Nail-fold capillaroscopy for the dermatologists

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Abstract

Nail fold is one of the most accessible sites for studying changes in the microcirculation in various microangiopathies. The characterization of changes in microvasculature can provide useful clues towards the diagnosis and prognosis of a disease. The diagnostic utility of nail fold capillaroscopy has improved and expanded over the past couple of decades. Beyond connective tissue diseases, it is now explored for its role in various systemic and dermatological diseases. Incorporation of nail-fold capillaroscopy in the diagnostic criteria of systemic sclerosis has generated interest among dermatologists. The current review is aimed at providing knowledge about nail-fold capillaroscopy to dermatologists. For the purpose of review, a PubMed search was done using the keywords "nail fold capillaries" and "nail fold capillaroscopy". All the articles were retrieved and classified into reviews and clinical studies of various types. The final data were then analyzed and presented in a narrative fashion.

Key words: Capillaroscope, capillaroscopy, dermatology, nail fold capillaroscopy, nail fold videocapillaroscopy

Introduction

Nail-fold capillaroscopy is a non-invasive imaging technique for *in vivo* assessment of microcirculation.[1,2] The easy availability of dermatoscopes (used as capillaroscopes) has ensured that more and more dermatologists use nail-fold capillaroscopy now, especially in conditions where it has established value such as Raynaud's phenomenon and connective tissue diseases.[1,3-10] The micro-vasculature is also affected in dermatoses like psoriasis,[11] metabolic diseases like diabetes mellitus,[12,13] autoimmune diseases and various other conditions.[14] Here too, nail-fold capillaroscopy helps to detect and monitor early microvascular changes which may precede development of clinically significant complications such as retinopathy, neuropathy and nephropathy.[13] This review aims to compile and present current knowledge of nail-fold capillaroscopy to serve as a ready reckoner for dermatologists.

Methodology

A PubMed search pertaining to published English articles using keywords "nail-fold capillaries," and "nail-fold capillaroscopy" was done. The search yielded 163 and 96 indexed articles, respectively, which were retrieved and classified into review articles (37) and clinical studies of various types (222). These were read and information pertaining to nail-fold capillaroscopy was collected. The cross references provided were also retrieved and studied. The final data were analyzed and presented in a narrative fashion.

Nail Fold Capillaroscopy

Nail-fold capillaroscopy is specialized dermatoscopy of proximal nail fold where incident light delivered at an acute angle enables "*in vivo*" visualization of vascular structures in the superficial papillary dermis, thus highlighting capillary architecture. Application of linkage fluid increases transparency of proximal nail fold and reduces surface reflection.[15]

Initial written description of nail fold capillary evaluation is available from 1663 when Johan Christophorous Kolhaus used a primitive microscope to observe small blood vessels surrounding the nails. Subsequently, Giovanni Rasori described a close relationship between conjunctival inflammation and the presence of "inextricable knots of capillary loops" using a magnifying glass.[1] Skin capillaries were also described by Purkinje (1823) while observing the nail fold with a magnifying lens.[2] However, nail-fold capillaroscopy was accorded the status of an important investigation by Raynaud (1862) through his thesis evaluating local ischemic damage of hands, feet, nose and tongue.[16]

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Lombard (1911) found that capillaries became visible on placing a drop of immersion oil. Much later, Maricq and Le Roy described specific capillaroscopic features in Systemic Sclerosis.[17] Cutolo *et al*. classified nail-fold video capillaroscopic patterns in patients with systemic sclerosis as "early," "active" and "late" patterns in 2000.[8]

Cutaneous micro-circulation

The cutaneous microcirculation is composed of superficial and deep horizontally-oriented plexuses. Superficial plexus, located 1–1.5 mm under the skin surface, gives rise to 1-3 capillary loops per dermal papilla, visible as dots or commas on the surface, as they are located at 90-degree angle to skin surface. They have an arterial and a venous limb connected by an apical loop.[6,15] However, capillary loops in the nail-fold region are uniquely located, as they lie increasingly parallel to the skin surface, enabling visualization of their size, shape and morphology across their full length [Figure 1].[17]

While capillaries can also be visualized and studied *in vivo* at sites such as conjunctiva and retina, the proximal nail fold offers the advantage of easy accessibility for repeated examination [Figures 2a and 2b].[18] The proximal nail fold, being an acral area, is also affected early as well as maximally, by disorders affecting microvasculature.

