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ORIGINAL ARTICLE

Comparison of qualitative and quantitative analysis of capillaroscopic findings in patients with rheumatic diseases

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Abstract No guidelines for the application of qualitative and quantitative analysis of the capillaroscopic examination in the rheumatologic practice exist. The aims of the study were to compare qualitative and quantitative analysis of key capillaroscopic parameters in patients with common rheumatic diseases and to assess the reproducibility of the qualitative evaluation of the capillaroscopic parameters, performed by two different investigators. Two hundred capillaroscopic images from 93 patients with different rheumatic diseases were analysed quantitatively and qualitatively by two different investigators. The distribution of the images according to the diagnosis and the microvascular abnormalities was as follows—group 1: 73 images from systemic sclerosis patients ("scleroderma" type pattern), group 2: 10 images from dermatomyositis ("scleroderma-like" pattern), group 3: 25 images from undifferentiated connective tissue disease and different forms of overlap (24 "scleroderma-like"), group 4: 26 images from systemic lupus erythematosus patients, group 5: 46 images from rheumatoid arthritis and group 6: 20 images from primary Raynaud's phenomenon patients. All the images were mixed and blindly presented to both investigators. For comparison of the quantitative and qualitative method, investigator 1 assessed presence of dilated, giant capillaries and avascular areas quantitatively by the available software programme and his estimates were compared with the results of investigator 2, who assessed the parameters qualitatively. In addition, the capillaroscopic images were evaluated qualitatively by the investigator 1 and 2 for presence of dilated, giant capillaries, avascular areas and haemorrhages. The comparison of the quantitative and qualitative assessment of the two investigators demonstrated statistically significant difference between the two methods for the detection of dilated and giant capillaries ($P < 0.05$) but no significant difference regarding the detection of avascular areas ($P > 0.05$). As we further analysed the results for the capillaroscopic images, demonstrating a "scleroderma" and a "scleroderma-like" pattern (170/200), analogous results were found for the evaluated parameters. Among the 20 capillaroscopic images from patients with primary RP, the estimates for the absence of giant capillaries and avascular areas were equal in 100% ($P > 0.05$). Comparing the qualitative assessment of the two investigators, a statistically significant difference between estimates of the two investigators was found for the presence of dilated capillaries ($P < 0.05$), while for giant capillaries, avascular areas and haemorrhages the difference was not statistically significant ($P > 0.05$). The results of the study have shown that qualitative assessment of capillaroscopic parameters in patients with rheumatic diseases is an adequate method for the everyday rheumatologic practice, especially in cases with primary RP for exclusion presence of microangiopathy. No significant difference between qualitative and quantitative methods of assessment was found for the detection of avascular areas. However, the quantitative analysis is more precise especially for the detection of capillary dilation. A good reproducibility of the qualitative evaluation, performed by two different investigators was also found.

Keywords Qualitative analysis · Quantitative analysis · Capillaroscopic image · Rheumatic diseases

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Background

The nailfold capillaroscopy is the only method for the evaluation of nutritional capillaries of the nailfold area. Digital videocapillaroscopy nowadays is a gold standard and consists of the combination of a microscope and a digital videocamera. It provides a significantly higher magnification as compared with other optical devices (from 50× to 1000×) and it allows capillaroscopic parameters to be measured precisely.

The following capillaroscopic parameters can be examined: capillary diameter (width), capillary length, shape, distribution, mean capillary density, presence of avascular areas, haemorrhages, neoangiogenic capillaries [1–13]. Some of the capillaroscopic parameters such as capillary width, length, mean capillary density can be exactly measured quantitatively by the current available software programs, while other parameters, e.g., shape, distribution and haemorrhages, are evaluated qualitatively. Counting the number of the haemorrhages, ramified capillaries per mm and evaluation of the degree of the derangement are methods for semiquantitative analysis of the capillaroscopic image. Nowadays, there are no guidelines for the application of the qualitative and quantitative analysis of the capillaroscopic images in the rheumatologic practice [12, 14, 15]. The capillary loops in the most areas of the human body are perpendicular to the skin surface, while at the nailfold they become parallel to the skin surface. This allows to be visualized with their whole length. The normal shape of the capillaries of the nailfold is like hairpin, capillaries are 1–3 in each dermal papilla, regularly orientated [2].

