Labial capillary microscopy in systemic sclerosis

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Abstract

Objectives—To investigate whether in vivo capillary microscopy of the lower lip mucosa can be used to assess microvascular disease in systemic sclerosis.

Methods—Thirteen patients with systemic sclerosis and 11 healthy control subjects were studied by conventional nailfold capillary microscopy and labial capillaroscopy. The following parameters were analysed: loop length; loop width (maximum distance between the arteriolar and venular limbs); loop density (number of capillaries/mm²); venular plexus visibility; megacapillaries; and the architectural arrangement of the capillary network.

Results—A typical 'scleroderma pattern' at the nailfold was observed in 12 of 13 (92%) patients with systemic sclerosis. Labial capillaroscopy showed a different morphological pattern of microangiopathy. A diffuse architectural derangement of the capillary network was the most striking abnormality in 12 (92%) patients. Labial capillaries in the patients with systemic sclerosis were shorter (mean (SD) loop length 133 (32.2) μ m) than in healthy controls (211 (48.4) μ m) and showed an increased loop width (41.7 (13.1) v 27.6 (5.5) μ m in controls. The loop density was 10.5 (4.6) capillaries/mm² in patients with systemic sclerosis and 9 (1.7) capillaries/mm² in controls.

Labial capillaroscopy in patients with systemic sclerosis did not provide definite evidence of enlarged capillaries or avascular areas, or both, even where such abnormalities were clearly evident at the nailfold.

Conclusions—This study shows that labial capillary microscopy is a simple, non-invasive technique which allows a careful morphological assessment of the mucosal microcirculation. Labial capillaroscopy in patients with systemic sclerosis showed significant microvascular changes with respect to the controls.

The results of labial and nailfold capillaroscopy are not superimposable, even if some common findings, such as architectural derangement, are present.

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Microvascular research in rheumatology has made consistent progress in the last decade. In vivo capillaroscopic studies have been

conducted using different techniques to detect morphological and dynamic changes of the microcirculation in many diseases.^{1–6}

Nailfold capillary microscopy, in particular, has become increasingly important in the diagnosis of scleroderma spectrum disorders.^{7–8} At present, nailfold capillary microscopy is one of the most sensitive and specific methods for the early recognition of systemic sclerosis in patients with Raynaud's phenomenon.⁹

The nailfold capillaries cannot be fully visualised in some subjects, however, because of low skin transparency (for example, manual workers) or excessive pigmentation.¹⁰ Moreover, the interpretation of capillary changes may be complicated by the coexistence of mechanical or chemical causes of microangiopathy at the nailfold.^{11–12} This study was designed to explore the capillary bed of the lower lip mucosa in patients with systemic sclerosis by in vivo capillary microscopy.

To our knowledge this is the first detailed capillaroscopic study of the labial mucosa in patients with systemic sclerosis.

Patients and methods

SUBJECTS

We studied 13 patients (all women) with systemic sclerosis diagnosed according to the criteria of the American Rheumatism Association.¹³ The mean age of the patients was 56 years (range 39–77 years). Four had limited cutaneous disease and nine the generalised form of the disease.

The results were compared with those obtained in 11 age matched healthy controls.

STUDY DESIGN

All the patients and controls underwent a capillary microscopy examination of the lower lip mucosa. A mean of four photographs at different magnifications was obtained for each subject.

The following features were quantitatively assessed: loop length; loop width (maximum distance between the arteriolar and venular limbs, including capillary lumen); and loop density (number of capillaries per mm²). For each subject the measurements of loop length and capillary width made on at least six contiguous capillaries were averaged, giving a mean value for each subject. Venular plexus visibility, the presence of megacapillaries, and the architectural arrangement of the capillary network were evaluated by a semiquantitative score. Coded photographs of all subjects were

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reviewed by the initial observer (PC) and a trained observer (WG). There was agreement in 23 of 24 subjects between the initial observer and the trained observer. Conventional nailfold capillary microscopy was also carried out on each subject.

TECHNIQUE

Capillary microscopy of the lower lip was performed using the same stereomicroscope (Stereo Star Zoom, American Optical) as used for the nailfold capillary microscopy. The microscope stand was partially modified to allow for a comfortable examination of the lower lip.

All subjects were resting in a supine position during the examination. They kept their lower lip between the first and second finger so that the mucosal surface was perpendicular to the optical axis of the microscope. A drop of castor oil solution was used to improve capillary visibility.

Quantitative assessment of the capillaroscopic images was performed by a computer aided system for morphometric analysis (Oculus 300 Frame Grabber, CORECO).¹⁴

STATISTICAL ANALYSIS

Results are expressed as mean (SD) unless stated otherwise. Testing for significant differences was carried out with the Mann-Whitney U test and χ^2 test. p Values less than 0.05 were considered to be significant.

