

Letter to the Editor

doi:10.1093/rheumatology/kex460

Reliability of simple capillaroscopic definitions in describing capillary morphology in rheumatic diseases**Rheumatology key message**

- The optimized simple definitions for normal and abnormal capillary morphology provide excellent reliability.

SIR, Nailfold capillaroscopy is emerging as a widely used tool to investigate the microvasculopathy in rheumatic diseases [1]. Through (semi-)quantitative and qualitative assessments of capillaroscopic images, valuable information on disease progression and outcome can be obtained [2–6]. In the literature, however, a variety of definitions are used to describe capillaroscopic findings of single capillaries, which hampers the interpretation of results in clinics and the interpretation of advancements made in research. One objective of the EULAR Study Group on Microcirculation in Rheumatic Diseases is to standardize and simplify the definitions used in describing capillaroscopic findings. In a first pilot study by the EULAR Study Group on Microcirculation in Rheumatic Diseases, a simple definition was proposed to describe the morphology of single capillaries as being normal or abnormal [7]. A moderate reliability of this definition was obtained between attendees of the sixth EULAR capillaroscopy course, held in Genoa, Italy in 2014. Attendees were rheumatologists with varying levels of expertise in performing capillaroscopy (of which the majority were novices). Subsequently, to further fine tune the previously proposed definition, convexity of the capillary head as a conditional criterion for normal capillary morphology was added (see Fig. 1). This optimized definition of the morphology of single capillaries was subsequently evaluated at the seventh EULAR capillaroscopy course, held in Genoa in 2016. Thirty images with good visibility of single capillaries were presented to the attendees of the course ($n = 119$). Attendees were asked to classify the 30 single capillaries (one highlighted capillary per capillaroscopic image) as having a normal or abnormal morphology. They were also asked to categorize themselves into one of the following levels of expertise in capillaroscopy: no experience (novices), $n = 69$; < 5 years of experience, $n = 41$ and > 5 years of experience, $n = 9$. In addition, five independent experts (A.H., F.I., A.S., M.C. and V.S.) evaluated the capillaries. The assessment of V.S. was considered as the gold standard. Interrater agreement was evaluated by calculation of Cohen's κ between each rater pair of all possible combinations of attendees and

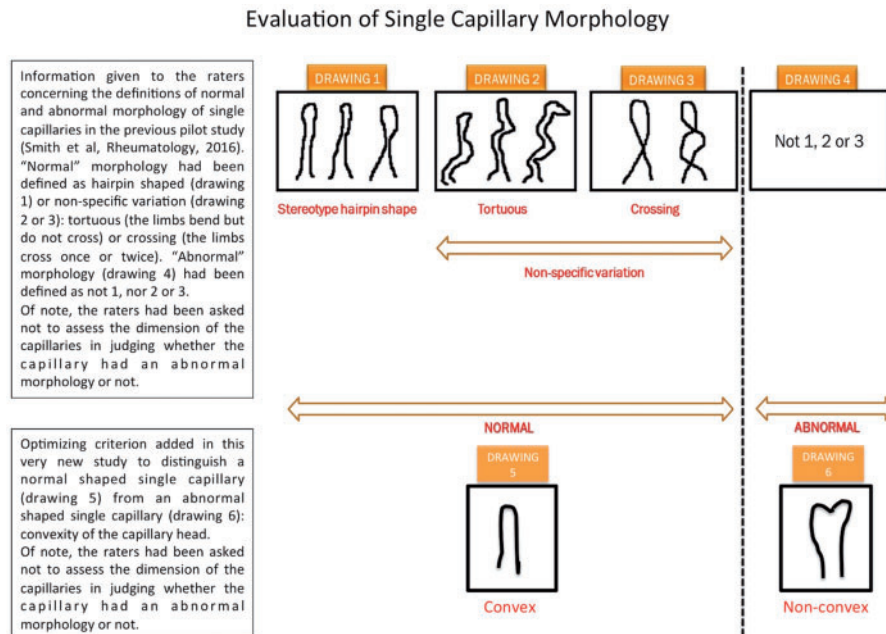
the gold standard and then averaged to provide the light κ [8]. Furthermore, the Cohen's κ scores between each attendee and the gold standard were averaged to obtain a mean index of reliability of the attendees to the gold standard. Finally, mean proportions of overall and specific agreement of attendees compared with the gold standard were reported. The study was conducted with the approval of the ethical committee of the Ghent University (EC2008/385).

The resulting light κ based on 30 capillaries was 0.78 for all EULAR course attendees and 0.82 for the five independent experts. More specifically, the light κ was 0.84 for experienced attendees, 0.78 for moderately experienced attendees and 0.77 for novices. The mean Cohen's κ coefficient of all attendees to the gold standard was 0.81 (95% CI 0.79, 0.83), with a mean proportion of overall agreement of 91%, a mean proportion of specific agreement for abnormal of 89% and for normal of 92%. Subgroup analyses according to the level of experience resulted in similar results for both reliability and agreement measures. Subgroup analyses demonstrated a mean Cohen's κ between each attendee and the gold standard of 0.83 (95% CI 0.78, 0.88) for experienced attendees, 0.81 (95% CI 0.77, 0.85) for moderately experienced attendees and 0.80 (95% CI 0.77, 0.83) for novices. Differences in mean agreement proportions between the subgroups and the total group of attendees were negligible. The mean Cohen's κ between each expert in capillaroscopy and the gold standard was 0.81 (95% CI 0.71, 0.92), with a mean proportion of overall agreement of 91%, a mean proportion of specific agreement for abnormal of 89% and for normal of 92%.

