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REVIEW ARTICLE

Practical issues in assessing nailfold capillaroscopic images: a summary

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Abstract

Nailfold capillaroscopy (NC) is a highly sensitive, safe, and non-invasive technique to assess involvement rate of microvascularity in dermatomyositis and systemic sclerosis. A large number of studies have focused on NC pattern description, classification, and scoring system validation, but minimal information has been published on the accuracy and precision of the measurement. The objective of this review article is to identify different factors affecting the reliability and validity of the assessment in NC. Several factors can affect the reliability of the examination, e.g., physiological artifacts, the nailfold imaging instrument, human factors, and the assessment rules and standards. It is impossible to avoid all artifacts, e.g., skin transparency, physically injured fingers, and skin pigmentation. However, minimization of the impact of some of these artifacts by considering some protocols before the examination and by using specialized tools, training, guidelines, and software can help to reduce errors in the measurement and assessment of NC images. Establishing guidelines and instructions for automatic characterization and measurement based on machine learning techniques also may reduce ambiguities and the assessment time.

Keywords Assessment · Measurement · Nailfold capillaroscopy

Introduction

Nailfold capillaroscopy (NC) is an old but inexpensive imaging technique used to study the morphology of nailfold dermal papillary capillaries. NC has been shown to have an important predictive role in identifying patients with Raynaud's phenomenon (RP), who are at an increased risk of progression to overt systemic sclerosis (SSc) spectrum disorders [1, 2]. After many years of intensive investigations, capillaroscopy has been included by the European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) as a diagnostic tool for the classification criteria of SSc [3]. Subsequent studies have identified the relationship between NC changes and some of the clinical features including digital ulcers [4], cardiopulmonary disease, heart failure severity [5, 6], diabetes mellitus (DM), general hypertension, and other diseases [7].

Most published studies on NC have focused on pattern description and classification, and very few have investigated how to improve the reliability of the assessment. To our knowledge, a few studies have shown the effect of imaging instrument factors, such as a specialized tool, on measurements [8] and magnification [9]. Some researchers in multicenter studies have focused on the reliability of capillaroscopic parameters [10] and simple

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capillaroscopic definitions [11]. Some studies have discussed the effect of training [12], suitable location [13], image quality [14], and a computerized image analysis system [15, 16] on the reliability of assessment. Machine learning techniques have also been used in two studies using non-linear support vector machine [17] and fuzzy logic [18] kernels for the classification of NC images in healthy, hypertensive, and diabetic subjects. Berks et al. also used this technique for measuring vessel morphology [19]. The small data set was a limitation of this study which increases the margin of error (455 images). Recently, a fully automated method to determine only the absolute capillary number on NC images has been proposed and validated in patients with SSc. Although the study had some limitations on well-valuable images and also a manual determination of the region of interest (ROI) by the observer was accomplished, the method made the assessment easier and quicker [15]. As a matter of fact, the absolute number of capillaries has been validated as the most important parameter for the patient follow up [20].

In particular, to our knowledge, no studies have pointed out different factors that have a high impact before, during, and after the imaging process. The aim of this study was to describe the factors that impact or modify the imaging process and assessment of NCV. This is typically a crucial problem in NC because identifying them can be helpful to improve the accuracy and precision of the measurement. In addition, it leads to a reliable scoring and classification of capillaroscopic patterns.

Method

Research strategy

To identify all available studies that fit the topic of review, we carried out a systematic search in Medline (PubMed) and Embase based on the following search terms in all possible combinations: capillaroscopy, nailfold capillary, capillary microscopy, and video capillaroscopy. The Boolean operators AND and OR have been used in combination with more key words to make the search more specific and to reduce the sensitivity of the search. The initial search of Medline (PubMed) and Embase abstract databases yielded 241 articles, which were narrowed down to 167 after eliminating duplicates. We included original articles concerning studies in NC, published between 1986 and 2018. The articles not published in English and case reports are excluded from this review. A careful analysis of titles, abstracts, and method found 50 studies that met our inclusion criteria in which full texts were available. Two independent authors (AK and ZE) reviewed and analyzed each article independently. In case of disagreement, two investigators were consulted (ME and AF). In addition, the reference lists of all retrieved papers were manually reviewed.

Results

The following factors could be considered as an important effective factor in the analysis of nailfold capillaroscopy images.

