

Capillaroscopy findings in lupus erythematosus*

*Achados capilaroscópicos no lúpus eritematoso**

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Abstract: BACKGROUND – Capillaroscopy is an useful diagnostic tool that is non-invasive, reproducible, able to assess the capillaries in the periungual region and that assists in the differential diagnosis of connective tissue diseases. OBJETIVOS - The aim of the study was to distinguish chronic cutaneous lupus erythematosus and systemic lupus erythematosus from controls assessed by nailfold capillaroscopy. METHODS - Seventy patients with lupus erythematosus (37 with chronic cutaneous lupus erythematosus and 33 with systemic lupus erythematosus) were studied by the technique of capillary microscopy and compared to 32 controls. RESULTS - The presence of ectatic ($p=0.027$; $p=0.001$), meandering ($p=0.001$; $p=0.007$), corkscrew capillaries ($p=0.011$; $p=0.005$) and nailfold bleeding ($p=0.004$; $p=0.001$) distinguished between the two groups of patients (chronic cutaneous lupus erythematosus and systemic lupus erythematosus) from controls. The variable meandering loops could be predictive for systemic lupus erythematosus (OR=8.308). The independent variables ectatic loops (OR=12.164) and nailfold bleedings (OR=5.652) were predictive for chronic cutaneous lupus erythematosus. CONCLUSIONS – Capillaroscopy can help in the management of patients, since the presence of typical capillaroscopic abnormalities seems to be related to the development of lupus erythematosus. The independent predictive variables for systemic lupus erythematosus were meandering loops, and, for chronic cutaneous lupus erythematosus, ectatic loops and nailfold bleedings.

Keywords: Capillaries; Lupus erythematosus, discoid; Lupus erythematosus, systemic; Microscopic angiography

Resumo: FUNDAMENTOS – A capilaroscopia é método não invasivo e reprodutível capaz de analisar diretamente os capilares na região periungueal, auxiliando no diagnóstico diferencial das doenças do tecido conectivo.

OBJETIVOS – Estudar, por meio da capilaroscopia periungueal, pacientes com lúpus eritematoso cutâneo crônico, lúpus eritematoso sistêmico e grupo controle.

MÉTODOS – Foram analisados 70 pacientes pela capilaroscopia periungueal, sendo 37 com lúpus eritematoso cutâneo crônico e 33 com forma sistêmica, comparados a 32 indivíduos sadios.

RESULTADOS - A presença de capilares ectasiados ($p=0,027$; $p=0,001$), enovelados ($p=0,001$; $p=0,007$) e em saca-rolhas ($p=0,011$; $p=0,005$), além de hemorragias capilares ($p=0,004$; $p=0,001$) foram parâmetros capazes de discriminar os dois grupos de pacientes do grupo controle. A variável capilar enovelado demonstrou ser preditiva para o diagnóstico de lúpus eritematoso sistêmico (OR=8,308). As variáveis independentes capilares ectasiados (OR=12,164) e hemorragias capilares (OR=5,652) foram preditoras para lúpus eritematoso cutâneo crônico.

CONCLUSÃO – A capilaroscopia é útil na prática clínica, pois pacientes com alterações capilaroscópicas específicas parecem ter maior probabilidade de desenvolver lúpus eritematoso. As variáveis preditoras independentes para lúpus eritematoso sistêmico foram capilares enovelados e para lúpus eritematoso cutâneo crônico foram capilares ectasiados e hemorragias capilares.

Palavras-chave: Angioscopia microscópica; Capilares; Lúpus eritematoso discóide; Lúpus eritematoso sistêmico

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INTRODUCTION

Lupus erythematosus is a chronic multifactorial inflammatory disorder caused by changes in the immune system with genetic, environmental and hormonal interactions. Its diagnosis is made by means of clinical history, physical examination and complemented by tests, such as histopathology, direct and indirect immunofluorescence and routine laboratory tests (complete blood count - CBC, erythrocyte sedimentation rate - ERS, type I urine analysis).¹

Nailfold capillaroscopy (NFC) is a method enabling direct assessment of capillaries of the perungual region by means of stereoscopic microscopy.^{2,3} This method combines several advantages: it is non-invasive; it is reproducible; it allows early distinction of primary Raynaud phenomenon (RP) from that secondary to connective tissue disorders.^{4,5} The microvascular changes found through capillaroscopy seen in lupus, dermatomyositis, Sjögren syndrome and scleroderma have been widely studied.^{4,7}