Objectives

The aims of the study were to compare qualitative and quantitative analysis of key capillaroscopic parameters in patients with common rheumatic diseases and to assess the reproducibility of the qualitative evaluation of the capillaroscopic parameters, performed by two different investigators.

Materials and methods

Two hundred capillaroscopic images from 93 patients with different rheumatic diseases were analysed quantitatively and qualitatively by two different investigators. The distribution of the images according to the diagnosis and the microvascular abnormalities was as follows—group 1: 73 images from systemic sclerosis (SSc) patients ("scleroderma" type), group 2: 10 images from dermatomyositis (DM) ("scleroderma-like"), group 3: 25 images from undifferentiated connective tissue disease (UCTD) and different forms of overlap (19 "scleroderma-like"), group 4: 26 from systemic lupus erythematosus (SLE), group 5: 46 from rheumatoid arthritis (RA) and group 6: 20 from primary Raynaud's phenomenon (RP). All the images were mixed and blindly presented to both investigators.

The following major capillaroscopic parameters were evaluated: presence of dilated and giant capillaries, haemorrhages, avascular areas. The above-mentioned definitions were used, e.g., capillaries with a diameter of the arterial limb wider than 0.015 mm (=15 μm) or a venous limb wider than 0.020 mm (=20 μm) were classified as dilated. As giant capillary loops were classified microvessels with a diameter of either an arterial or a venous limb wider than 0.050 mm (=50 μm) and as elongated—capillaries with length greater than 0.300 mm (=300 μm). The avascular area was defined as a distance between two adjacent capillary loops from the distal rows longer than 0. 500 mm (=500 μm) or above 0.300 mm (=300 μm) in the proximal area [15]. The reliability of quantitative and qualitative methods, and the reproducibility of the qualitative assessment performed by two different investigators, was evaluated specifically for the "scleroderma" and "scleroderma-like" images and for images of primary RP patients.

1. For comparison of the quantitative and qualitative methods, investigator 1 assessed *presence of dilated, giant capillaries and avascular areas, according to the above-mentioned definition* by the available software program and his estimates were compared with the results of investigator 2, who assessed the parameters qualitatively.
2. For evaluation the reproducibility of the qualitative method performed by two different investigators, the mixed and blindly presented capillaroscopic images were evaluated qualitatively by the investigator 1 and investigator 2 for the presence of the following capillaroscopic changes—*dilated capillaries, giant capillaries, haemorrhages and avascular areas*.

For statistical analysis of the data, variational analysis, t-criterion of V. Goset (Student-Fisher) and χ^2 test were used. Results are shown as mean value/average ± standard deviation (SD). The values of P less than 0.05 were considered as statistically significant.

Results

Quantitative and qualitative assessment performed by two different investigators

The quantitative and qualitative analysis resulted in identical estimates in 74% (148/200) of the cases for the

