Medicina Clínica 166 (2026) 107426

Contents lists available at ScienceDirect

Medicina Clínica

journal homepage: www.elsevier.es/medicinaclinica

Original article

Value of nailfold capillaroscopy in the classification of the systemic sclerosis pattern

Valor de la capilaroscopia ungueal en la clasificación del patrón de esclerosis sistémica

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ARTICLE INFO

Keywords:
Nailfold videocapillaroscopy
Scleroderma patterns
Reliable diagnosis
Nailbed images
Nailbed areas

ABSTRACT

Objectives: Nailfold videocapillaroscopy (NVC) is the gold-standard to identify scleroderma patterns. Our aim was to establish the minimum requirements; number of fingers, length of nailbed samples, location of nailbed areas, to diagnose the existence of systemic sclerosis patterns (SSc-P) and further identify non-SSc-P and SSc-P subtypes reliably.

Methods: NVCs were taken during routine explorations by capillaroscopists from 12 hospitals, who made four diagnosis per patient according to the examination of the following: 32 images (4 images/finger, mean 59.43 mm); 16 images (2 medial images/finger [mean 29.28 mm]); 8 images (1 medial image/finger [mean 14.50 mm]); 4 images (1 medial image per middle fingers [mean 7.22 mm]). Diagnosis matches and discrepancies considering 32 versus 16, 8 or 4 images, were calculated, with the goal of estimating the information loss when not covering the whole nailbed. The same analysis was performed using the CAPI-Score and CAPI-Detect algorithms.

Results: A total of 2,387 NVCs were used. Disagreement in pattern assignment was 26.7%, 36.6% and 41.5% when the analysis was performed over 16, 8 or 4 images, respectively. When 16 images were used, 18.5% of expert observers changed their assigned pattern in 18.5% of cases from SSc-P to non-SSc-P, and >30% of patients diagnosed were assigned a different subtype. Although to a lesser extent, diagnosis discrepancies were observed when CAPI-Score and CAPI-Detect algorithms were applied.

Conclusion: All fingers but thumbs have to be considered to identify scleroderma patterns accurately. Four nailbed areas in the analysis demonstrated to be superior than using a partial sample.

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https://doi.org/10.1016/j.medcli.2026.107426
Received 2 January 2026; Accepted 24 February 2026

R E S U M E N

Objetivos: La videocapilaroscopia del lecho ungueal (NVC) es el método de referencia para identificar los patrones de esclerodermia. Nuestro objetivo era establecer los requisitos mínimos (número de dedos, longitud de las muestras del lecho ungueal, ubicación de las áreas del lecho ungueal) para diagnosticar la existencia de patrones esclerodérmicos (SSc-P) e identificar de forma fiable los subtipos no SSc-P y SSc-P.
Métodos: Los NVC se tomaron durante exploraciones rutinarias realizadas por capilaroscopistas de 12 hospitales, quienes realizaron cuatro diagnósticos por paciente según el examen de lo siguiente: 32 imágenes (4 imágenes/dedo, media de 59,43 mm); 16 imágenes (2 imágenes mediales/dedo [media de 29,28 mm]); 8 imágenes (1 imagen medial/dedo [media de 14,50 mm]); 4 imágenes (1 imagen medial por dedo medio [media de 7,22 mm]). Se calcularon las coincidencias y discrepancias en el diagnóstico considerando 32 frente a 16, 8 o 4 imágenes, con el objetivo de estimar la pérdida de información cuando no se cubre todo el lecho ungueal. Se realizó el mismo análisis utilizando los algoritmos CAPI-Score y CAPI-Detect.
Resultados: Se utilizaron un total de 2387 NVC. El desacuerdo en la asignación de patrones fue del 26,7%, 36,6% y 41,5% cuando el análisis se realizó sobre 16, 8 o 4 imágenes, respectivamente. Cuando se utilizaron 16 imágenes, el 18,5% de los observadores expertos cambiaron el patrón asignado en el 18,5% de los casos de SSc-P a no SSc-P, y a más del 30% de los pacientes diagnosticados se les asignó un subtipo diferente. Aunque en menor medida, se observaron discrepancias en el diagnóstico cuando se aplicaron los algoritmos CAPI-Score y CAPI-Detect.
Conclusión: Para identificar con precisión los patrones de esclerodermia, es necesario tener en cuenta todos los dedos, excepto los pulgares. Las cuatro áreas del lecho ungueal analizadas demostraron ser superiores al uso de una muestra parcial.