The typical capillaroscopic pattern in systemic lupus erythematosus (SLE pattern) consists basically of increased capillary tortuosity, which may affect the three branches of the capillary loop, with changes like meandering, corkscrew or circumvolutions and lengthening of loops, which at times resemble glomeruloid structures.^{3,7} Andrade et al.³ performed quantitative analytical assessment in 40 patients with SLE and concluded that very long and abundant meandering capillaries may suggest the diagnosis of systemic lupus. Jaramillo et al.⁸ studied 15 SLE patients and observed capillary tortuosity in all of them. Tortuosity is a relevant morphological criterion, which, nonetheless, may be considered a normal finding when found in less than 5% of capillaries. Reduction in the number of capillaries may also be part of this pattern.^{4,6,8} Studer et al.⁹ reported that SLE patients had a statistically significant higher number of bleedings, greater rate of plexus depiction, larger diameter in the three parts of the capillary loop (arterial, transitional and venous) than controls. It is worth emphasizing that a normal examination does not rule out the possibility of connective tissue disease, and it is unlikely in the case of progressive systemic sclerosis, for which the negative predictive value is 99.4%.¹⁰

With the aim of improving the characterization of SLE and chronic cutaneous lupus erythematosus (CCLE), the present study attempts to correlate the capillaroscopic findings in both conditions and to compare them to those of controls.

PATIENTS AND METHODS

Patients

Patients seen at the Collagen Disease Outpatient's Clinic of the Department of

Dermatology and of the Rheumatology Course of the Universidade Federal de São Paulo – Escola Paulista de Medicina – Hospital São Paulo, from February 1997 to September 1999, took part in this study. The study had been previously approved by the Ethics Committee of Hospital São Paulo and all patients signed informed consent forms.

Patients were randomly selected, and the exclusion criterion was presence of other systemic diseases, such as hypertension, diabetes mellitus and lung diseases. Patients suspected of other associated collagen diseases were also excluded. People with systemic diseases and with suspected Raynaud phenomenon were excluded from the control group.

One hundred and two subjects were studied and assigned to three different groups: SLE (33), CCLE (37) and control (32).

The CCLE and the SLE groups were identified according to the ARA criteria¹¹ by means of history (photosensitivity) and laboratory tests (CBC, urine I, 24-hour proteinuria, indirect immunofluorescence, histopathology).

Capillaroscopy

a – Microscope

A stereomicroscope Olympus SZ 40, with six to 40 times magnification was used. To count the capillaries in the fourth and fifth fingers, 10 times magnification was employed and to assess the morphology of capillary loops, a 15-times magnification was performed in 10 fingers.

A precision reticulum with 10 divisions corresponding to one millimeter of the field observed, for 10mm was set in the right eye piece. This allowed immediate counting of the number of capillaries in each millimeter of the distal row.

b – Lighting

A low voltage tungsten incandescent lamp (6 volts and 15 watts) that releases small amount of heat on the skin at study, not causing dilatation of the vessels, was used. Its light is collimated by means of a convergent lens and the light beam shines on the skin surface at a 45 degree angle, and uncomfortable glare is prevented.

Dry oil is rubbed on the skin surface to reduce refraction and to add transparency, thus improving the visualization of vessels.

A plastic green filter was used to enhance contrast between the capillaries and surrounding tissues.

Capillaroscopy was performed in all 10 fingers with the hand at the heart level. The readings were double-blind and done by two independent examiners. The agreement rate of the two capillaroscopic readings was greater than 80% for each parameter,

showing good reproducibility.

The parameters analyzed were: number of loops per millimeter, presence of ectatic capillaries, presence of corkscrew capillaries, presence of meandering capillaries and nailfold bleeding.^{3,7,12}

Statistical Analysis

Qualitative variables are depicted in tables displaying absolute (n) and relative (%) frequencies. The association between these variables was assessed by the chi-square test or by the likelihood ratio, or the Fisher exact test. Quantitative variables were assessed by analysis of variance with one classification factor. The statistically significant variables in the univariate analysis were used to adjust the logistic regression model. Results of logistic regression were expressed as the odds ratio and their 95% confidence intervals. The level of significance adopted was $p < 0.05$.¹³

RESULTS

Mean age among the three groups was not statistically different (Table 1). The groups were homogeneous regarding sex and skin color (Tables 2 and 3, respectively).

The distribution of the mean number of loops in the two types of lupus erythematosus and in the control group was not different (Table 4).

