Capillaroscopic Pattern at the Toes of Systemic Sclerosis Patients

Does It ''Tell'' More Than Those of Fingers?

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Purpose: The aim of the study was to compare nail fold capillaroscopic findings of the fingers with those of the toes in patients with systemic sclerosis (SSc).

Methods: Thirty-six patients with SSc were included in the study: 30 patients had limited SSc, 5 patients had diffuse SSc, and 1 patient had an overlap syndrome. Of these 36 patients, 30 were women and 6 were men (mean [SD] age, 56 [14] years). The severity of the Raynaud phenomenon (RP), the presence of digital ulcers, and skin scores at the fingers and feet were assessed. Nail fold capillaroscopy was performed with a videocapillaroscope (Videocap 3.0; DS Medica).

Results: All 36 patients (100%) reported about symptoms of RP in the hands and 34 (94.4%) reported episodes of RP in the feet; the difference is not significant ($P > 0.05$). In most patients with RP symptoms of both hands and feet, the symptoms were more severe at the hands (82%, 28/34). Digital ulcers of the fingers were found in 36% (13/36) of the case and those of the toes were found in 8.3% (3/36) of the cases. Nail fold capillaroscopy of the hands showed the classic "scleroderma"-type capillaroscopic pattern in 97.2% (35/36) of the patients. In the toes, a scleroderma-type capillaroscopic pattern was found only in 66.7% (24/36) of patients ($P < 0.05$). With respect to distinct differences, in the toes, the dilated capillaries were found in 72.2% (26/36) of the cases, giant capillaries in 30.6% (11/36) of the cases, hemorrhages in 8.3% (3/36) of the cases, avascular areas in 41.7% (15/36) of the cases, and neoangiogenesis in 22.1% (8/36) of the cases. This difference in frequency of the findings regarding the toes and the fingers of patients with SSc was statistically significant for all parameters.

Conclusions: Capillaroscopy of the toes of SSc also shows patterns characteristic of SSc. However, these patterns differ from the respective patterns of the fingers, which is probably related to less-severe RP and lower skin score at the feet.

Key Words: capillaroscopy, systemic sclerosis, toes

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In rheumatology, nail fold capillaroscopy is important particularly for patients with systemic sclerosis (SSc) owing to the specific findings that support early diagnosis and are present in most patients with SSc. Microvascular abnormalities are associated with a high frequency of Raynaud phenomenon (RP) in SSc. The specific capillaroscopic pattern in SSc has been described for the first time by Maricq et al.[1] in 1980 and is called "scleroderma type" capillaroscopic pattern.[2–5] It is found in a great number of cases with overt scleroderma (70%–93%) and is characterized by the presence of dilated capillaries, loss of capillaries, avascular areas, hemorrhages, and neoangiogenesis.[1,6–8]

RP affects both hands and feet of patients with SSc, but usually, hand problems are given more serious consideration.[9] Nail fold capillaroscopy of the fingers of patients with SSc is a common method for evaluating abnormal microcirculation, and the presence of the specific scleroderma-type pattern supports the early diagnosis. In 2001, Le Roy and Medsger[10] suggested certain criteria for the early diagnosis of SSc. According to these criteria, cases with scleroderma-type capillaroscopic pattern and/or SSc-specific autoantibodies in patients with RP have to be diagnosed as "prescleroderma" or limited SSc irrespective of the presence or absence of other symptoms of the disease. Despite the fact that patients frequently complain of RP of the feet, nail fold capillaroscopy of the toes is not used in clinical practice, and there are no data in the current literature concerning the capillaroscopic findings of the toes of patients with SSc.

La Montagna et al.[11] examined the involvement of the feet of 100 patients with SSc and monitored these patients between 1 and 28 years (median, 7 years). Among 100 patients with SSc included in the study, 90% of patients presented with features of RP of the feet versus 100% in RP of the hands. In 43% of the patients, RP of the feet presented at initial evaluation, whereas 47% developed it in the course of the follow-up. RP in the hands was registered in 100% of the patients at the initial evaluation. The onset of clinically evident involvement of the feet was noted to come later in limited SSc than in the diffuse form of the disease. Lower rates of necrotizing RP, tendon friction rubs, and skin thickening scores were found in the feet of patients with SSc as compared with the hands, whereas arthralgias affected the feet significantly more often. Acroosteolysis, calcinosis, and erosions were observed significantly more often in the hands of patients with SSc. The final statistical analysis has led to the authors' conclusion that the involvement of the feet in SSc seems to be less frequent and with later onset, but can be similarly disabling.

In contrast to the now widely used microscopic examination of the nail folds of the fingers, at present, this technique is not established for feet examination in the everyday rheumatologic clinical practice.