Palabras clave:
Videocapilaroscopia del pliegue ungueal
Patrones de esclerodermia
Diagnóstico fiable
Imágenes del lecho ungueal
Áreas del lecho ungueal

Introduction

Detection of abnormal capillaries by nailfold videocapillaroscopy (NVC) is among the classification criteria for scleroderma or systemic sclerosis patterns (SSc-P) in the American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR).[1] NVC SSc-Ps correspond to three stages: early, active, and late according to Cutolo's proposal. These patterns represent endothelial dysfunction and microangiopathy progression, and can be identified by capillaroscopic changes (Supplementary Data S1).[2] An early SSc diagnosis is important to consider therapeutic strategies to prevent or delay adverse outcomes. For many years, NVC analyses did not cover more than one finger.[3] However, it became apparent in the last decade that this practice led to misdiagnosis, and that all fingers but thumbs should be considered to assign disease patterns accurately.[4,5] In any case, consensus statements have not been published regarding the minimum length of the nailbed sample or the nailbed's area to cover, i.e., if considering medial territories is enough.

With this background, we hypothesized that choosing uniquely medial fields could jeopardize SSc-P diagnosis or correct staging, and, thus, that the gold-standard to execute NVC should comprise both medial and lateral territories of the eight fingers, i.e., 32 images of 1.5–2.5 mm each. To accomplish this purpose, a nationwide, quantitative study of concordance was designed where capillaroscopists were invited to recruit patients assessed in consultations for Raynaud's phenomenon and diagnose them as having or not having SSc-P and, where applicable, assign SSc-P stage, on the basis of examining 32 or less images per patient. Furthermore, taking advantage of the clinically validated Capillary.io software to assess capillary density and count and categorize abnormalities,[6,7] which allowed us to develop the CAPI-Score and the machine learning (ML)-based CAPI-Detect algorithms,[8,9] we studied if these models were able to assign patients the same disease pattern regardless of the number of images analyzed was 32, 16, 8 or 4.

Methods

Patient recruitment

NVC images were taken by researchers from 12 Spanish and American hospitals with expertise in capillaroscopy-based diagnosis of connective tissue disorders (Supplementary Table S1). Each examiner studied 200 patients from their own hospitals. Image collection was performed during routine explorations. The digital video capillaroscopes used are listed in Supplementary Table S2. Thirty-two images were recorded per patient: four images per finger except thumbs (two medial, one left lateral, one right lateral) (Supplementary Fig. S1A).

Poor quality images

The experts discarded those NVCs considered, at their discretion, not to have enough quality. Discarded NVCs were not used in the automated analyses. Therefore, manual and automated analyses were performed on the same sets of NVCs.

Assessment of disease pattern diagnosis according to the number of fields examined

Manual analysis

Each expert manually examined the NVCs of their own patients. Diagnoses were given according to examination of, in this order, 4, 8, 16 and 32 images (Supplementary Fig. S1A–D). The increasing order in the number of images to analyze was decided to minimize the risk of biased diagnosis. To further prevent biased disease pattern assignments, the examiner was blinded to the patient's identification, and the NVCs were randomly analyzed. 200× magnification was always used for analysis. In each phase, both the order of the capillaroscopies and the order of the images included were randomized in order to avoid carry-over bias. The time allowed was 30 days for each phase, with an average total of 143 days to complete the four phases. At no point during the study did the researcher know which images he was interpreting or the purpose of the study.

