Nailfold Capillaroscopy
Capilaroscopia ungueal

Borja Gracia Tello[1,2] Eduardo Ramos Ibañez[3]

Borja del Carmelo Gracia Tello [1]Hospital Clínico Universitario Lozano Blesa Zaragoza, Zaragoza. SPAIN. [2]Instituto de Investigación Sanitaria de Aragón (ISSA)
Corresponding author: Borja del Carmelo Gracia Tello. bcgracia@salud.aragon.es

Eduardo Ramos Ibañez [3]Ingeniero informático. Universidad de Zaragoza. SPAIN.

Conflict of interest: none.

Funding: none.

Ethical considerations: This study does not include the participation of patients, therefore it was not not written informed consent was obtained.

Nailfold Capillaroscopy
Capilaroscopia ungueal

Borja Gracia Tello[1,2] Eduardo Ramos Ibañez[3]
[1]Hospital Clínico Universitario Lozano Blesa Zaragoza, Zaragoza. SPAIN. [2]Instituto de Investigación Sanitaria de Aragón (ISSA)
[3]Ingeniero informático. Universidad de Zaragoza. SPAIN.

Capillaroscopy is a simple, non-invasive and accessible technique that allows physicians to analyze the microvasculature of patients by observing the capillaries of the nailfold.

Capillaroscopy makes it possible to see the shape and size of the capillaries, as well as any changes in their structure or function. These changes can be indicators of vascular diseases, such as Raynaud's phenomenon and scleroderma. This technique, first described in the 17th century by Johan Christophorus Kolhaus, has been limited throughout its history by the available technology at the time (1).

During the development of the technique, the difficulty in obtaining lenses with sufficient magnification to allow correct visualization of the capillaries and, likewise, contact oils to improve the refractoriness of the applied light prevented widespread use of the technique. Even so, in the 18th century Giovanni Rasori made the first association between the findings of the conjunctiva with capillaroscopic alterations in the nail bed. In the first quarter of the 20th century, Lombard described for the first time a capillaroscopy performed with immersion oil (2). These technical difficulties resulted in large and expensive apparatus, difficult to handle and learn, and scarcely adapted to the exploration of patients in real practice.

Well into the 20th century, technological advances translated into the availability of increasingly modern lenses, called stereomicroscopes, an optical microscope variant designed for low magnification observation of a sample, typically using light reflected from the surface of an object rather than transmitted through it, accessible to a greater number of hospitals, but a new limitation appeared: the heterogeneity in their interpretation and inter-observer variability, derived from the difficulty for the objective and individual analysis of each of the observed capillaries (3-

4). For this reason, different authors such as Weiss, Maricq and Cutolo successively (5-6), proposed different classifications that sought to solve this "impossibility" of individual analysis by classifying the images in a few "patterns", which combined the most outstanding findings allowing a global analysis of the exploration, without the need to know the individual details of each capillary. These patterns, widely used, have made capillaroscopy a more useful tool in the classification of Raynaud's phenomenon and in the classification, activity, and prognosis of patients with scleroderma (7-11). In addition, in recent years the association of clinical manifestations in systemic sclerosis with capillaroscopy findings has been revealed, considering capillaroscopy as a promising biomarker (10, 12-14).

However, with the beginning of the 21st century great progress was made in capillaroscopy. On the one hand, the increasingly widespread use of video capillaroscopes; easy to use, inexpensive and portable devices that allow image processing and storage have been replacing the classic stereomicroscopes, generalizing the use of the technique, and making capillaroscopy possible during the patient consultation or even bedside. On the other hand, in recent years the use of artificial intelligence applied to capillaroscopy has brought its development to new limits that were not previously conceivable and establishes a very promising future for capillaroscopy.

Artificial intelligence is increasingly being used as a tool to support physicians in different areas of medicine. For example, artificial intelligence systems are being developed that can analyze medical images and detect patterns that may indicate disease. This can help physicians make accurate diagnoses and save time in image interpretation.