Physiological factors

Different physiological factors affect the NC images quality. It is impossible to avoid all physiological artifacts in most cases; however, in some cases, the influence of these factors can be reduced using the following limitations:

Removing fingernail cuticles

The cuticle is a barrier layer between the skin and the nail plate merging these two structures. The red blood cells traveling within loop-shaped capillaries carry out the supply and waste disposal. It is preferable to image this area since the epidermis layer is thin compared with other areas in the nailfold region [21]. Cuticles are ordinarily soft and cutting them can make them hard and then more likely to break. Hence, patients are requested not to remove their fingernail cuticle for 1 month prior to the test to prevent microtraumas that could damage the precision of the test [22].

Drinking and smoking

Smoking and drinking can alter the capillary diameters and capillary blood circulation. To decrease the influence of this aspect, patients are asked not to smoke or drink caffeine-containing beverages 4–6 h before testing [23].

Stress and tension

Psychological stress and tension may affect the rate of blood flow to the heart and other important organs in elderly and young patients [24]. Patients are acclimatized and relaxed prior to the test to avoid creating stress during the test. Moreover, explaining the equipment's function to patients may reduce tension prior to the capillaroscopy test; this is particularly the case in children [25].

Skin transparency

Conditions of the skin are another source of image variability. The nailfold capillaries viewed using an optical microscope depend on the transparency of the overlying skin; however, thickening the skin due to the scleroderma causes a noticeable transparency reduction [26]. Moreover, some NC parameters depend remarkably on the skin transparency, such as the subpapillary venous plexus and capillary length. These parameters are relatively variable, and their assessment is more problematic due to skin transparency differences [27].

Typically, for better observation and improving skin transparency, a drop of neutral oil can be applied prior to the test [28]. However, either too much or too little oil can cause resolution reduction and should be avoided.

Physically injured fingers

Physically injured fingers cannot be tested in this research because the blood flow to the fingers is altered due to the injuries. Moreover, by using in-contact videocapillaroscopy, the patient feels pain, and this pain can lead to stress [28].

Skin pigmentation

The development of SSc causes skin pigmentation disturbances and must be recognized for diagnosis [29]. Melanin, the skin pigment, absorbs light considerably in the visible spectrum, and as a result, capillaroscopy is complicated in highly pigmented skin [30]. For skins with light pigmentation, capillaroscopy is achievable but is of limited use in people with thick and dark skin [31].

Nailfold imaging instrument factors

The function of the immersion oil

We can maximize the amount of light and improve image quality by immersing oils on the skin. Uniformly distributing the oil on the skin obtains a homogeneous thin layer, which is favorable. The oil layer on the skin has a skin refractive index (Fig. 1) as similar as possible to the optical refractive index and decreases superficial reflection (scattering) that causes a dazzling effect, leading to images with less information. Vegetable oils (neutral oils) are good choices since they are skin-friendly. Skin and mucous membrane irritations may be created by applying common immersion oils used in microscopy [32].

Scanning system

The two probe-scanning systems with immersing techniques commonly utilized in NVC are the following:

Non-contact: Non-contact videocapillaroscopy in immersion (Fig. 1, left) uses a spacer that maintains a fixed distance to determine a completely free superficial layer of the area under the test. The main advantage of this method is that no pressure on the skin surface exists, and this causes no obstructions of the capillary lumen introduced by mechanical compression [32]. The non-contact NVC in immersion is a probe-scanning system that has little or no use in clinical rheumatology.

In-contact: In-contact videocapillaroscopy in immersion (Fig. 1, right) is implemented by attaching a slide to the end of the spacer. The slide can be either made of optical quality glass with polished edges or plastic. This system improves the quality determinations. The oil surface uniformity is increased, and light reflections are reduced, which are often unpleasant in non-contact systems. This