Software-based analysis

The same images analyzed manually were submitted to analysis using the Capillary.io software.[6,7]

CAPI-Score algorithm. Taking advantage of the information of each bunch of 32, 16, 8 or 4 images per patient provided by Capillary.io, the CAPI-Score algorithm was applied to assign disease patterns according to rules explained in detail elsewhere (Supplementary Data S2).[8]

CAPI-Detect algorithm. The use of ML to develop the CAPI-Detect algorithm was described previously.[9] Twenty-four variables related to capillary density and architecture were quantified by Capillary.io. Disease pattern assignment was performed taking advantage of the ML-based classification models previously trained using CatBoost software on a bank of 1490 NVCs whose disease pattern had been assigned by an expert consensus.[9]

Ethics

Capillary.io, its database and the projects to build the CAPI-Score and CAPI-Detect algorithms were approved by the Clinical Research Ethics Committee of Aragón, Spain (record number PI18/336 [20/2018]). All patients signed an informed consent form. The images were always anonymized.

Statistical analysis

Proportions of disease patterns were calculated for manual or automated analyses using 32, 16, 8 or 4 images per patient. Comparisons of proportions of coincidences among analyses performed with 32, 16, 8 or 4 images per patient were carried out using the chi square test. Proportion of Capillary.io-detected capillary abnormalities, as defined elsewhere,[6,7] were calculated for right and left hand with all available images. Violin plots were generated to compare the distribution of abnormalities according to the nail sectors analyzed.

Agreement between classifications obtained with different numbers of images was assessed using Cohen's kappa coefficient (κ) for binary classification (SSc-P vs non-SSc-P) and weighted kappa (quadratic weights) for the five-category ordinal classification (normal, non-specific, SSc-early, SSc-active, SSc-late). Kappa values are reported with 95% confidence intervals (CI). Paired comparisons of binary SSc-P versus non-SSc-P classification (32 images vs 16, 8 or 4 images) were performed using McNemar's test. Disagreement proportions were reported with 95% CI (Wilson method). To evaluate homogeneity across investigators, disagreement rates were calculated separately for each examiner, and presented with 95% CI.

Results

Up to 2387 NVCs of 2387 patients were recorded. After discarding 107 of them for poor quality or inability to make a diagnosis by manual examination, 2280 NVCs were selected for manual and automated analysis (Supplementary Fig. S2). The mean (standard deviation [SD]) size of each image captured was 1.88 (0.32) mm wide. Of the capillaroscopies analyzed, 78.99% belonged to women and 21.01% to men. Similarly, 63.48% of patients were Caucasian, 33.38% were Amerindian, 2.18% were African American, and 0.87% were Asian. The reported clinical diagnosis was primary Raynaud's phenomenon in 47.85% of cases, scleroderma in 35.73% of cases, and other pathologies such as inflammatory myopathy (10.19%), undifferentiated connective tissue disease (8.37%), mixed connective tissue disease (4.18%), systemic lupus erythematosus (9.23%), and others such as antiphospholipid syndrome (1.72%) or Buerger's disease (0.32%). The mean age of the patients included was 49.96 years (SD 37.5).

Manual analysis

Considering the examination of 32 images per patient (59.43 [10.16] mm, mean [SD]) as the gold-standard, disagreement mounted up to 26.7%, 36.6% and 41.5% when the analysis was performed over 16 (29.28 [4.23] mm), 8 (14.50 [2.2] mm) or 4 (7.22 [1.23] mm) images, respectively ($P < 0.001$) (Fig. 1A). When comparing diagnosis of non-SSc-P versus SSc-P according to examining 32 or 16 images, 18.5% of patients diagnosed with SSc-P over 32 images were considered not to have a pathological pattern when the examination was performed over 16 images (Fig. 1B).

Patients were further assigned a normal, non-specific, SSc-early, SSc-active or SSc-late pattern. The results of these analyses according to examination of 32, 16, 8 or 4 images are shown in Supplementary Fig. S3A. The proportion of ungradable NVCs was increasing as the number of analyzed images decreased. Table 1 focuses on the examinations performed with 32 or 16 images, and describes, for each pattern assigned by the gold-standard, the magnitude of the erroneous assignment of other diagnoses when 16 images were analyzed. The wrong assignment of normal pattern to patients diagnosed with non-specific pattern was the most common error when 16 images instead of 32 were analyzed. Wrong attributions of non-specific pattern were frequent in patients who had really a SSc-early pattern. Misdiagnosis among SSc patterns was also detected.