Since 2014, several groups have been investigating different ways to apply artificial intelligence in a useful way in capillaroscopy. In 2019, the Automated Nailfold Capillary Counting System (AUTOCAPI system), was presented that demonstrated that there were no significant differences when using artificial intelligence versus manual counting in the analysis of 183 capillaroscopies of patients diagnosed with scleroderma (15). However, this system did not perform morphologic interpretation of the capillaries, nor did it allow the detection of avascular areas, microhemorrhages, or other morphologic findings. Recently, a proposal for the use of artificial intelligence for the

automated detection of the patterns described by Cutolo et al. (6) in capillaroscopy images according to their general appearance has been published (16). The proposed system is based on the global analysis of the image, without providing an individualized or detailed analysis of each image. Although this may seem to be a great advance, in our opinion it is a limited approach since it does not allow comparing different capillaroscopies in an objective and quantitative manner. A patient can be classified with the same pattern even when presenting very different findings in terms of mean capillary loop diameter or number of dilations, megacapillaries or microhemorrhages. In addition, these systems are based on an incomplete analysis of the nail bed, which necessarily leads to bias because the information is not available for the entire image.

From our perspective, for a true advance in capillaroscopy that allows it to be applied not only to continue the great current advances on Systemic Sclerosis where exists the largest series and better evidence (12-14), and autoimmune diseases or Raynaud's phenomenon (7-9), but also to all pathologies that present microvascular involvement, we need to count, measure, and rigorously classify all capillaries from patients (17, 18). Only in this way will we be able to assess the increasingly proven usefulness of capillaroscopy in diseases other than scleroderma, measure the progression of capillaries in the same patient or compare them in a completely objective manner with other patients. Other initiatives or perspectives, although they will represent a short-term improvement and an advance with respect to the current situation, will not allow a comprehensive capillaroscopic assessment to be made.

In our opinion, the way to solve this problem is to use artificial intelligence to automate the analysis of individual capillaries (19-20), allowing an automated identification, measurement and classification that facilitates the interpretation of the very large number of capillaries that make up a complete capillaroscopy. This information will assess not only the presence or absence of morphological alterations but also the average size of each of the groups in each of its parts (afferent, efferent and apex loops) as well as quantitatively the number of microhemorrhages, the presence of avascular areas or other findings.

The availability of supporting software will greatly simplify capillaroscopic interpretation, significantly reducing the intraobserver variability that is so limiting at present. Likewise, it will make it possible to obtain reports and statistics of a complete

capillaroscopy in less time, which until now would have required hours to be done manually. Also, by presenting a support based on artificial intelligence, it will allow greater accessibility to healthcare professionals with less experience doing the technique.

Likewise, with this analysis system we will be able to classify the capillaroscopies by means of the described patterns, so useful currently, but without losing objective and quantitative information, fundamental in modern medicine, which will allow us to advance deeper into the capillaroscopy applications.

In conclusion, capillaroscopy has been limited by technology throughout its history. However, the use of portable video capillaroscopes and artificial intelligence are driving the development of the technique, both in research and clinical use, and establish a promising future for capillaroscopy not only for autoimmune diseases, but for all diseases with microvascular involvement.