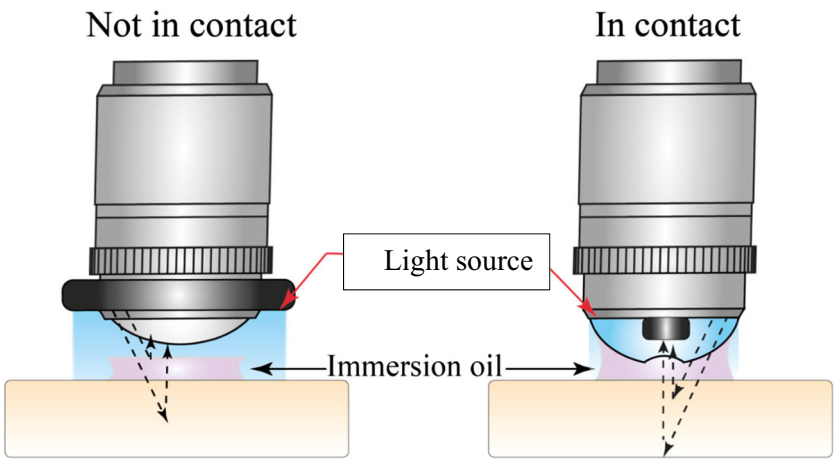


Fig. 1 Use of immersion oil can minimize the refractive index differences between the objective and the sample

	Refractive index
Air	1
Water at 20 °C	1.33
Sugar solution (80%)	1.49
Cedar or synthetic oil	1.51
Glass	1.53

technique requires operators with greater manual skills and experience. For certain, more accurate results, images with better quality, are obtained using this system [32].

Specialized tools

We can increase the observer accuracy by using a highly specialized tool. Different instruments with different specifications, such as cost, magnification, training period, portability, image quality, and image analysis software and storage are available to accomplish the examination [33]. A variety of different devices used to examine nailfold capillaries are the following:

Ophthalmoscopes are devices used to examine the interior of the eye. The ophthalmoscope was developed into a model that was later used for endoscopy. The device includes a strong light that is conducted into the eye using a small mirror or prism. Through a small hole in the ophthalmoscope, the light reflects off the retina. Consequently, physicians can observe a non-stereoscopic magnified image of the anatomy of the back of the eye in conjunction with the optic disk, retina, retinal blood vessels, macula, and choroid. Ophthalmoscopes are notably valuable devices used to screen various ocular diseases, such as diabetic retinopathy (see Table 1).

Dermatoscopy (magnification on the order of × 10): Dermatoscopes are small, inexpensive, and conveniently portable devices used to see nailfold capillaries with good intra- and inter-observer reliability [34]. One issue is how the nailfold capillary visualization by dermatoscopy compares with visualization by NVC. Given its more availability and simplicity use, dermatoscopy could help in daily practice to differentiate the patients with primary vs secondary RP [8] (see Table 1).

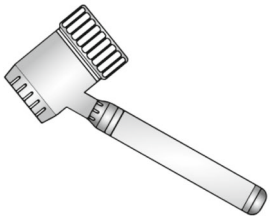
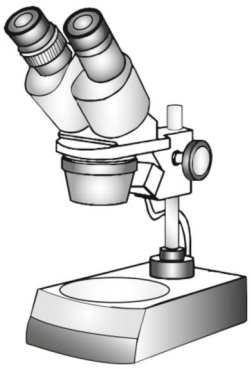
Wide-field microscope is an easy and inexpensive technique mostly studied by Maricq et al. 30–40 years ago [35]. This technique is routinely carried out with a stereomicroscope at × 10–200 magnification allowing the overall viewing of the whole capillary network at the nailfold region. By using a common camera or a digital camera, images can be obtained and saved. Moreover, through the use of an attached digital video camera, video recording can be achieved. The saved image quality depends on the resolution of the camera and the optics. Wide-field microscopy appears to be a satisfactory method for the semi-quantitative and quantitative measurement of the capillary density [36] (see Table 1).

A digital video capillaroscope fuses a microscope with a digital video camera and is treated as a particular tool for assessing capillaroscopic parameters. In videocapillaroscopy, an electronic sensor is known as CCD (charge-coupled device) functions as the operator's eye. The intensities of the magnetic radiations of the light reflected by subcutaneous structures are transformed into this device, which treats them as electric signals. Then, the signals are transmitted to a computer that displays them as images. The optical part is quite comparable with the one obtained by the stereomicroscope with all related procedures [32]. The instrument has a low magnification capability; however, a sequential high-magnification function that can help distinguish the capillaries with clear detail is achievable. Additionally, direct contact with the nailfold is attainable, and testing patients with serious finger flexion contracture is achievable. There is particular software that determines the detailed specific parameters, such as the dimensions of individual capillary loops, and the afferent and efferent luminal diameters are provided by videocapillaroscopy. Nevertheless, because of the high-magnification power used in this method, only a limited portion of the nailfold region can be examined at one time [28] (see Table 1).