In 84 healthy subjects, Noy-Delcourt and Thébaut[12] observed that most feet parameters are similar to those of the hands, for example, shape and capillary width. For other parameters, the authors found some differences, such as a smaller number of capillary loops per millimeter on average, greater number of minor dystrophic forms, and shorter capillary loops at the feet compared with those at the hands. In addition, in the feet of the healthy individuals examined, there were more frequent pericapillary haziness because of the physiological edema and frequent irregularity in the distribution of capillary loops compared with those in the hands. No major dystrophy

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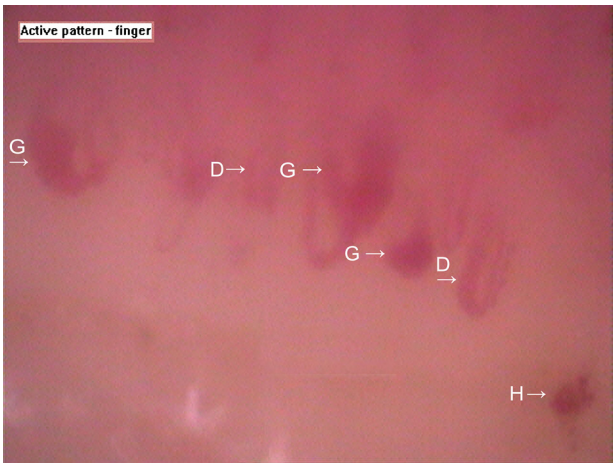

FIGURE 1. Scleroderma capillaroscopic pattern in the active phase at the finger of a 48-year-old man with limited form of SSc. Color online-figure is available at http://www.jclinrheum.com.

was seen, and traumatic hemorrhages were no more frequent in the foot than in the hand.

On the basis of these data and because of the lack of information in the current literature about the capillaroscopic pattern in the toes of patients with SSc, this study aimed to compare nail fold capillaroscopic findings of the fingers with those of the toes in patients with SSc and to evaluate whether the respective patterns are similar or different.

PATIENTS AND METHODS

A total of 36 patients with SSc, diagnosed according to the current American College of Rheumatology classification criteria,[13] were included in the study; 30 patients had limited SSc, 5 patients had diffuse SSc, and 1 patient had an overlap syndrome. There were 30 women and 6 men, with a mean (SD) age of 56 (14) years (range, 30–76 years). The severity of RP in the hands and feet was assessed with a visual analog scale (100 mm) by the physician and the patient. Patients were asked by the physician, "Please evaluate the severity and frequency of RP in the last month according to the disability that vasospastic attacks cause to your everyday activities." The presence of digital ulcers in the hands and feet was documented. Fingers and feet were assessed using the Rodnan skin score: 0 indicates uninvolved skin; 1, mild; 2, moderate; 3, severe thickening.[14] Nail fold capillaroscopy was performed using a high-end videocapillaroscope (Videocap 3.0; DS Medica, Milan, Italy). Measurements were performed with the device's software program, and all measurements were made in millimeters (0.001 mm = 1 μm). The following capillaroscopic parameters were evaluated: distribution, shape of capillaries, diameter of the arterial and the venous limbs of the capillary loop, capillary length, mean capillary density, presence of avascular areas, hemorrhages, and neoangiogenesis. The capillary loops most areas of the human body are perpendicular to the skin's surface, whereas at the nail fold, they become parallel to the skin's surface. This allows capillaries at the distal row to be visualized at their whole length. Normally, capillaries of the nail fold are shaped like a hairpin or a U. They follow regular distribution with a single capillary loop in each dermal papilla. Every single capillary loop consists of a thinner arterial limb, a wider venous limb, and a connecting part between them—an apical loop. Those capillaries of the arterial limb with a diameter greater than 15 μm (0.015 mm) or venous limb greater than 20 μm (0.020 mm) were classified as dilated. Those microvessels of either the arterial or the venous limb with a diameter greater than 50 μm (0.050 mm) were classified as giant capillary loops. The mean diameter of the arterial and the venous limb was calculated as the mean value of the 3 arterial venous limbs, respectively, at their widest part. The length of the capillary loop was measured as the distance between the papillary plexus (if visible) or the visualized base of the capillary loop and the apical part. The mean capillary length was calculated as the mean value of the 3 longest capillaries. Those capillary loops with length greater than 300 μm (0.300 mm) were classified as elongated. Hemorrhages are the extracapillary brown aggregations of erythrocytes. The mean capillary density was calculated as the number of capillary loops in the distal row per 1 mm. The avascular areas were defined as the distance between 2 adjacent capillary loops from the distal rows greater than 500 μm (0.500 mm) or greater than 300 μm (0.300 mm) in the proximal area. Meandering capillaries, presence of more than 1 capillary loop in a single dermal papilla, and ramified and bushy capillaries are the characteristic features of neoangiogenic capillaries.[15]

Twenty-two age- and sex-matched individuals were used as the healthy controls. The mean (SD) age of the healthy controls was 51 (12) years ($P > 0.05$); of them, 19 were women and 3 were men ($P > 0.05$). For the statistical analysis of data, variational analysis, t criterion of V. Goset (Student-Fisher), and χ^2 test were used. The study was approved by the local ethical committee, and all patients signed an informed consent. Results are shown as mean ± standard deviation. We considered $P < 0.05$ as statistically significant.