The discriminatory power of the presence of ectatic capillaries was, on the contrary, demonstrated. No difference was found between the SLE and the CCLE groups. Between the SLE and control groups and between the CCLE and control groups, differences were found with $p = 0.005$, that is, they were statistically significant (Table 5).

Regarding the presence of meandering capillar-

ies, no difference was found between SLE and CCLE patients. However, the difference between SLE and control groups and between CCLE and control groups was at $p = 0.001$ (Table 6).

As to corkscrew capillaries, the two lupus groups were not different, opposed to what was found when both, the CCLE and the SLE groups were compared with control groups, $p = 0.003$ (Table 7).

The presence of nailfold bleeding was not statistically different between the SLE and the CCLE groups. Comparing the SLE with controls and CCLE with controls, $p = 0.001$ (Table 8).

By using logistic regression for the CCLE group relative to the control group, nailfold bleeding and ectatic capillaries were predicted variables for CCLE, and this model was adjusted for age (Table 9). On the other hand, meandering capillaries were a predictive variable for SLE (Table 10).

The presence of nailfold bleeding increased the risk for CCLE five fold and that of ectatic capillaries, by 12 fold. The finding of meandering capillaries increased the risk for SLE by eight fold.

DISCUSSION

Panoramic periungual capillaroscopy has become a relevant diagnostic tool in connective tissue diseases. Many investigators have analyzed pictures of the periungual bed, seeking patterns in the capillaries that could distinguish different connective tissue diseases.^{7,15,14-16} Others have nailfold capillaroscopy using more powerful lenses in order to measure the diameters of loops and their curvature.^{4,9,16-23} Some authors have attempted the use of the dermatoscope, such as Dermalite® with the same purpose.^{24,25} After the method was established by Maricq², using panoramic PUC with variable magni-

TABLE 1. Distribution of the variable age in two forms of lupus and control

Variable	SLE (n=33)	CCLE (n=37)	Control (n=32)
Age	(Mean + SE) 34.12 + 1.99	(Mean + SE) 42.22 + 2.06	(Mean + SE) 34.78 + 1.89

$p = 0.1743$ (Variance analysis) SE - Standard error

TABLE 2. Distribution of the variable sex in two forms of lupus and control

Sex	SLE		CCLE		Control		Total	
	N.	%	N.	%	N.	%	N.	%
Female	29	87.9	31	81.1	22	68.8	81	79.4
Male	4	12.1	6	18.9	10	31.2	21	20.6
Total	33	100.0	37	100.0	32	100.0	102	100.0

$p = 0.123$ (chi-square test)

TABLE 3. Distribution of the variable skin color in two forms of lupus and control

Skin color	SLE		CCLE		Control		Total	
	N.	%	N.	%	N.	%	N.	%
Non-white	15	45.4	15	37.8	11	34.4	40	39.2
White	18	54.6	22	62.2	21	65.6	62	60.8
Total	33	100.0	37	100.0	32	100.0	102	100.0

p= 0.660 (chi-square test)

Table 4. Distribution of number of loops in the groups in two forms of lupus erythematosus and in the control group

Variable	LES (n=33)	CCLE (n=37)	Control(n=32)
Number of loops	(Mean +SE) 9.08 ± 0.19	(Mean +SE) 9.50 ± 0.23	(Mean +SE) 9.53 ± 0.11

p=0.143 Variance analysis

fication from 10 to 20 times, several studies have followed these standardization.^{3,26}

Some investigators have found a reduction in the total number of capillary loops in lupus patients.^{7,12,27} In the present study the number of capillaries per millimeter was not different among patients with SLE, CCLE and controls, the mean number of capillaries per millimeter being 9.08 in SLE, 9.50 in CCLE and 9.53 in controls, in accordance to the findings of Andrade *et al.*³

Kabasakal *et al.*¹⁹ observed difference in the number of ectatic loops in 22 SLE patients and 38 healthy individuals (p<0.005). Studer *et al.*,⁹ assessed

12 patients with CCLE, 10 with SLE and 15 controls and found that loop diameter was greater in SLE than in CCLE and controls, but no difference was found between the CCLE and control groups. Dancour *et al.*²⁸ found statistical difference in capillary diameter between 21 SLE patients and 21 controls.

In this study, the presence of ectatic capillary discriminated SLE and CCLE patients from controls (p=0.027) and (p=0.001) respectively, but did not differentiate the CCLE and the SLE groups from each other (p=0.321), and was a predictive parameter (odds ratio = 12.164) for the CCLE group (Table 9).