The benefit of the NVC is that repeatability and reproducibility can often be high, but this often comes with associated conditions, unfortunately. For instance, when NVC itself was assessed for repeatability, it was found to be high for a single observer [37], when assessed for intra- and inter-observer reliability, also was high only when the NVC images were evaluable [38].

Comparison of different capillaroscopic techniques is limited to NVC, dermoscopy, and stereomicroscope in SSc patients. Sekiyama et al. examined intra- and inter-observer reliability for both stereomicroscope (× 10–25) and for videocapillaroscope (× 200 magnification) in a study with 20 subjects in two separate occasions and by two observers. The κ-value and intra-class correlation coefficient (ICC) analysis showed excellent (ICC > 0.90) intra- and inter-observer reproducibility for all parameters evaluated by stereomicroscope and videocapillaroscope [39]. Another study compared three capillaroscopic methods to determine the capillary density in patients with SSc. Two of the three methods involved stereozoom microscopy (× 20) used either for direct counting or for working with a camera and the third method was NVC with × 300 magnification. The results demonstrated good agreement between methods. All methods could differentiate SSc patients with controls cases [40]. Sibel et al. compared the diagnostic value of dermatoscopy and NVC and demonstrated both of them could reveal a distinct nailfold capillary pattern in SSc. Moreover, they also suggested dermatoscopy is an efficient method to identify pathognomonic changes [41]. Recently, a group of researcher from seven European centers compared dermoscopy (× 10) and NVC (× 300) in the assessment of nailfold capillaries. They reported that dermoscopy images have a high level of subjective grade ability (70.9%)

Table 1 Various common instruments for nailfold capillaroscopy

Device	Advantages and disadvantages	Shape
Ophthalmoscopes, Traditional microscopes	***Advantages*** - Low-cost options - Widely available - Can be used with minimal training ***Disadvantages*** - Only low magnification, 10–20× - Can visualize only gross NFC changes - Difficult to use for the operator - Poor reproducibility	
Dermatoscopes	***Advantages*** - Intermediate cost - Portable devices - Easy availability in dermatology practice - Acceptable magnification 20–40× - Acceptable resolution and sensitivity for major NFC changes ***Disadvantages*** - Same as ophthalmoscope	
Stereomicroscopes	***Advantages*** - Intermediate cost - Main tools used in national centers - Ease of use - Acceptable magnification 10–200× ***Disadvantages*** - Either low- or high-level magnification - Can be difficult to use on patients with joint contractures. - Time-consuming - Specialized training required - Additional camera and fiber optic light source required	
Videocapillaroscope	***Advantages*** - Handheld probe - Excellent image quality reproducibility - Acceptable magnification, 200–600× - Portable system allowing for easy clinical use considered the gold standard for noninvasive examination of the microcirculation - Can be used for bedside examination or in patients with severe flexion contractures - Variable magnification (with different lenses) ***Disadvantages*** -A most expensive option - Either low- or high-level magnification. - Requires specialized training	

but lower than NVC (79.3%). In addition, specificity and sensitivity were higher (92.5–84.6%) and lower (60.2–81.6%) for dermoscopy and NVC, respectively [42].

Another recent study evaluated two novel capillaroscopy techniques in suspected scleroderma-spectrum disorders. They compared smartphone-lens and smartphone-dermatoscope techniques to evaluate their diagnostic performance. Wide-field microscopy was applied in both of them as a reference standard. The observed sensitivity and specificity of smartphone-dermatoscope were 77% and

95%, respectively, which showed higher values than those for smartphone-lens technique (65% and 90%, respectively) [43]. In a recent international survey on non-invasive assessment of RP patients, observed dermatologists may prefer to use dermoscopy, whereas rheumatologists tend to prefer NVC among different common instruments for NC [44].

Magnification

An appropriate magnification is selected according to the specific application needs. Typically, the NVC device is a mobile hand-held instrument with an optical magnification of × 20–200. For better results, two magnifications (× 50 and × 200) are tested on each finger. The lower magnification shows the general architecture while the higher magnification for assessing morphological details of a single capillary [45]. The blood cells inside the capillaries are shown better with the increased magnification. More information regarding this subject can be found in Etehad Tavakol et al. [28].