Agreement analysis confirmed a progressive decline in concordance when nailfold coverage was reduced. For 32 vs 16 images, binary agreement (SSc-P vs non-SSc-P) was $\kappa = 0.829$ (95% CI: 0.804–0.854). Five-category agreement was $\kappa = 0.640$ (95% CI: 0.612–0.668), while weighted kappa (quadratic weights) was $\kappa w = 0.860$ (95% CI: 0.837–0.883). McNemar's test showed significant asymmetry in paired binary misclassification ($P < 0.001$), indicating a systematic bias toward underdiagnosis of SSc-P when fewer images were analyzed.

The degree of agreement was analyzed individually, yielding the following results. Overall disagreement (all researchers combined) was 26.7% (95% CI 24.9–28.6). By investigator, disagreement ranged from 17.3% to 34.2%, with relatively narrow 95% CIs (Supplementary Table 3).

Automated analyses

CAPI-Score algorithm

Disagreement in diagnosis was close to 20% when only 16 images were considered, and mounted up to almost 30% and 40% with 8 and 4 images per patient, respectively ($P < 0.001$) (Fig. 1C). When 16 images were examined, 9.3% of patients diagnosed with SSc-P over 32 fields were assigned a non-SSc-P (Fig. 1D). Within those patients diagnosed not to have SSc-P, more than 10% of those considered normal were diagnosed as non-specific with 16 images, and vice versa. In the group of SSc-P patients, 15.1% of those diagnosed with SSc-early pattern were assigned a non-SSc pattern when only 16 images were used. Furthermore, 19.8% of those diagnosed with SSc-late pattern were assigned a different SSc-P (Table 1). Supplementary Fig. S3B shows the proportion of each pattern when the CAPI-Score algorithm was applied to 32, 16, 8 or 4 images.

For 32 vs 16 images, binary agreement (SSc-P vs non-SSc-P) was $\kappa = 0.855$ (95% CI: 0.831–0.879). Five-category agreement was $\kappa = 0.746$ (95% CI: 0.719–0.773), and weighted kappa was $\kappa w = 0.874$ (95% CI: 0.851–0.897). McNemar's test confirmed significant asymmetry in paired binary classification ($P < 0.001$).

CAPI-Detect algorithm

Disagreements between the gold-standard and the other analyses were lower when the CAPI-Detect algorithm was used, but remained significant ($P < 0.001$) (Fig. 1E). Although only 1.2% and 6.6% of those patients diagnosed with non-SSc-P and SSc-P, respectively, by the gold-standard were considered to belong to the opposite group in the analysis performed using 16 images (Fig. 1F), further pattern assignment revealed remarkable disagreements. Within the non-SSc-P group, 17.2% of those diagnosed as non-specific were considered to exhibit a normal pattern. Within the SSc-P group, roughly 20% of those diagnosed with either SSc-early, SSc-active or SSc-late pattern were assigned a different one (Table 1). The proportion of patterns according to the number of analyzed images is shown in Supplementary Fig. S3C.

CAPI-Detect showed the highest agreement. For 32 vs 16 images, binary κ was 0.927 (95% CI: 0.909–0.945). Five-category κ was 0.789 (95% CI: 0.764–0.814), and weighted κw was 0.920 (95% CI: 0.901–0.939). McNemar's test remained significant ($P < 0.001$), although misclassification rates were lower than in manual and CAPI-Score analyses.