BIBLIOGRAPHY

1. Ross JB. Nailfold capillaroscopy. A useful aid in the diagnosis of collagen vascular diseases. J Inv Derm 1966; 47: 282-285
2. Grassi W, De Angelis R. Capillaroscopy: questions and answers. Clin Rheumatol. 2007;26:2009.
3. Rodriguez-Reyna TS, Bertolazzi C, Vargas-Guerrero A, Gutiérrez M, Hernández-Molina G, Audisio M, et al; PANLAR Capillaroscopy Group. Can nailfold videocapillaroscopy images be interpreted reliably by different observers? Results of an inter-reader and intra-reader exercise among rheumatologists with different experience in this field. Clin Rheumatol. 2019;38:205-210.
4. Sáez-Comet L, Fanlo-Mateo P, Gracia-Tello B; en representación del GREC (Grupo Español de Capilaroscopias); Otros miembros del Grupo Español de Capilaroscopias. Nailfold capillaroscopy in the Spanish Group of Systemic Autoimmune Diseases (GEAS). Results of an electronic survey. Med Clin (Barc). 2020;155:509-510.
5. Maricq HR, Spencer G, Leroy EC. Skin capillary abnormalities as indicator of organ involvement in scleroderma (Systemic sclerosis), Raynaud's syndrome and dermatomyositis. Am J Med 1976; 61: 862- 870.
6. Cutolo M, Sulli A, Pizzorni C, Accardo S. Nailfold videocapillaroscopy assessment of microvascular damage in systemic sclerosis. J Rheumatol. 2000;27:155-60.
7. Koenig M, Joyal F, Fritzler MJ, Roussin A, Abrahamowicz M, Boire G, et al. Autoantibodies and microvascular damage are independent predictive factors for the progression of Raynaud's phenomenon to systemic sclerosis: a twenty-year prospective study of 586 patients, with validation of proposed criteria for early systemic sclerosis. Arthritis Rheum. 2008;58:3902-12.
8. Van den Hoogen F, Khanna D, Fransen J, Johnson SR, Baron M, Tyndall A, et al. 2013 classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative. Ann Rheum Dis. 2013;72:1747-55.
9. Ingegnoli F, Boracchi P, Gualtierotti R, Lubatti C, Meani L, Zahalkova L, et al. Prognostic model based on nailfold capillaroscopy for identifying Raynaud's phenomenon patients at high risk for the development of a scleroderma spectrum disorder: PRINCE (prognostic index for nailfold capillaroscopic examination). Arthritis Rheum. 2008;58:2174-82.
10. Sebastiani M, Manfredi A, Colaci M, D'amico R, Malagoli V, Giuggioli D, et al. Capillaroscopic skin ulcer risk index: a new prognostic tool for digital skin ulcer development in systemic sclerosis patients. Arthritis Rheum. 2009;61:688-94.
11. Sebastiani M, Manfredi A, Vukatana G, Moscatelli S, Riato L, Bocci M, et al. Predictive role of capillaroscopic skin ulcer risk index in systemic sclerosis: a multicentre validation study. Ann Rheum Dis. 2012;71:67-70.
12. Vanhaecke A, Cutolo M, Distler O, Riccieri V, Allanore Y, Denton CP, et al. Nailfold capillaroscopy in SSc: innocent bystander or promising biomarker for novel severe organ involvement/progression? Rheumatology (Oxford). 2022;61:4384-4396.
13. Avouac J, Lepri G, Smith V, Toniolo E, Hurabielle C, Vallet A, et al. Sequential nailfold videocapillaroscopy examinations have responsiveness to detect organ progression in systemic sclerosis. Semin Arthritis Rheum. 2017;47:86-94.

14. Guillén-Del-Castillo A, Simeón-Aznar CP, Callejas-Moraga EL, Tolosa-Vilella C, Alonso-Vila S, Fonollosa-Pla V, et al. Quantitative videocapillaroscopy correlates with functional respiratory parameters: a clue for vasculopathy as a pathogenic mechanism for lung injury in systemic sclerosis. Arthritis Res Ther. 2018;20:281.
15. Sulli A, Vanhaecke A, Pizzorni C, Ferrari G, Tomatis V, Pendolino M, et al. Automated Nailfold Capillary Counting System (AUTOCAPI) in Systemic Sclerosis Patients with Different Capillaroscopic Patterns [abstract]. Arthritis Rheumatol. 2019; 71 (suppl 10).
16. Garaiman A, Nooralahzadeh F, Mihai C, Perez Gonzalez N, Gkikopoulos N, Becker MO, et al. Vision Transformer Assisting Rheumatologists in Screening for Capillaroscopy Changes in Systemic Sclerosis: An Artificial Intelligence Solution [abstract]. Arthritis Rheumatol. 2022; 74 (suppl 9).
17. Anderson ME, Allen PD, Moore T, Hillier V, Taylor CJ, Herrick AL. Computerized nailfold video capillaroscopy--a new tool for assessment of Raynaud's phenomenon. J Rheumatol. 2005;32:841-8.
18. Cutolo M, Trombetta AC, Melsens K, Pizzorni C, Sulli A, Ruaro B, et al. Automated assessment of absolute nailfold capillary number on videocapillaroscopic images: Proof of principle and validation in systemic sclerosis. Microcirculation. 2018;25:e12447.
19. Herrick AL, Berks M, Taylor CJ. Quantitative nailfold capillaroscopy-update and possible next steps. Rheumatology (Oxford). 2021;60:2054-2065.
20. Gracia Tello B, Ramos Ibañez E, Fanlo Mateo P, Sáez Cómet L, Martínez Robles E, Ríos Blanco JJ, et al. The challenge of comprehensive nailfold videocapillaroscopy practice: a further contribution. Clin Exp Rheumatol. 2022;40:1926-1932.