Illumination and wavelength

The illumination and wavelength are two essential light source specifications in a microcirculation imaging system. Selecting an appropriate wavelength for the light source to gain detailed images is crucial. A green light source with a 500–550-nm wavelength is theoretically suitable to obtain high-quality images [46]. The relationship of the image contrast with the illumination was studied using green and white colors as the light sources. The green light demonstrated better contrast than the generally used white light [47]. The experimental findings are similar to the theoretical findings.

Dust on lenses

This parameter is also responsible for image quality reduction. To obtain clear capillaroscopy images, controlling and removing dust from the lenses and cleaning the capillaroscope optics are necessary. Due to the nature of the optical surface and the type of dirt, it is essential to select the best cleaning technique. Sometimes spots that are difficult to remove are found on the lenses; in this situation, the surface should first be wiped with a tissue moistened with 95% alcohol and then desiccated with a dry tissue.

Software for the analysis

Providing powerful image analysis software that is user-friendly and has the potential to assist technicians acquire valuable information from the images quickly is very important. Converting images into analytical data is possible via software with a library of powerful measurement options. In addition, software design for NVC can maximize the workflow for an experienced user and fast learning curve for new user [48]. OptiPix and Videocap are two common capillaroscopy software which are designed for analyzing and reporting nailfold capillary images [14]. To our knowledge, no study has investigated the advantages of different software types or has performed a comparison between them.

Human factors

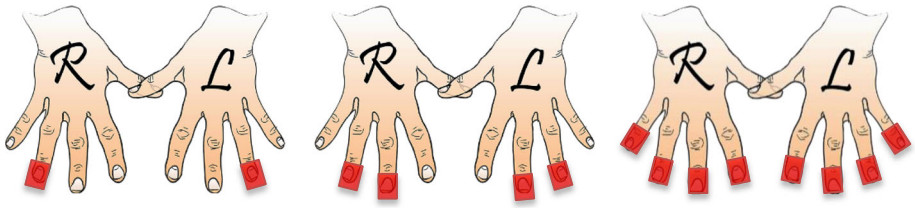
The operator who obtains the NC images

Operators can play a key role in obtaining capillaroscopy images. He or she is required to have sufficient information and knowledge regarding the nailfold imaging instrument. He/she should prevent factors leading to the reduction of images qualities, such as blurred images that resulted from finger micromotion or device movement while taking images.

The observer who examines the NC images

Scientists are human beings who have the potential to make mistakes. It is important to reduce factors leading to mistakes that affect the collected data. Observer effects on subjects such as observer error, observer bias, accuracy, precision, and intra- and inter-observer reliability have been discussed in many methodological texts in different fields [49]. This limitation has been recognized for a long time by many researchers in this field; however, the nature of the study (such as field studies where the "group," "treatment," or "individual" are unavoidably known) or the fact that only one researcher has conducted a study that provides blind data collection is almost impractical or is very difficult [50]. Few approaches have been presented to reduce possible bias: (1) Two different observers are selected to perform the task, and the assessed NC images are blind to the group. (2) It is recommended that two different experts with no previous knowledge of a patient's clinical conditions should analyze the obtained images because evaluating capillary dimensions by hand is time-consuming and may be inaccurate [26]. (3) The observers should be trained and motivated to be accurate. Additionally, only those observers who were consistent during training should be invited. (4) Measurement time is important to assess the measurement. Observation sessions should be sufficiently short such that the observers do not become tired. (5) Categories should be defined carefully such that all observations will be interpreted according to a consistent and uniform set of standards. (6)

Table 2 Sensitivity for the presence of two markers of capillary abnormality in a combination of two-finger and four-finger of both middle and ring fingers compared with the assessment of all eight fingers

Finger combination			
Sensitivity	59.8%	66.7%	74.6%

Replacement of human observers and human recorders with computers or automatic counters may be considered for some of the parameters [51] (Table 2).

