics Committee and informed consent was obtained from all patients. VCP examinations were performed by the same experienced investigator (RDA) with more than ten years of experience in VCP at baseline (T0) and after 4, 8, and 12 weeks (T1, T2, and T3 respectively) using a Videocap 9.0 software (DS Medica, Milan, Italy) at a room temperature of 22–25°. All patients were asked to refrain from caffeinated drinks for at least four hours before the VCP assessment. Four consecutive fields were examined bilaterally in the middle of the nailfold for any single finger ($2^{nd}$, $3^{rd}$, $4^{th}$ and $5^{th}$). The linear extension of the corresponding images was 1.57 mm. A second investigator (CB) with less than three years of experience in VCP, performed a visual reading of the basal VCP images in order to determine the inter-reader agreement. This observer was fully blinded to the clinical information and lectures of the first operator. The images were captured, coded and stored and in order to minimise reader bias, all the images coded remained anonymous. Prior to the study, both investigators reached a consensus on the VCP findings interpretation (using a core set of images of patients not included in the study).

The following internationally accepted definitions for the capillary abnormalities were adopted: homogeneous enlarged capillaries (width >30 and <50 micron), giant capillaries (a homogeneous enlarged diameter of both afferent and efferent limb >50 micron), irregularly enlarged capillaries (an irregular enlarged branch diameter >50 micron), microhaemorrhages, microaneurysms (normal portion alternating with a circumscribed increase of the capillary diameter) (3, 7, 12, 13). Capillary density was calculated as the number of capillaries in the end row per each image, and even capillaries appearing as normal (hairpin and/or crossed) were counted. Neoangiogenesis was defined as extremely tortuous, bushy, branching, ramified and coiled capillaries, four or more capillaries within a single dermal papilla, very elongated loops, thin and branching interconnected capillaries originating from a single loop. For study purposes, all types of neoangiogenesis were considered as 1 loop in the total count. An avascular area was defined as the lack of two or more consecutive capillaries.

Among the 4 images per each finger, the best visible was selected and then tracked and re-assessed for T1, T2 and T3. A total of 120 images (baseline) and 360 (follow-up) were studied.

*Statistical analysis*

All statistical analyses were performed using MedCalc®, version 10.0 (MedCalc software, Mariakerke, Belgium) for Windows XP (Microsoft Corp, Redmond WA).

The results were expressed as mean and standard deviation (SD). Comparison between capillaroscopic abnormalities at baseline was performed by chi-square analysis. For longitudinal assessment, the cumulative scores for each capillaroscopic variable were estimated by time-integrated values (area under the curve-AUC) and the comparison of AUC values by the Fisher's test. A $p$-value <0.05 was considered significant. The inter-reader agreement was calculated using a weighted kappa (k) test. A κ-value of 0–0.20 was considered poor, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 good and 0.81–1.00 excellent.

**Table I.** Disease activity of DM patients obtained using the Myositis Disease Activity Assessment (MYOACT).

| | VASs | VASs | VASs | VASs | VASs | VASs | Mean (SD) |
|---|---|---|---|---|---|---|---|
| Patient n. | 1 | 2 | 3 | 4 | 5 | 6 | |
| Constitutional disease activity | 0 | 9 | 72 | 18 | 12 | 38 | 24.8 (26.3) |
| Cutaneous disease activity | 0 | 62 | 48 | 28 | 27 | 22 | 31.1 (21.5) |
| Skeletal disease activity | 7 | 12 | 27 | 22 | 8 | 11 | 14.5 (8.1) |
| Gastrointestinal disease activity | 0 | 0 | 0 | 0 | 0 | 0 | 0 (0) |
| Pulmonary disease activity | 0 | 0 | 48 | 0 | 0 | 0 | 8 (19.5) |
| Cardiac disease activity | 0 | 0 | 0 | 0 | 0 | 0 | 0 (0) |
| Other disease activity | 0 | 0 | 0 | 0 | 0 | 0 | 0 (0) |
| Extra-skeletal muscle disease activity | 5 | 32 | 72 | 25 | 22 | 28 | 30.6 (22.2) |
| Muscle Disease activity | 0 | 0 | 0 | 0 | 0 | 42 | 7 (17.1) |
| Global Disease activity | 5 | 10 | 71 | 19 | 18 | 30 | 25.5 (23.8) |

VASs: 100-mm visual analogue scales to measure the physician's evaluation of disease activity in different domains.