detection of dilated capillaries, in 84% (168/200) for giant capillaries and in 91% (182/200) for the presence of avascular areas. The distribution of the equal estimates from the quantitative and qualitative analysis of the investigators divided according to the diagnosis is presented in Table 1. In Table 2, the numbers of capillaroscopic images with presence and absence of dilated, giant capillaries and avascular areas evaluated quantitatively and qualitatively, respectively, are shown. Using the χ^2 test, the number of the images with the presence and absence of a certain capillaroscopic parameter, e.g., dilated, giant capillaries and avascular areas, evaluated quantitatively by investigator 1 and qualitatively by investigator 2, was compared. A statistically significant difference between the two methods for the detection of dilated and giant capillaries was found ($P < 0.05$), but no significant difference regarding the detection of avascular areas ($P > 0.05$) (Table 2). The quantitative and qualitative methods were further compared for the assessment of images with "scleroderma" and "scleroderma-like" type capillaroscopic pattern and from patients with primary RP. Among the analysed images, 107 were from "scleroderma" and "scleroderma-like" type (73 from patients with SSc, 10 from DM, 19 from UCTD and 5 patients with different form of overlap syndrome). Twenty images were from patients with primary RP and showed the classic finding with presence of dilated capillaries, but without signs for microangiopathy. Results are presented in Tables 3 and 4. Among the "scleroderma" and "scleroderma-like" images, we have again found a statistically significant difference between the quantitative and qualitative method for the detection of dilated and giant capillaries ($P < 0.05$), while for the presence of avascular areas the difference was not significant ($P > 0.05$). Among the 20 capillaroscopic images from patients with primary RP, the estimates for absence of giant capillaries and avascular areas were equal in 100% ($P > 0.05$). For these groups of capillaroscopic images, a statistically significant difference between the quantitative and the qualitative for the detection of dilated capillaries was also not found ($P > 0.05$).

Qualitative assessment performed by two different investigators

The qualitative assessment by two different investigators showed identical estimates as follows, 81% (164/200) for the presence of dilated capillaries, 89% (177/200) for the detection of giant capillary loops, 85% (172/200) for the presence of avascular areas and in 100% (200/200) of the cases for the haemorrhages (Table 5). The distribution of the equal estimates, divided according to the diagnosis is presented in Table 5. Using the χ^2 test, the number of the images with presence or absence of a certain capillaroscopic parameter, e.g., dilated, giant capillaries, haemorrhages and avascular areas, evaluated qualitatively by both investigator 1 and 2, was compared. For the detection of dilated capillaries, a statistically significant difference between estimates of the two investigators was found ($P < 0.05$), while for giant capillaries, avascular areas and haemorrhages, the difference was not statistically significant ($P > 0.05$). As the key capillaroscopic parameters for microangiopathy are giant capillaries, avascular areas, haemorrhages, their detection is of crucial importance for differentiation of primary RP from RP in the context of SSc and scleroderma-spectrum disorders. Thus, the nonsignificant difference for qualitative detection of these capillaroscopic changes between two different investigators demonstrates the high reproducibility of the qualitative assessment for the detection of microvascular damage in rheumatic disease irrespective of the examiner. Here, we have to emphasize that

Table 1 The distribution of the equal estimates from the quantitative and qualitative analysis of the investigators, divided according to the diagnosis

Capillaroscopic parameters	Dilated capillaries	Giant capillaries	Avascular areas
Distribution of the capillaroscopic images according to the diagnosis			
Systemic sclerosis, $n = 73$	64/73	54/73	64/73
Early: 8	Early: 3/8	Early: 3/8	Early: 5/8
Active: 54	Active: 54/54	Active: 38/54	Active: 49/54
Late: 11	Late: 7/11	Late: 8/11	Late: 10/11
Dermatomyositis, $n = 10$ "scleroderma-like" pattern 10/10	10/10	8/10	8/10
UCTD and different forms of overlap associated with secondary RP, $n = 25$ "scleroderma-like" pattern, $n = 19$	21/25 "scleroderma-like" pattern 19/19	19/25 "scleroderma-like"pattern 14/19	22/25 "scleroderma-like"pattern 19/19
SLE, $n = 26$	17/26	23/26	23/26
RA, $n = 46$	29/46	44/46	45/46
Primary RP, $n = 20$	7/20	20/20	20/20
Total number of equal estimates	148/200	168/200	182/200

Table 2 Comparison of number of images with presence or absence of a certain capillaroscopic parameter evaluated by investigator 1 (quantitatively) and investigator 2 (qualitatively)

Investigator 1—quantitative/investigator 2—qualitative assessment	Investigator 1—quantitative assessment—number of images with presence or absence of a certain parameter	Investigator 2—qualitative assessment—number of images with presence or absence of a certain parameter
Capillaroscopic parameters		
Dilated capillaries $\chi^2 = 15.87$, $P < 0.05$	168 presence	117 presence
	32 absence	83 absence
Giant capillaries $\chi^2 = 5.30$, $P < 0.05$	69 presence	40 presence
	131 absence	160 absence
Avascular areas $\chi^2 = 0.210$, $P > 0.05$	65 presence	59 presence
	135 absence	141 absence