Work experience and training program

Recently, capillaroscopy was mentioned as one of the SSc classification criteria. Therefore, adequate training to identify normal and SSc patterns is relevant for all rheumatologists. Correct recognition and/or interpretation of both normal NVC pattern and the SSc patterns require more time, better work experience, and more-precise standardization. In a pilot study to test the learning curve of operators with different experience in NVC, five investigators (1 senior, 1 junior, and 3 beginners) participated in an intensive training program. After 1-week training the result showed, sensitivity and specificity of the participants increased after training and κ-scores of qualitative and quantitative assessments improved from poor to excellent from the beginning to the end of the exercise [12]. Another study was evaluated normal and scleroderma pattern of the nailfold capillary, thirteen expertise's with different experience in NVC received training to standardize reading different criteria. The result showed higher κ-scores among experienced vs inexperienced observers in both inter-observer ($\kappa = 0.58$ vs 0.34) and intra-observer ($\kappa = 0.65$ vs 0.37). In addition, they reported the identification of early microvascular changes might require more training and experience [52].

Assessment rules and standards

The number of fingers

According to the study design, there were no limitations when selecting the number of fingers or the number of fields for the test. The fourth and fifth fingers of both hands have been selected by some authors [54], while all fingers on both hands except the thumbs were selected by the others [39]. In some cases, all fingers on both hands were selected [55]. The question of how many (and which) fingers should be routinely assessed with NC was answered recently by one study involving many images (1600). Different finger combinations were tested for the sensitivity of presence of two markers of capillary abnormality based on the presence of giant capillaries and an SSc pattern (early, active, or late) classification defined by Cutolo et al. [56]. They suggested that examining fewer than eight nailfolds reduces the sensitivity to detect capillary abnormalities (Table 2). However, if an observer is pressed for time, the best two-finger combination is both ring fingers [57].

Capillaroscopy procedure

Capillaroscopy procedures that can help improve the quality of the measurement are the following:

Washing the hands or toes: Before capillaroscopy of the toes, the patients are required to clean their toenails with a soft brush to remove any dirt or bacteria that may have become stuck in the nail corners while being careful to not damage the neighboring skin [28] (Fig. 2a).

Acclimatization: Generally, minimal or no capillary flow exists when the examination room is cool, or the patient is under stress. To enhance blood flow to the affected limb, warm body temperature should be maintained. Before the examination, patients should be seated at room temperature (20–25 °C) for 15–20 min to become acclimatized and to relax. Then, the patient's hands are placed at her or his heart level based on the temperature outside [28] (Fig. 2b).

Improving the visibility of capillaries: Before the test, a drop of vegetable oil is placed on the nailfold of each finger or toe to improve the image resolution [28] (Fig. 2c).

Contact of videocapillaroscope: A videocapillaroscope directly contacts a patient's nailfold. The contact angle and the direction of the videocapillaroscope may be altered to reduce reflections. By adjusting the focusing system manually and using the camera head, a sharp image of the capillary branches can be obtained [28] (Fig. 2d).

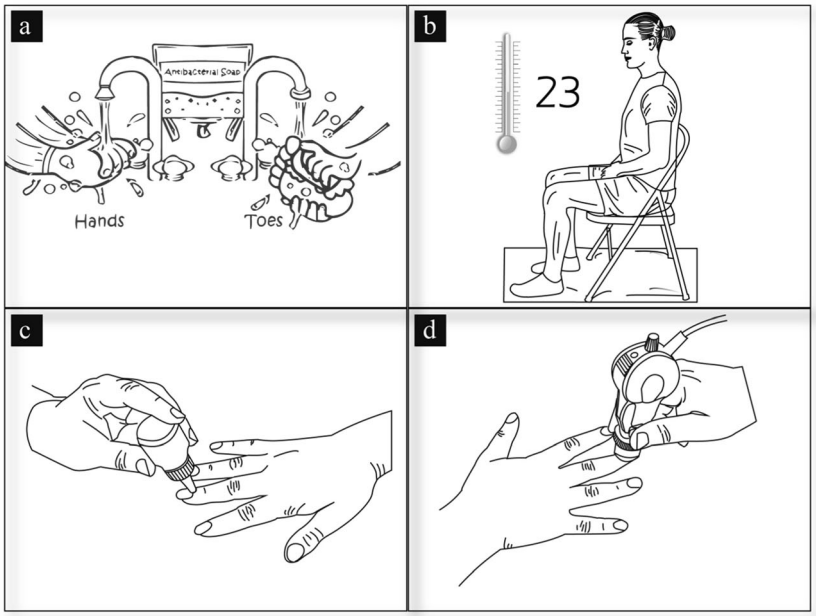


Fig. 2 Various steps required for a nailfold capillaroscopy procedure [53]