RESULTS

All 36 patients (100%) reported symptoms of RP in the hands and 34 patients (94.4%) reported episodes of RP in the feet; this difference was not significant ($P > 0.05$). In most patients with RP symptoms of both hands and feet, the symptoms were more severe at the hands (82%, 28/34). Digital ulcers of the fingers were found in 36% (13/36) of the cases and those of the toes were found in 8.3% (3/36) of the cases. The skin score of the hands and fingers (2.05 [0.67]) was significantly higher than that in the feet (0.69 [0.57]; $P < 0.05$).

Nail fold capillaroscopy of the hands of patients with SSc showed the classic feature of scleroderma-type capillaroscopic pattern in 97.2% (35/36), with the following typical features: dilated and giant capillaries, hemorrhages, avascular

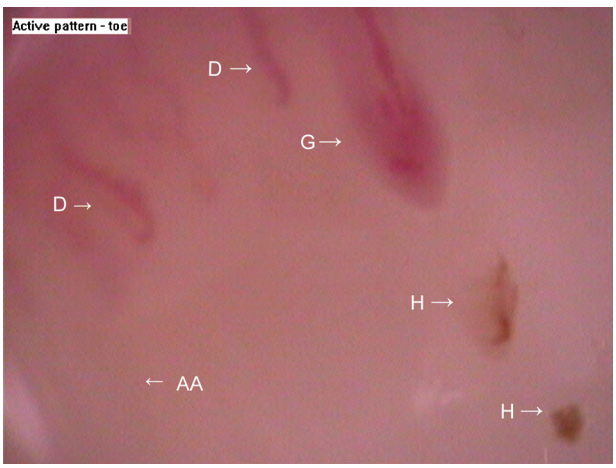

FIGURE 2. Scleroderma capillaroscopic pattern in the active phase at the toe of the same patient in Figure 1. Color online-figure is available at http://www.jclinrheum.com.

TABLE 1. Frequency of Capillaroscopic Parameters of the Scleroderma-Type Pattern in the Fingers and Toes of the SSc Patients

	Fingers	Toes
Dilated capillaries $\chi^2 = 8.69$, $P < 0.05$	97.2% (35/36)	72.2% (26/36)
Giant capillaries $\chi^2 = 16.16$, $P < 0.05$	77.7% (28/36)	30.6% (11/36)
Hemorrhages $\chi^2 = 18.06$, $P < 0.05$	58.3% (21/36)	8.3% (3/36)
Avascular areas $\chi^2 = 17.7$, $P < 0.05$	88.8% (33/36)	41.7% (15/36)
Neoangiogenesis $\chi^2 = 7.17$, $P < 0.05$	52.7% (19/36)	22.2% (8/36)

areas, and neoangiogenesis (Fig. 1). In contrast, in the toes, the scleroderma-type capillaroscopic pattern was found only in 66.7% (24/36) of the patients, and this difference in the frequency of specific changes of the fingers and toes was statistically significant ($P < 0.05$; Fig. 2).

With respect to distinct differences, in the toes, the dilated capillaries were found in 72.2% (26/36) of the cases, giant capillaries in 30.6% (11/36) of the cases, hemorrhages in 8.3% (3/36) of the cases, avascular areas in 41.7% (15/36) of the cases, and neoangiogenesis in 22.1% (8/36) of the cases. This difference in frequency of the findings regarding the toes and the fingers of patients with SSc was statistically significant for all parameters (Table 1).

In addition, the mean values of the arterial diameter, the venous diameter, and the capillary length were statistically significantly higher in the fingers when compared to the toes. The mean capillary density was found to be significantly lower in the hands compared with that in the toes ($P < 0.05$; Table 2).

When comparing the mean values of the main capillaroscopic parameters at the toes of patients with SSc with those of the healthy controls, it was observed that the mean diameter of the arterial and the venous capillary limb was significantly higher in patients with SSc ($P < 0.05$). The mean capillary length was found to be greater in patients with SSc compared with that in healthy individuals, but the difference did not reach statistical significance ($P > 0.05$). Furthermore, the mean capillary density of the toes of patients with SSc was found to be significantly lower (7 ± 3 capillaries/mm) than that of the toes of healthy volunteers (10 ± 1.13 capillaries/mm) ($P < 0.05$) (Fig. 3).