Table 3 Comparison of number of images from "scleroderma" and "scleroderma-like" capillaroscopic patterns with presence or absence of a certain capillaroscopic parameter, evaluated by investigator 1 (quantitatively) and investigator 2 (qualitatively)

Investigator 1—quantitative/investigator 2—qualitative assessment	Investigator 1—quantitative assessment—number of images with presence or absence of a certain parameter	Investigator 2—qualitative assessment—number of images with presence or absence of a certain parameter
Capillaroscopic parameters		
Dilated capillaries $\chi^2 = 7.49$, $P < 0.05$	107 presence	93 presence
	0 absence	14 absence
Giant capillaries $\chi^2 = 6.33$, $P < 0.05$	64 presence	38 presence
	43 absence	69 absence
Avascular areas $\chi^2 = 0.084$, $P > 0.05$	57 presence	54 presence
	50 absence	53 absence

Table 4 Comparison of number of capillaroscopic images of patients with primary RP with presence or absence of a certain capillaroscopic parameter, evaluated by investigator 1 (quantitatively) and investigator 2 (qualitatively)

Investigator 1—quantitative/investigator 2—qualitative assessment	Investigator 1—quantitative assessment—number of images with presence or absence of a certain parameter	Investigator 2—qualitative assessment—number of images with presence or absence of a certain parameter
Capillaroscopic parameters		
Dilated capillaries $\chi^2 = 2.727$, $P > 0.05$	15 presence	18 presence
	5 absence	2 absence
Giant capillaries $\chi^2 = 0$, $P > 0.05$	0 presence	0 presence
	20 absence	20 absence
Avascular areas $\chi^2 = 0$, $P > 0.05$	0 presence	0 presence
	20 absence	20 absence

haemorrhages were the most reliable parameter that is evaluated equally in 100% of the cases. Results are presented in Table 6. We have further evaluated the reproducibility of the qualitative assessment between two different investigators in the different type of capillaroscopic images for the 107 capillaroscopic images from "scleroderma" and "scleroderma-like" type and for the 20 images from primary RP. Results are presented in Tables 7 and 8. Among the "scleroderma" and "scleroderma-like" images, there were no significant difference between the estimates of the two investigators for all of the examined capillaroscopic changes, e.g., dilated capillaries, giant capillaries, avascular areas, haemorrhages ($P > 0.05$). Analogous results were achieved for the 20 capillaroscopic images from patients with primary RP that revealed 100% equal answers for the absence of giant capillaries, avascular areas and haemorrhages. The group with primary RP was used as a group for comparison. The full coincidence of the results in primary RP regarding the absence of signs of microangiopathy was a motive not to be included comparison with analysis of images in healthy controls. Regarding the detection of dilated capillaries in these patients, no statistically significant difference between the estimates of the two investigators was found ($P > 0.05$).

Table 5 The distribution of the equal estimates from the qualitative analysis of the two investigators, divided according to the diagnosis

Capillaroscopic parameters	Dilated capillaries	Giant capillaries	Avascular areas	Haemorrhages
Distribution of the capillaroscopic images according to the diagnosis				
Systemic sclerosis, $n = 73$	66/73	59/73	61/73	73/73
Early: 8	Early: 4/8	Early: 4/8	Early: 5/8	
Active: 54	Active: 54/54	Active: 45/54	Active: 46/54	
Late: 11	Late: 8/11	Late: 10/11	Late: 10/11	
Dermatomyositis, $n = 10$ "scleroderma-like" pattern 10/10	10/10	8/10	6/10	10/10
UCTD and different forms of overlap associated with secondary RP, $n = 25$ "scleroderma-like" pattern, $n = 19$	21/25 "scleroderma-like" pattern 19/19	20/25 "scleroderma-like" pattern 15/19	22/25 "scleroderma-like" pattern 19/19	25/25
SLE, $n = 26$	20/26	24/26	19/26	26/26
RA, $n = 46$	34/46	46/46	44/46	46/46
Primary RP, $n = 20$	13/20	20/20	20/20	20/20
Total number of equal estimates	164/200	177/200	172/200	200/200