Results

The table gives the demographic, clinical, and capillaroscopic features of the patients with systemic sclerosis.

Nailfold capillary microscopy showed a typical 'scleroderma pattern'¹⁵ in 12 of 13 (92%) patients. Seven patients (54%) showed a 'slow' pattern as described by Chen *et al* (extremely dilated nailfold capillaries with little or no capillary loss, or else capillary telangiectases combined with nailfold capillaries of differing size but with little or no capillary loss).¹⁶ An 'active' pattern (enlarged capillaries with moderate or extensive capillary loss) was observed in five patients (38%).

Labial capillary microscopy of the lower lip was easy to perform. Detailed images were obtained in the patients and controls. Figure 1 shows a typical capillaroscopic pattern from a healthy subject.

The most striking morphological change in the patients with systemic sclerosis was the widespread disorganisation of the normal architecture of the mucosal capillary bed (fig 2). This finding was observed in 12 of 13 patients but in no control subject (p=0.002).

The architectural derangement was characterised by a loss of the normal 'U' shape of the mucosal capillaries with a high degree of shape heterogeneity (fig 3), anarchic orientation of the major axis of contiguous capillaries (fig 4), and a non-homogeneous loop density.

It is of interest that the only patient (patient 6) without nailfold 'scleroderma-type' changes showed labial capillary disorganisation (loop tortuosity and shape heterogeneity) (fig 5).

The capillary loop length was easy to assess because of the transparency of the labial mucosa. The mean (SD) loop length was 133 (32.2) μ m in the patients with systemic sclerosis and 211 (48.4) μ m in the controls. The difference was significant (p=0.0017).

Clinical, laboratory, and capillaroscopic data of 13 patients with systemic sclerosis

	Patient No												
	1	2	3	4	5	6	7	8	9	10	11	12	13
Clinical characteristics													
Age (years)	51	44	64	77	56	44	39	67	72	69	50	42	53
Disease duration (years)	1	1	12	5	3	3	1	5	20	7	2	13	38
Raynaud's phenomenon duration (years)	6	11	11	4	4	9	19	9	46	21	4	20	39
Digital ulcers	-	-	+	-	+	+	-	+	+	+	+	-	+
Sclerodactyly alone	-	-	-	-	-	-	+	-	+	-	+	-	+
Acrosclerosis	-	+	+	+	+	+	-	+	-	+	-	+	-
Truncal scleroderma	+	-	+	+	+	-	-	-	-	-	-	+	-
Telangiectases	-	+	+	+	+	+	-	+	+	+	-	+	+
Calcinosis	-	-	+	-	+	-	-	+	+	-	-	-	-
Sjögren's syndrome	+	-	+	-	-	-	-	+	+	-	-	-	-
Pulmonary disease	-	+	+	+	+	-	-	+	-	-	-	-	-
Renal disease	-	-	-	-	-	-	-	-	-	-	-	-	-
Gut hypomotility	-	-	+	+	+	+	+	+	+	+	+	+	+
Antinuclear antibody titre	1/1280	1/1280	1/320	1/1280	1/1280	1/160	1/1280	1/160	1/1280	1/1280	1/1280	1/1280	1/1280
Antibodies to RNP	-	-	-	-	-	-	-	-	-	-	-	+	-
Anticentromere antibodies	+	+	-	-	-	-	+	-	+	+	+	-	+
Antibodies to Scl-70	-	-	-	+	+	-	-	-	-	-	-	-	-
Nailfold capillaroscopy													
Interstitial oedema	-	+	-	-	-	+	+	+	-	-	-	-	-
Irregularly enlarged capillaries	+	+	+	+	+	-	+	+	+	+	+	-	+
Megacapillaries	-	+	-	+	+	-	+	-	-	-	+	-	-
Disorganised capillary pattern	-	-	-	+	+	-	-	+	-	+	+	-	+
Avascular areas	-	-	-	-	+	-	-	+	-	+	+	+	-
Venular plexus visibility	-	-	-	-	-	-	-	-	-	-	-	+	-
Neoangiogenesis	+	-	+	-	+	-	-	+	+	+	+	+	-
Labial capillaroscopy													
Mean loop length (μ m)	86.3	183.9	97.2	140.4	143.7	157.5	107.8	186.7	111.3	156.0	138.9	121.1	102.8
Mean loop width (μ m)	63.3	40.6	62.2	32.8	26.7	38.1	46.1	62.9	38.4	32.5	27.5	38.1	33.3
Loop density (No/mm ²)	9	7	19	9	6	18	8	7	6	8	13	17	9
Irregularly enlarged capillaries	-	-	-	+	+	-	-	-	-	-	-	-	-
Megacapillaries	-	-	-	-	-	-	-	-	-	-	-	-	-
Avascular areas	-	-	-	-	-	-	-	-	-	-	-	-	-
Disorganised capillary pattern	+	-	+	+	+	+	+	+	+	+	+	+	+
Venular plexus visibility	-	+	-	+	+	-	+	+	+	+	-	-	+

Figure 1 Capillary bed of the labial mucosa in a representative healthy subject. Labial capillaries show an evident shape and size homogeneity.