TABLE 2. Comparison of the Mean Values of the Main Capillaroscopic Parameters of the Fingers and Toes of the SSc Patients

	Fingers	Toes
Mean (SD) diameter of the arterial limb ($P < 0.05$), mm	0.035 (0.013)	0.021 (0.009)
Mean (SD) diameter of the venous limb ($P < 0.05$), mm	0.052 (0.020)	0.037 (0.04)
Mean (SD) capillary length ($P < 0.05$), mm	0.284 (0.11)	0.200 (0.11)
Mean (SD) capillary density ($P < 0.05$), capillaries/mm	5 (1.7)	7 (3)

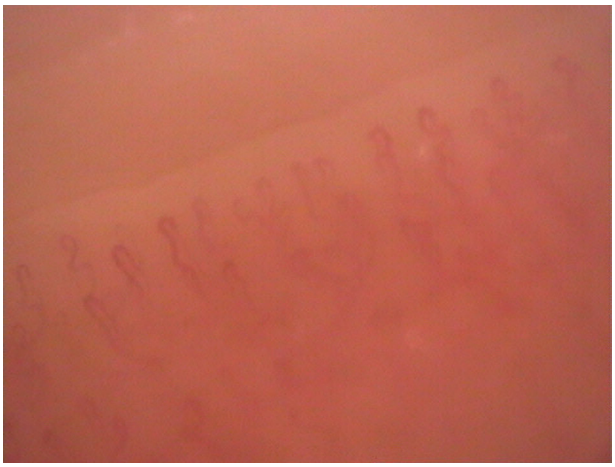

FIGURE 3. Normal capillaroscopic pattern at the toe of a healthy volunteer. Color online-figure is available at http://www.jclinrheum.com.

Values of the main parameters of the toes of patients with SSc and healthy controls are shown in Table 3.

DISCUSSION

We have registered symptoms of RP of the feet in a high proportion (94.4%) of patients with SSc, and our results are similar to those of La Montagna et al.[11] Digital ulcers of the fingers were found in 36% (13/36) of the case and those of the toes were found in 8.3% (3/36) of the cases. Our percentage is smaller compared with that in the study of La Montagna et al.,[11] who report necrotizing RP with a frequency of 52% in the hands and 31% in the feet.

Although the specific scleroderma-type capillaroscopic pattern of the fingers of patients with SSc facilitates early diagnosis, the capillaroscopic pattern of the toes has not been studied in the current literature on rheumatology. Results from our study demonstrate that the capillaroscopic pattern of the toes of patients with SSc also shows the characteristic features of microangiopathy in 66.7% of the examined group. This frequency is significantly lower than that of the hands (97.2%; $P < 0.05$). The abnormal scleroderma-type capillaroscopic pattern was observed in the hands of all but 1 patient with limited SSc—a woman with limited SSc who had not obeyed the obligatory period of 1 month without cutting her nail folds and presented at the consultation with a recent manicure. Capillaries

TABLE 3. Comparison of the Mean Values of the Main Capillaroscopic Parameters of the Toes of the SSc Patients and Healthy Volunteers

	Toes of SSc Patients	Toes of Healthy Volunteers
Mean (SD) diameter of the arterial limb ($P < 0.05$), mm	0.021 (0.009)	0.012 (0.002)
Mean (SD) diameter of the venous limb ($P < 0.05$), mm	0.037 (0.04)	0.017 (0.002)
Mean (SD) capillary length ($P > 0.05$), mm	0.200 (0.11)	0.165 (0.09)
Mean (SD) capillary density ($P < 0.05$), capillaries/mm	7 (3)	10 (1.13)

in the distal row were not visualized in this patient, and the picture was hazy with traumatic hemorrhages. On examination of the feet, the classic scleroderma-type capillaroscopic pattern was observed. Another clinical situation in patients with SSc where toe capillaroscopy may help is when capillaroscopic examination of the fingers is impeded by severe contractures. In these difficult circumstances, nail fold capillaroscopy of toes may offer an opportunity for assessment of microcirculation because it also reveals specific microvascular changes and thus possesses a diagnostic potential although in a smaller percentage.

CONCLUSIONS

Although better protected from exposure to low temperatures, nail fold capillaroscopy of the toes of patients with SSc also shows patterns characteristic of SSc. However, these patterns differ from the respective patterns of the fingers, which are probably also related to less-severe RP and lower skin score at the feet. Therefore, the results of this study not only illustrate the systemic vascular pathophysiology of SSc but also reveal the distinct differences of "similarly" affected vessels in different parts of the body. Therefore, examination of the toes may be considered in the algorithm of the capillaroscopic evaluation of microcirculation in these patients, especially when SSc is suspected, but capillaroscopic examination at the fingers is hampered by different factors.

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