Table 6 Comparison of number of images with presence or absence of a certain capillaroscopic parameter, evaluated by both investigator 1 and 2 qualitatively

Investigator 1 and 2—qualitative assessment	Investigator 1—qualitative assessment—number of images with presence or absence of a certain parameter	Investigator 2—qualitative assessment—number of images with presence or absence of a certain parameter
Capillaroscopic parameters		
Dilated capillaries $\chi^2 = 5.127$, $P < 0.05$	146 presence	117 presence
	52 absence	83 absence
Giant capillaries $\chi^2 = 2.189$, $P > 0.05$	58 presence	40 presence
	142 absence	160 absence
Avascular areas $\chi^2 = 0.223$, $P > 0.05$	53 presence	59 presence
	147 absence	141 absence
Haemorrhages $\chi^2 = 0$, $P > 0.05$	40 presence	40 presence
	160 absence	160 absence

Table 7 Comparison of the number of images from "scleroderma" and "scleroderma-like" capillaroscopic pattern with presence or absence of a certain capillaroscopic parameter, evaluated by both investigator 1 and 2 qualitatively

Investigator 1 and 2—qualitative assessment	Investigator 1—qualitative assessment—number of images with presence or absence of a certain parameter	Investigator 2—qualitative assessment—number of images with presence or absence of a certain parameter
Capillaroscopic parameters		
Dilated capillaries $\chi^2 = 3.032$, $P < 0.05$	103 presence	93 presence
	4 absence	14 absence
Giant capillaries $\chi^2 = 2.15$, $P > 0.05$	53 presence	38 presence
	54 absence	69 absence
Avascular areas $\chi^2 = 0.149$, $P > 0.05$	50 presence	54 presence
	54 absence	53 absence
Haemorrhages $\chi^2 = 0$, $P > 0.05$	33 presence	33 presence
	74 absence	74 absence

The results of the study have shown that qualitative assessment of the capillaroscopic parameters in patients with rheumatic diseases is an adequate method for the everyday rheumatologic practice especially in cases with primary RP for exclusion presence of microangiopathy. No significant difference between qualitative and quantitative methods of assessment was found for the detection of avascular areas. However, the quantitative

Table 8 Comparison of the number of capillaroscopic images of patients with primary RP with presence and absence of a certain capillaroscopic parameter, evaluated by both investigator 1 and 2 qualitatively

Investigator 1 and 2—qualitative assessment	Investigator 1—qualitative assessment—number of images with presence or absence of a certain parameter	Investigator 2—qualitative assessment—number of images with presence or absence of a certain parameter
Capillaroscopic parameters		
Dilated capillaries $\chi^2 = 1.79$, $P > 0.05$	7 presence	2 presence
	13 absence	18 absence
Giant capillaries $\chi^2 = 0$, $P > 0.05$	0 presence	0 presence
	20 absence	20 absence
Avascular areas $\chi^2 = 0$, $P > 0.05$	0 presence	0 presence
	20 absence	20 absence
Haemorrhages $\chi^2 = 0$, $P > 0.05$	0 presence	0 presence
	20 absence	20 absence

analysis is more precise especially for the detection of capillary dilation.

A good reproducibility of the qualitative evaluation, performed by two different investigators was found. It supports the idea, that interpretation performed by different investigators produces results that can be reliably compared in the daily practice.

Discussion

The qualitative analysis is more simple, accessible and fast for everyday application. The results of the study have shown that qualitative assessment of the capillaroscopic parameters in patients with rheumatic diseases is an adequate method for the everyday rheumatologic practice, especially in cases with primary RP for exclusion presence of microangiopathy. However, the quantitative analysis is more precise especially for the detection of capillary dilation.