## Results

*Longitudinal capillaroscopy*

Mean and SD of AUC for capillaroscopic abnormalities in DM and SSc, respectively, were as follows: normal capillaries 11.9±8.5 and 27.7±44.4; microhaemorrhages 4.3±3.5 and 0.1±0.3; neoangiogenesis 50±19.8 and 42.4±13.6; homogeneous enlarged capillaries 7.2±2.6 and 6.5±8.3; irregular enlarged capillaries 23±8.2 and 11.7±10.8; microaneurysms 5.7±5.2 and 1.3±2; giant capillaries 16.3±15 and 13.4±8.4; avascular areas 9.2±5.8 and 2.7±2.9. A significant turn-over was detected in DM patients respect to SSc patients for microhaemorrhages ($p$=0.009), avascular areas ($p$=0.024), neoangiogenesis ($p$=0.001), microaneurysms ($p$=0.001), and irregular enlarged capillaries ($p$=0.044). No differences were found for homogeneous enlarged ($p$=0.140), giant ($p$=1.0) and normal capillaries ($p$=0.516).

*Basal inter-reader agreement*

κ-values showed moderate to excellent agreement between the two investigators: homogeneous enlarged capillaries (0.577); irregularly enlarged capillaries (0.883), giant capillaries (0.961), microhaemorrhages (0.651), microaneurysms (0.561), neoangiogenesis (0.915), avascular areas (0.960).

## Discussion

We observed a rapid change of the capil-

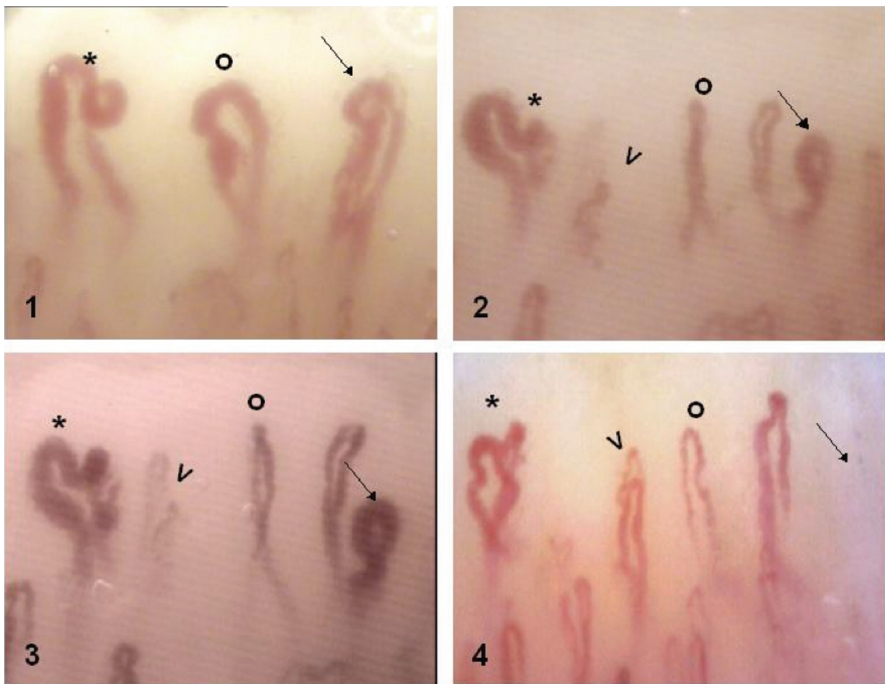


**Fig. 1.** Nailfold capillaroscopy (x200). Monthly image follow-up of a DM patient. Asterisk: reference loop; arrowhead: neoformation of a capillary; circle: from irregular enlargement to tiny capillary; arrow: from neoangiogenesis to giant capillary then disappearance.