In conclusion, this multicentre, international study, conducted at the seventh EULAR course on capillaroscopy, demonstrated that the reliability of the optimized simple capillaroscopic definition of normal and abnormal morphologies of capillaries is excellent, even when used by rheumatologists with varying levels of expertise in capillaroscopy. Further, large-scale validation with random selection of single capillaries is needed to validate these findings.

Acknowledgements

We are grateful to all attendees of the seventh EULAR course on capillaroscopy, held in Genoa, Italy in 2016, for participating in this study. We also thank the collaborators of the EULAR Study Group on Microcirculation in Rheumatic Diseases. V.S. is Senior Clinical Investigator of the Research Foundation – Flanders (Belgium) (FWO) (grant number 1.8.029.15N).

Fig. 1 Evaluation of single capillary morphology

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Disclosure statement: O.D. had a consultancy relationship and/or has received research funding from Actelion, Bayer, Biogen Idec, Boehringer Ingelheim, ChemomAb, EspeRare Foundation, Genentech/Roche, GlaxoSmithKline, Inventiva, Italfarmaco, Lilly, Medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sinoxa and UCB in the area of potential treatments of scleroderma and its complications and has a licensed patent (miR-29) for the treatment of systemic sclerosis. The other authors have declared no conflicts of interest.

Maurizio Cutolo^{1,*}, Karin Melsens^{2,3,*}, Ariane L. Herrick⁴, Ivan Foeldvari⁵, Ellen Deschepper⁶, Filip De Keyser^{2,3}, Oliver Distler⁷, Francesca Ingegnoli⁸, Yora Mostmans^{9,10,11}, Ulf Müller-Ladner^{12,13}, Carmen Pizzorni¹, Valeria Riccieri¹⁴, Barbara Ruaro¹, Alberto Sulli¹, Amelia C. Trombetta¹, Amber Vanhaecke^{2,3} and Vanessa Smith^{2,3}; for the EULAR Study Group on Microcirculation in Rheumatic Diseases

¹Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of

Genoa, Genoa, Italy, ²Department of Rheumatology, Ghent University Hospital, ³Department of Internal Medicine, Ghent University, Ghent, Belgium, ⁴Centre for Musculoskeletal Research, University of Manchester, Manchester Academic Health Science Centre, Manchester, UK, ⁵Hamburg Centre for Pediatric and Adolescent Rheumatology, Schön Klinik Hamburg Eilbek, Hamburg, Germany, ⁶Biostatistics Unit, Department of Public Health, Ghent University, Ghent, Belgium, ⁷Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland, ⁸Division of Rheumatology, Istituto Gaetano Pini, Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy, ⁹Department of Dermatology, Universitair Ziekenhuis Brussel (UZ Brussel), ¹⁰Department of Dermatology, Vrije Universiteit Brussel (VUB), ¹¹Department of Immunology and Allergology (CIA), Centre Hospitalier Universitaire (CHU) Brugmann, Université Libre de Bruxelles (ULB), Brussels, Belgium, ¹²Department of Rheumatology and Clinical Immunology, Kerckhoff Clinic Bad Nauheim, Bad Nauheim, ¹³Department of Internal Medicine and Rheumatology, Justus-Liebig University Giessen, Giessen, Germany and ¹⁴Department of Internal Medicine and Medical Specialties, University Sapienza Rome, Rome, Italy
 *Maurizio Cutolo and Karin Melsens contributed equally to this study.

Revised version accepted 26 October 2017

Correspondence to: Vanessa Smith, Department of Rheumatology, Ghent University Hospital – P6, De Pintelaan 185, 9000 Ghent, Belgium.

E-mail: vanessa.smith@ugent.be

References

- 1 Cutolo M, Smith V. State of the art on nailfold capillaroscopy: a reliable diagnostic tool and putative biomarker in rheumatology? *Rheumatology* 2013;52:1933–40.
- 2 Sulli A, Secchi ME, Pizzorni C, Cutolo M. Scoring the nailfold microvascular changes during the capillaroscopic analysis in systemic sclerosis patients. *Ann Rheum Dis* 2008;67:885–7.
- 3 Smith V, Riccieri V, Pizzorni C *et al.* Nailfold capillaroscopy for prediction of novel future severe organ involvement in systemic sclerosis. *J Rheumatol* 2013;40:2023–8.
- 4 Smith V, Pizzorni C, De Keyser F *et al.* Reliability of the qualitative and semiquantitative nailfold videocapillaroscopy assessment in a systemic sclerosis cohort: a two-centre study. *Ann Rheum Dis* 2010;69:1092–6.
- 5 Melsens K, Wijnant S, Ingegnoli F *et al.* Capillaroscopy in systemic lupus erythematosus: a systematic review and critical appraisal [abstract]. *Ann Rheum Dis* 2017;76(Suppl 2):299.
- 6 Cutolo M, Sulli A, Pizzorni C, Accardo S. Nailfold video-capillaroscopy assessment of microvascular damage in systemic sclerosis. *J Rheumatol* 2000;27:155–60.
- 7 Smith V, Beeckman S, Herrick AL *et al.* An EULAR study group pilot study on reliability of simple capillaroscopic definitions to describe capillary morphology in rheumatic diseases. *Rheumatology* 2016;55:883–90.
- 8 Light RJ. Measures of response agreement for qualitative data: some generalizations and alternatives. *Psychol Bull* 1971;76:365–77.