The mean (SD) loop width was $27.6 (5.5) \mu\text{m}$ in the controls and $41.7 (13.1) \mu\text{m}$ in the patients with systemic sclerosis ($p=0.0066$).

The number of capillaries ranged between six and 12 in the controls and between six and 19 in the patients with systemic sclerosis. The mean (SD) loop density was $10.5 (4.6)$ capillaries/ mm^2 in the patients with systemic

sclerosis, and $9 (1.7)/\text{mm}^2$ in the controls ($p=\text{NS}$). Venular plexus was detected in nine (82%) of the controls and in eight (62%) of the patients with systemic sclerosis ($p=\text{NS}$).

Only two patients (15%) showed some enlarged capillaries, but no labial megacapillary was observed in either the patients or the controls.

Figure 2 High degree architectural derangement in a patient with systemic sclerosis (patient 9).

Figure 3 Strikingly disorganised labial capillaroscopic pattern in a patient with systemic sclerosis. A diffuse shape and size heterogeneity is the main feature. No 'normal' shaped capillary can be detected (patient 13).

Discussion

There is ample evidence showing that widespread microangiopathy is a hallmark of systemic sclerosis.¹⁷ Although nailfold capillary microscopy is the gold standard for the in vivo study of microcirculation, it would be of interest to have a 'second window'.^{18, 19} An alternative to conventional nailfold capillary microscopy would contribute to our knowledge

of various aspects of microangiopathy in systemic sclerosis (topography, physiopathology, influence of local factors). Moreover, in some patients with systemic sclerosis nailfold capillary microscopy gives only limited information because of the low visibility of the nailfold capillary network (due to dark pigmentation or the presence of interstitial oedema).

Figure 4 Definite disruption of the orderly appearance of labial capillary bed in a patient with systemic sclerosis (patient 8).

Figure 5 Low degree disorganisation (loop tortuosity and shape heterogeneity) of the labial capillary pattern in the only patient (patient 6) without typical 'scleroderma-type' changes at the nailfold.

Labial capillaroscopy appears to be an interesting complementary or alternative technique to nailfold capillary microscopy for several reasons.^{20 21} Firstly, the capillary bed of the lower lip is easily accessible by the same instruments used for conventional nailfold capillary microscopy. Secondly, the microcirculation of the oral mucosa is not influenced by the local stimuli (mechanical or chemical) that may act on the nailbed. Thirdly, the oral mucosa is less subject to cold stress. Consequently, capillaroscopic abnormalities of the labial mucosa in systemic sclerosis may represent an easily detectable expression of widespread microangiopathy in systemic sclerosis.

Compared with healthy controls, patients with systemic sclerosis showed two main changes in their labial capillaroscopic pattern, recognisable even by direct qualitative evaluation: widespread disruption of the orderly arrangement of the mucosal bed and shape heterogeneity. These changes were so striking as to be easily detected even by observers without specific training in capillaroscopic examination.

Capillaroscopic abnormalities of the labial mucosa in patients with systemic sclerosis showed some similarities to those seen at the nailfold. Two main differences should be stressed, however. Firstly, definitely enlarged capillaries were not observed in the labial mucosa. Secondly, there was no obvious loss of labial capillaries even in patients with definite avascular areas at the nailfold.

The lack of definite, widespread enlargement of the labial capillaries in patients with systemic sclerosis (particularly in those with megacapillaries at the nailfold) was unexpected. It could be hypothesised that local

factors, such as capillary pressure, temperature, mechanical stress, and mechanisms of flow regulation, may modulate the morphological expression of microvascular disease in systemic sclerosis at different sites.

The lack of significant labial capillary loss in the patients with systemic sclerosis was another unexpected and remarkable finding. Definitive conclusions about labial capillary density in systemic sclerosis cannot be drawn from the present data, however, because of the small group of patients and the scattered distribution of the individual density values.

Compared with healthy controls, patients with systemic sclerosis showed a decrease in the mean loop length ($p=0.0017$) and an increase in the mean loop width ($p=0.0066$). These findings may be partly related to the widespread architectural derangement and the high degree of shape heterogeneity seen.

From this study, we can conclude that the 'scleroderma pattern' of the labial mucosa is characterised by widespread disorganisation of the microvascular network. The labial capillaries are short, unevenly distributed, and show variable morphological changes with a high degree of shape heterogeneity. These findings suggest that labial capillaroscopy may be a useful additional method to explore microvascular disease in systemic sclerosis.

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