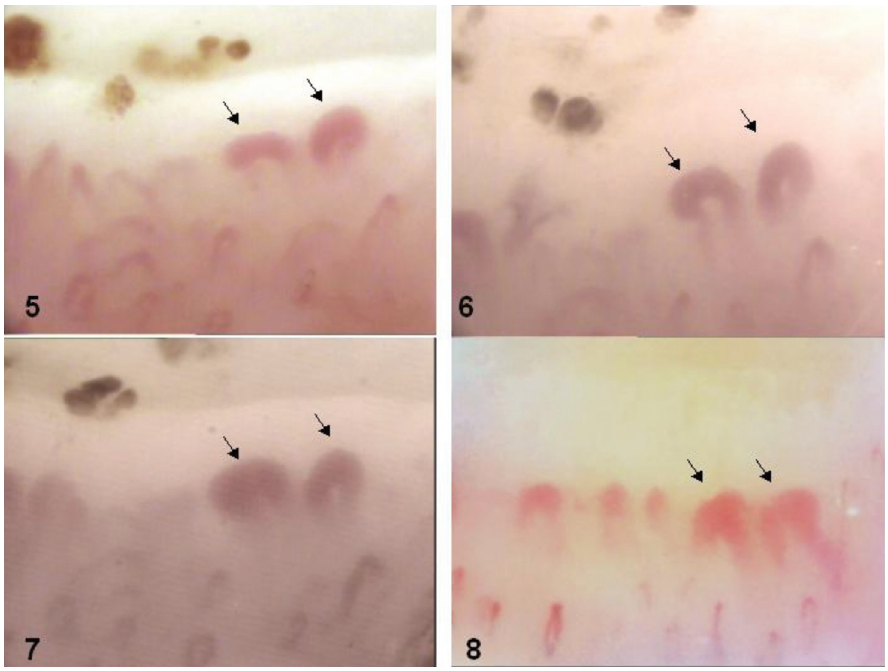


**Fig. 2.** Nailfold capillaroscopy (x200). Monthly image follow-up of a SSc patient. Two giant capillaries appearing the same during the tight control.

lary morphology and architecture in DM patients with respect to SSc patients. The appearance of avascular areas in DM patients proceeded at the same rate with a contextual reduction in the total loop number. The number of microhaemorrhages and microaneurysms increased and then decreased quickly or vice versa, as well as irregular enlarged capillaries and neoangiogenesis (Fig. 1). Additionally, we confirmed the good inter-reader reliability in identifying the major capillaroscopic findings, when measured with a quantitative method (12, 13).

Based on our observations, a particular microvascular environment in DM patients may be hypothesised, perhaps supported by the inflammatory status and the reversible endothelial damage (4, 5, 6), characterised by the rapid break of some pre-existing widened capillaries, with a development of microhaemorrhages, fast capillary loss and replacement with newly formed capillaries. Conversely, capillary morphology and architecture in SSc patients seems to remain stable during our follow-up period (Fig. 2), suggesting that the changes may develop within a longer time, according to the typical progression of the microvascular injury in this disease, due to the critical tissue hypoxia and the unremitting endothelial damage (2, 14, 15).

We are aware that our paper presents strong limitations. First, the small sample enrolled does not allow to extrapolate the results to a wider population. Second, the differences in disease duration may raise the doubt that changes depends on the earlier disease course in DM patients. This can be verified in long term studies on a large patients series. Third, the observation period should be extended, in order to see whether the changes observed are maintained over time.

In conclusion, our preliminary study demonstrated a more rapid progressive morphologic changes of capillaries in DM patients with respect to SSc patients. Additional investigations studying larger series of patients may be useful to support more strongly our observations, especially to examine comprehensively a variety of factors that may influence microvascular changes, including age, gender, comorbid conditions, disease activity, disease duration, and medications.

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