Results from the study demonstrate a good reproducibility of the qualitative evaluation, when performed by two different investigators. They suggest that interpretation, performed by different investigators, who are experienced with capillaroscopic images in the context of rheumatic disease, produces results that can be reliably compared in the daily practice.

Conclusion

In the current study, it has been demonstrated that the qualitative assessment of capillaroscopic parameters in patients with rheumatic diseases is a reliable method for the everyday rheumatologic practice especially in cases with primary RP to exclude the presence of microangiopathy. No significant difference between qualitative and quantitative methods of assessment was found for the detection of avascular areas. However, the quantitative analysis is more precise especially for the detection of capillary dilation.

Results from the present study demonstrate also a good reproducibility of the qualitative evaluation, performed by two different investigators.

Conflict of interest None.

References

1. Bergman R, Sharony L, Schapira D, Nahir MA, Balbir-Gurman A (2003) The handheld dermatoscope as a nail-fold capillaroscopic instrument. Arch Dermatol 139:1027–1030
2. Bollinger A, Fagrell B (1990) Clinical capillaroscopy—a guide to its use in clinical research and practice. Hogrefe & Huber Publishers, Toronto, pp 1–123
3. Bredemeier M, Xavier RM, Capobianco KG, Restelli VG, Rohde LE, Pinotti AF et al (2004) Nailfold capillary microscopy can suggest pulmonary disease activity in systemic sclerosis. J Rheumatol 31:286–294
4. Cutolo M, Pizzorni C, Sulli A (2005) Capillaroscopy. Best Pract Res Clin Rheumatol 19(3):437–452
5. Cutolo M, Sulli A, Secchi ME, Olivieri M, Pizzorni C (2007) The contribution of capillaroscopy to the differential diagnosis of connective autoimmune diseases. Best Pract Res Clin Rheumatol 21(6):1093–1108
6. Dolezalova P, Young SP, Bacon PA, Southwood TR (2003) Nailfold capillary microscopy in healthy children and in childhood rheumatic diseases: a prospective single blind observational study. Ann Rheum Dis 62(5):444–449
7. Kabasakal Y, Elvins DM, Ring EF, McHugh NJ (1996) Quantitative nailfold capillaroscopy findings in a population with connective tissue disease and in normal healthy controls. Ann Rheum Dis 55:507–512
8. Lee P, Leung FY, Alderdice C, Armstrong SK (1983) Nailfold capillary microscopy in the connective tissue diseases: a semiquantitative assessment. J Rheumatol 10(6):930–938
9. Lefford F, Edwards JCW (1986) Nailfold capillary microscopy in connective tissue disease: a quantitative morphological analysis. Ann Rheum Dis 45:741–749

10. Maricq HR, Le Roy EC, D'Angelo WA, Medsger TA Jr, Rodnan GP, Sharp GC, Wolfe JF (1980) Diagnostic potential of in vivo capillary microscopy in scleroderma and related disorders. Arthritis Rheum 23(2):183–189
11. Maricq HR, Harper FE, Khan MM, Tan EM, LeRoy EC (1983) Microvascular abnormalities as possible predictors of disease subsets in Raynaud phenomenon and early connective tissue disease. Clin Exp Rheumatol 1(3):195–205
12. Maricq HR (1986) Comparison of quantitative and semiquantitative estimates of nailfold capillary abnormalities in scleroderma spectrum disorders. Microvasc Res 32(2):271–276
13. Redisch W (1970) Capillaroscopic observations in rheumatic diseases. Ann Reum Dis 29:244–253
14. Ohtsuka T (1999) Quantitative analysis of nailfold capillary abnormalities in patients with connective tissue diseases. Int J Dermatol 38(10):757–764
15. Schmidt JA, Caspary L, von Bierbrauer A, Ehrly AM, Jünger M, Jung F, Lawall H (1997) Standardisierung der Nagelfalz-Kapillarmikroskopie in der Routinediagnostik. Vasa 25:5–10