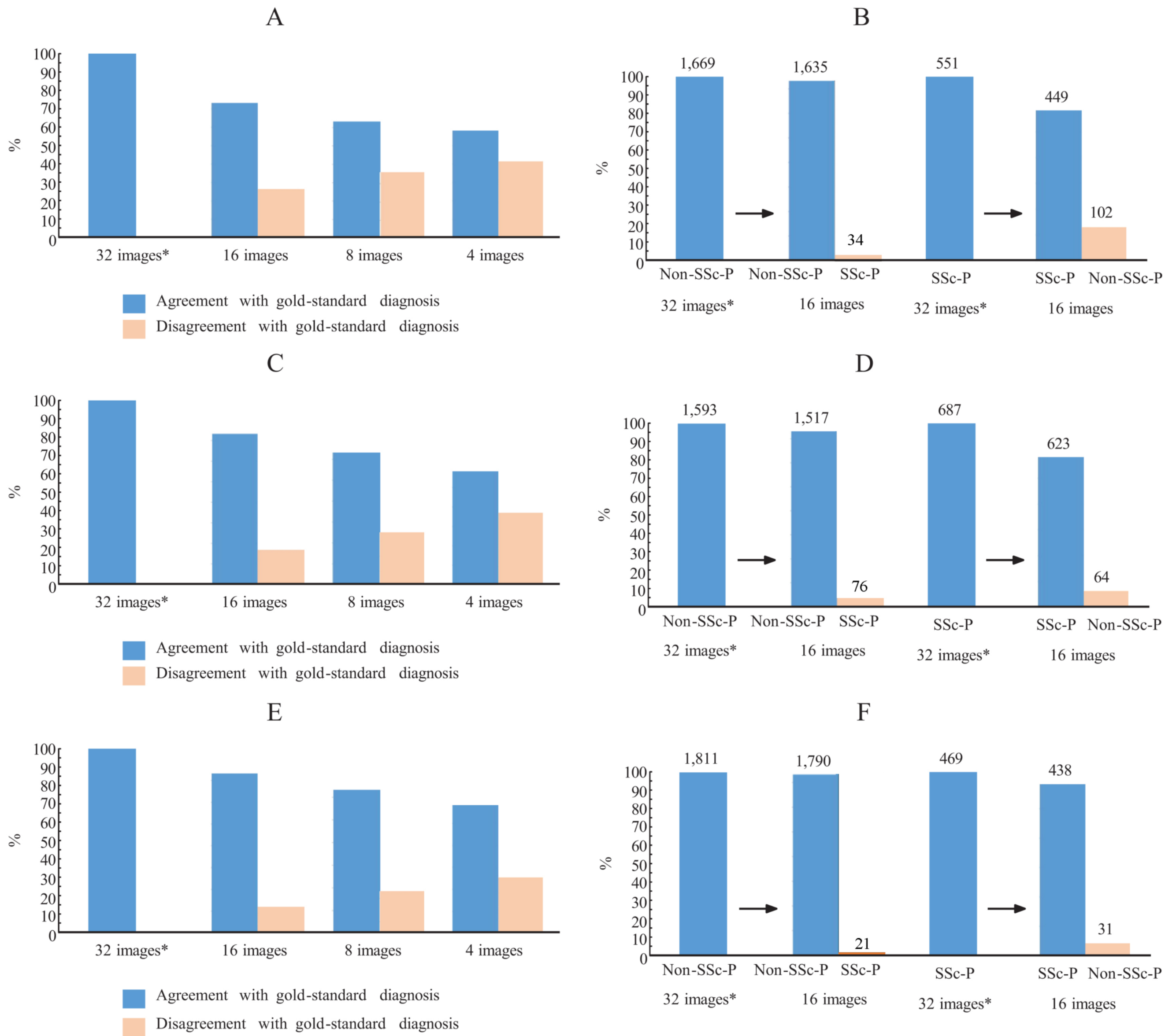

Fig. 1. Agreement between the pattern based on the number of images analyzed. (A) Agreement in manual analysis. (B) Percentage of patients who change their pattern based on the number of images. (C) Agreement in analysis with CAPI-Score algorithm. (D) Percentage of patients who change their pattern based on the number of images according to CAPI-Score. (E) Agreement in the analysis with CAPI-Detect algorithm. (F) Percentage of patients who change their pattern based on the number of images according to CAPI-Detect.

Right hand versus left hand

No remarkable differences regarding number and type of abnormalities were observed between right and left hands (Supplementary Fig. S4). Differences between finger lateral and medial images were not observed either (Supplementary Fig. S5).