Normal and abnormal capillary morphology

Definitions of normal and abnormal capillary morphology play a key role in the reliability of the assessment. Every capillary loop has a regular structure in each dermal papilla. A wider venous limb connected with a thinner arterial limb, a connecting part between the venous and arterial limbs, and an apical loop are present in every single capillary loop [59]. In general, the normal nailfold capillary pattern under physiological conditions is characterized by the following: (i) a density of 9–13/mm; (ii) the orderly comb-like arrangement; (iii) a capillary length of 200–500 mm; (iv) an efferent branch with 8–21 mm and afferent branch width of 7–14 mm [60]. Apart from the stereotype hairpin-shaped loop, there are common subtle morphological variations and abnormal distinctive morphological changes in the distal row of capillaries. There is no general agreement about some of the definition of the abnormal capillary. Table 3 showed the definition of different capillary and capillary finding in a healthy subject according to the previous studies [28, 45, 53, 59, 63, 64].

The EULAR study group on microcirculation proposed a simple definition to describe the morphology of a single capillary. In this study, the normal morphology had been defined as hairpin-shaped or non-specific variation, and tortuous or crossing while abnormal morphology had been defined as not hairpin, not tortuous and not crossing. Moderate reliability of this definition was obtained in this multicenter, international study [11] (Fig. 3a). Excellent reliability was reported in the seventh EULAR course on capillaroscopy by an optimized simple capillaroscopic definition of normal and abnormal morphologies of a single capillary. They suggested that the convexity of the capillary head can be a factor of distinguishing normal and abnormal capillaries [58] (Fig. 3b). In both studies, the raters had been asked not to judge capillary morphology by the assessed capillaries dimensions.

Additionally, it is not known which morphometric measurements would be the most reproducible and if the method has an acceptable inter- and intra-observer variability. Among different capillaroscopy parameters, capillary density is evaluated by different techniques such as NVC, stereomicroscopes, and dermatoscopy with different automated and semi-automated methods [15, 59]. In this study, ICC showed good inter-observer variability for the intercapillary distance (ICC = 0.58) and the capillary width (ICC = 0.86), but the poor correlation (ICC = 0.3) in the measurement of capillary length. In addition, an excellent intra-observer reproducibility for all of this parameter was demonstrated [65].

Automated evaluation techniques

A few studies have focused on automated quantitative assessment of capillaroscopy images. In one study, a semi-automated image analysis (CapiAna) has been developed to evaluate skin capillary density. The capillary density derived with CapiAna was slightly higher compared with the manual counting procedure. A manual correction was necessary to control counting the capillary. Although this application has a better reproducibility as compared with

Table 3 Definitions of elementary abnormalities and capillary finding in a healthy subject [28, 61, 62]

Shape	Definition
Normal	A regular capillary is shaped similar to a hairpin or an upside-down letter "U" with a slimmer arterial arm, an upper part, and a venous arm.
Tortuous	Arterial and venous limbs are curled, but alterations do not cross.
Crossed	Arterial and venous limbs cross at a minimum of one point.
Dilated	A capillary with a venous limb diameter > 20 μm or arterial limb > 15 μm.
Giant	A capillary with an arterial or venous limb diameter > 50 μm.
Bushy	Capillaries with small and multiple branching limbs.
Meandering	Presence of more than one capillary loop in a single dermal papilla.
Ramified	Abnormal connections between arterial and venous limbs, different capillaries, or vascular neoplasms.
Elongated	Capillary loops longer than 300 μm.
Bizarre	Variations of very abnormal branching although not conforming to the three previously defined categories are classified as unusual distinctive morphological variations.
Qualitative parameter	
Subpapillary plexus visibility	The vascular network at the base of a finger nailfold into which capillaries drain is called the subpapillary plexus.
Intercapillary distance	The longest distance that exists between two neighboring capillary loops.
Avascularity	The lack of two or more successive capillaries.
Microhemorrhages	Dark masses attributable to hemosiderin deposit.
Skin transparency	The possibility of seeing the vessels beneath the skin reflecting the level of vascularization and the skin thickness.
Capillary disorganization	The complete distortion of a normal and regular capillary pattern.
Capillary in a healthy subject	
Capillaroscopic parameter	The normal healthy subject image
Capillary density	9–13 in 1 mm
Capillary blood flow	Dynamic, no stasis, or thrombosis
Skin transparency and visibility pericapillary	In skin without pigment capillaries clearly visible
Subpapillary venous plexus	Visible in up to 30% of healthy people
Capillary array and architecture	Straight capillaries, perpendicular to the skin surface
Capillary morphology	Hairpin or an elongated upside-down letter "U"
Tortuosity	Usually absent
Hemorrhages	Usually absent, may be present after local trauma
Pericapillary edema	Absent
Avascular areas	Absent
Dilated and giant loops	Absent
Ramified, elongated, bizarre capillaries	Absent
Neoangiogenesis	Absent