Caspary *et al.*¹⁷ reported less than 10% incidence of tortuous capillaries in 29 controls, of 15% in 29 SLE patients with associated Raynaud phenomenon and 18% in 29 lupus patients with no associated Raynaud phenomenon. Ricciéri *et al.*²⁹ found that in 44 SLE patients, meandering capillaries were present in 16%. Jaramillo *et al.*⁸ reported 12/15 (80%) capillaries in SLE and Maricq *et al.*¹², in 25 of 60 patients (42%). Opposing this, Bongard *et al.*,¹⁸ described a reduction in meandering capillaries in 16% of SLE patients. Ercole²⁷ also found an increase in the mean number of meandering capillaries in SLE patients

TABLE 5. Distribution of ectatic capillaries in two forms of lupus erythematosus and in the control group

Ectatic capillaries	SLE		Control		CCLE	
	N.	%	N.	%	N.	%
Present	8	24.2	1	3.1	13	35.1
Absent	25	75.8	31	96.9	24	64.9

p=0.005 (chi-square test)

TABLE 6. Distribution of meandering capillaries in two forms of lupus erythematosus and in the control group

Meandering capillaries	SLE		Control		CCLE	
	N.	%	N.	%	N.	%
Present	20	60.6	5	15.6	17	46.0
Absent	13	39.4	27	84.4	20	54.0

p=0.001 (chi-square test)

TABLE 7. Distribution of corkscrew capillaries in two forms of lupus erythematosus and in the control group

Corkscrew capillaries	SLE		Control		CCLE	
	N.	%	N.	%	N.	%
Present	7	21.6	2	6.3	8	21.6
Absent	26	78.4	32	100.0	29	78.4

p=0.003 (likelihood ratio test)

TABLE 8. Distribution of nailfold bleeding in two forms of lupus erythematosus and in the control group

Nailfold bleeding	SLE		Control		CCLE	
	N.	%	N.	%	N.	%
Present	22	66,7	10	31,2	29	78,4
Absent	11	33,3	22	68,8	8	21,6

p=0.001 (chi-square test)

(p<0.01) compared to controls.

In the present study, the parameter meandering capillaries did not discriminate between the CCLE and the SLE groups (p=0.220), but it discriminated either group from the control group (p=0.011 and p=0.005, respectively) (Table 6) and was predictive of SLE (odds ratio of 8.308).

Corkscrew capillaries were found in 7/33 (21.2%) patients with SLE, 8/37 (21.6%) with CCLE and in no control subject, in the present study. The method separated the CCLE and the SLE from the control groups, but not between each other. No reference was found in the literature on such association of the presence of corkscrew capillaries and lupus.

In the present study, the parameter nailfold bleeding besides separating the SLE and the CCLE from the control group (p=0.004 and p=0.001, respectively) (Table 8), was also predictive of CCLE (odds ratio of 5.6520) (Table 9). Previous studies also reported higher frequency of nailfold bleeding in SLE patients than in normal subjects.^{22,29}

Andrade *et al.*³ inferred that the occurrence of micropetechiae of focal distribution was related to everyday microtrauma that may occur in healthy individuals. They also stated that because it is a dynamic phenomenon, agreement may be low in two consecutive readings (72%) with variable intervals from weeks to months. They also observed that of 112 healthy subjects with more than three micropetechiae at capillaroscopy, 106 had clustered lesions, and only six had disseminated distribution.³

The findings of the present study regarding the CCLE group may perhaps be explained by the fact

TABLE 9. Logistic regression results for the CCLE group as compared to the control group as to the variables nailfold bleeding and ectatic capillaries

CCLE Variable	Odds ratio	IC 95%	P
Nailfold bleeding	5.652	1.756 18.189	0.0037
Ectatic capillaries	12.164	1.359	0.0254

Adjusted per age

TABLE 10. Logistic regression results for the SLE group as compared to the control group as to the variable meandering capillaries

SLE Variable	Odds ratio	IC95%	P
Meandering capillaries	8,308	2,547 27,102	0,0004

that many patients of this group had often times, in addition to localized cutaneous LE lesions, disseminated skin lesions aside from presenting arthralgia or arthritis, although not fulfilling the ARA criteria for SLE

CONCLUSION

Capillaroscopy proved to be useful when applied in clinical practice, and that patients with specific capillaroscopic changes have higher probability of having lupus erythematosus, and the independent predictive variables were meandering capillaries for SLE, and ectatic capillaries and nailfold bleeding for CCLE. It was also concluded that the capillaroscopic variables were not useful for discriminating the groups with CCLE from SLE between each other. □

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