Discussion

We have revisited the minimum requirements needed to assign SSc patterns reliably. Early studies stated that analyzing ring finger capillaries was enough to discriminate between primary Raynaud's phenomenon (PRP) and SSc.[3] Later, it was said that best capillaroscopic predictions, at least regarding SSc digital ulcers, were attained when the middle finger of the dominant hand was chosen.[10] More recent reports claim that all fingers but thumbs must be considered for analysis. One study showed that better accuracy was gained when the eight fingers were analyzed instead of the middle and ring fingers only, although whether or not the number of images per finger influenced diagnostic decision was not addressed.[4] Importantly, a pivotal review that provided comprehensive recommendations regarding how to use NVC in daily practice, confirmed the requirement to examine the eight fingers.[5] The authors had earlier recommended to analyze four fields, two medial and two lateral, 1 mm each, per each of the eight fingers, to perform a semi-quantitative assessment of the hallmarks of the SSc-P.[2] Nowadays, when the quantitative assessment is being increasingly used, the authors recommend to count capillaroscopic characteristics per mm and perform calculations over 32 images, or 16 images if two medial fields per finger have been taken.[5] Nevertheless, direct comparisons of SSc-P diagnosis accuracy when 32 or 16 images are used have not been performed, and the loss of information that may occur when lateral fields are not included in the analysis has not been addressed either. We provide quantitative evidence regarding matching in disease pattern assignment according to the number and length of the nailbed samples analyzed. Discrepancies with respect to those results obtained with 32 images (8 fingers, ~60 mm overall) were not only observed with 8 (8

Table 1
Agreement in diagnosis when examination was performed with 32 (gold-standard) or 16 images per patient.

Manual analysis

32 images/patient	16 images/patient					
(gold-standard)	Normal	Non-specific	SSc-early	SSc-active	SSc-late	U.G.[a]
Normal ($N = 838$)	730 (87.1)	88 (10.5)	3 (0.4)	0 (0)	0 (0)	17 (2.0)
Non-specific ($N = 875$)	237 (27.1)	580 (66.3)	25 (2.9)	1 (0.1)	5 (0.6)	27 (3.1)
SSc-early ($N = 258$)	13 (5.0)	67 (26.0)	155 (60.1)	17 (6.6)	2 (0.8)	4 (1.6)
SSc-active ($N = 220$)	1 (0.4)	16 (7.3)	29 (13.2)	147 (66.8)	22 (10.0)	5 (2.3)
SSc-late ($N = 89$)	0 (0)	5 (5.6)	5 (5.6)	13 (14.6)	59 (66.3)	7 (7.9)

CAPI-Score algorithm

32 images/patient	16 images/patient					
(gold-standard)	Normal	Non-specific	SSc-early	SSc-active	SSc-late	U.G.
Normal ($N = 720$)	600 (83.3)	94 (13.1)	24 (3.3)	0 (0)	2 (0.3)	n.a.
Non-specific ($N = 873$)	92 (10.5)	731 (83.7)	44 (5.0)	5 (0.6)	1 (0.1)	n.a.
SSc-early ($N = 365$)	17 (4.7)	38 (10.4)	271 (74.2)	18 (4.9)	21 (5.7)	n.a.
SSc-active ($N = 231$)	0 (0)	9 (3.9)	21 (9.1)	190 (82.2)	11 (4.8)	n.a.
SSc-late ($N = 91$)	0 (0)	0 (0)	9 (9.9)	9 (9.9)	73 (80.2)	n.a.

CAPI-Detect model

32 images/patient	16 images/patient					
(gold-standard)	Normal	Non-specific	SSc-early	SSc-active	SSc-late	U.G.
Normal ($N = 1084$)	1002 (92.4)	80 (7.4)	2 (0.2)	0 (0)	0 (0)	n.a.
Non-specific ($N = 727$)	125 (17.2)	583 (80.2)	15 (2.1)	0 (0)	4 (0.5)	n.a.
SSc-early ($N = 206$)	4 (1.9)	22 (10.7)	168 (81.5)	8 (3.9)	4 (1.9)	n.a.
SSc-active ($N = 132$)	1 (0.8)	0 (0)	15 (11.4)	109 (82.6)	7 (5.3)	n.a.
SSc-late ($N = 131$)	2 (1.5)	4 (3.0)	8 (6.1)	13 (9.9)	104 (79.4)	n.a.