the manual counting procedure, it was limited in the skin regions where the capillary loop is arranged perpendicularly to the skin surface [66]. In another study, another semi-automated system has been described to extract quantitative biomarkers from capillaroscopy images, using a layered machine learning approach. They used random forest algorithm which is a powerful supervised learning algorithm for classification [19]. The large data set was the limitation of this study because a large amount of training data plays a critical role in machine learning models to be successful. In 2016, the same authors developed the NC system that enables panoramic imaging of the whole nailfold at high magnification. It incorporates new software to make fully automated estimates of capillary structure and blood flow velocity [67]. In 2018, they showed that structural and blood flow measurements are both able to distinguish patients with SSc from those with primary RP/healthy controls [3]. Providing a panoramic image with high magnification is one of the strengths of this NC system. It allows the selection of the most specific alterations and highly reproducible approach for quantitative assessment [13].

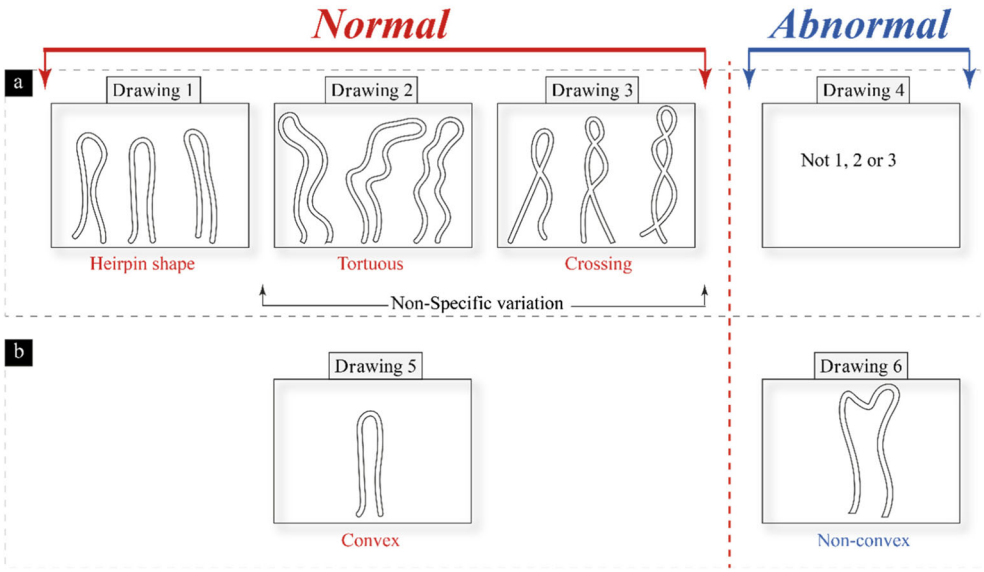


Fig. 3 Definition of normal and abnormal single capillary morphology. **a** Study by Smith et al. [11]. **b** Optimized definitions by Cutolo et al. [58]

Conclusion

Prior studies have documented the effectiveness of different factors such as physiological, nailfold imaging instrument, human factors, and assessment rules and standards in improving the quality of an assessment. In the current study, all previous investigations including recommendations, assessment rules, and standardizations that could contribute to increasing the reliability of the measurement were reviewed. Following these rules and standards can be used to design and develop semiautomatic even automatic measuring system. We found that the assessment of 8 fingers by using videocapillaroscope with × 200, suitable software, and a trained observer can increase the accuracy of the assessment in both clinical decisions making and researches.

Compliance with ethical standards

Disclosures None.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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