n.a., not applicable; SSc, systemic sclerosis; U.G., ungradable.
Results are *n* (%).
[a] Ungradable due to poor quality or inability of the examiner to make an accurate diagnosis.

fingers, ~15 mm overall) or 4 (4 fingers, ~7.5 mm overall) images, but also when 16 images (8 fingers, ~30 mm overall) were used. In this case, discrepancies mounted up to 25% when the analysis was performed manually. Importantly, disagreements were not limited to discrepancies within the SSc-P or non-SSc-P categories. Almost one fifth of those patients who had been assigned a SSc-P after the examination of 32 images were considered to have a non-SSc-P when 16 images were used. The manual analysis also revealed that the proportion of normal patterns increased while that of non-specific patterns decreased as the number of analyzed images gradually declined. Finally, the proportion of patients who had been assigned a SSc-early, SSc-active or SSc-late pattern by the gold-standard and, subsequently, had a different diagnosis with 16 images, was never lower than 33%. Although at a lesser extent, remarkable discrepancies could also be seen when the automated analyses, either the CAPI-Score algorithm or the CAPI-Detect model, were applied.

Whether the examination of lateral in addition to medial areas is advisable when looking for abnormalities in nailbeds has not been addressed in depth elsewhere.[4,5,10] In our study, the main difference between the analyses based on the examination of 16 or 32 images, was that, in the first case only medial territories were included. It is conceivable that abnormalities not detected in medial nailbed areas be present in the lateral ones, which could contribute to the observed discrepancies. Thus, limiting the examination to the medial area may prevent access to valuable information, in spite of overall differences in abnormality proportions between nailbed sectors, or between hands, were not observed.

The present work should formally be interpreted as a diagnostic concordance study. Weighted kappa coefficients confirmed that agreement progressively declines as nailbed coverage is reduced, even when 16 images (~30 mm) are analyzed. Importantly, McNemar's test demonstrated a systematic asymmetry in paired binary classification, revealing a consistent bias toward underdiagnosis of SSc-P when fewer images are considered.

With reliable automated analysis now widely available for nailfold capillaroscopy, there is no reason to restrict image acquisition to partial segments. Capturing the entire nailbed (medial and lateral) of all eight fingers should be the default to avoid length-driven bias and preserve diagnostic accuracy. Currently, the existence of AI software specialized in capillaroscopy allows any commercially available capillaroscope to be used with automatic quantitative interpretation practically simultaneous with the performance of the technique (an average of 10 seconds for recognition, measurement and report writing), enabling a completely objective interpretation of the capillaroscopy without any additional cost or time.

In summary, we provide evidence to support that all fingers but thumbs must be considered to assign SSc/non-SSc patterns accurately. Our results also suggest that both medial and lateral nailbed areas (≥6 mm per finger overall) should be examined.

Contributors

BGT designed research, contributed to patient recruitment and NVC analysis and wrote the manuscript. ER developed the software, trained ML-based models and wrote the manuscript. The rest of the authors contributed to patient recruitment and NVC analysis and reviewed the final manuscript. BGT is responsible for the overall content as guarantor.

Ethical considerations

The project was approved by the Clinical Research Ethics Committee of Aragón, Spain (record number PI18/336 [20/2018]). All patients signed an informed consent form. The images were always anonymized.

Funding

Boehringer Ingelheim funded the open access publication of this article via the Aragon Health Research Institute. Boehringer Ingelheim did not participate in the design, analysis or interpretation of the results of this study. Boehringer Ingelheim was given the opportunity to review the manuscript for medical and scientific accuracy as it relates to Boehringer Ingelheim substances, as well as intellectual property considerations.

Conflict of interest statement

The authors declare that there are no conflicts of interest regarding the publication of this paper. All authors have participated in the work and have reviewed and agree with the content of the article.

Data availability statement

Data are available upon request. All relevant data are either in the article or in the Supplementary appendix.

Acknowledgments

Medical writing assistance funded by the Fundación Instituto de Investigación Sanitaria (IIS) de Aragón. The promoter of the study was the Systemic Autoimmune Diseases Group (GEAS) of the Spanish Society of Internal Medicine (SEMI).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.medcli.2026.107426.

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