Equipment used

Equipment reported to visualize proximal nail fold capillaries include hand-held magnifying glass, ophthalmoscope, light stereomicroscope,[19] wide-field microscope, dermatoscope,[10,18,20] and videodermatoscope.[21] Digital videocapillaroscopy, the gold standard technique to examine nail fold capillaries, consists of a microscope with digital video-camera providing a magnification from ×50 to ×1000. However, it is expensive and not widely available. Ophthalmoscopes and hand-held dermatoscopes offer less magnification (×10 mostly), but enable examination of a wider area of the nail fold. USB dermatoscopes are not that costly and offer magnification from ×20 to ×200.[17] There are studies affirming their reliability in studying the nail-fold capillaroscopy changes.[10,18-20]

Technique

Nail-fold capillaroscopy should be done after minimum 15–20 min stay in a room with normal ambient temperature (20–22°C). The patient is made to sit comfortably with hands kept at the level of heart.[6,8-10,22] Most precise morphologic evaluation is obtained from 4th and 5th fingers, because of highest transparency of skin and least proneness to day-to-day trauma.[23] Nevertheless, it is advisable to perform nail-fold capillaroscopy in all fingers since early and initial microvascular changes may manifest in few fingers only. Use of linkage fluid (immersion oil, ultrasound gel, etc.) increases the transparency and resolution of images. Additional considerations are outlined in Table 1.

The images taken are stored in JPEG/PNG/BMP formats and assessed in detail. An estimate of mean capillary density is made from the distal-most row of capillaries. Abnormal capillaroscopic changes (identified in at least two digits) are recorded as a part of overall nail-fold capillaroscopy findings.[23] Overall evaluation of capillaries depends on the equipment used (quality and visibility of images); observer experience; and transparency of skin, which may be compromised in pigmented, thickened or fibrosed skin.[21]

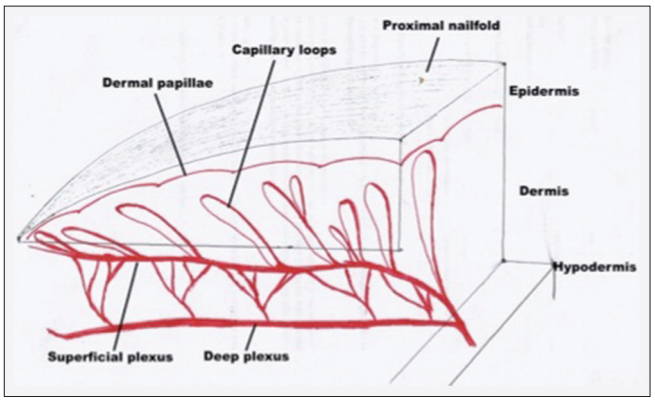

Figure 1: Diagrammatic representation of the sagittal anatomy of the proximal nail fold. The skin fold over itself forming the dorsal as well as the ventral surface of the proximal nail fold. Thus, the papillary capillaries lie increasingly horizontal near the folding edge

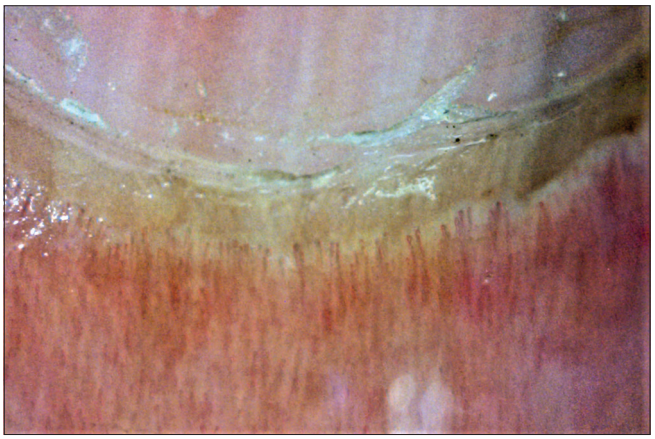

Figure 2a: Normal proximal nail-fold capillaries seen as regular hairpin bends (Dinolite AM7515MZT, polarized ×65)

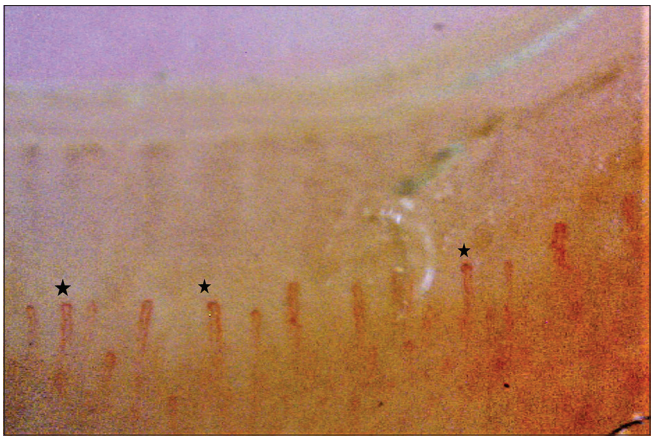

Figure 2b: Normal proximal nail-fold capillaries seen at higher magnification (Dinolite AM7515MZT polarized, ×180). Also note the tortuosity seen in many vessels

Table 1: Important consideration before doing nail-fold capillaroscopy

- Caffeine and smoking to be avoided 4–6 h before examination
- Nail paint to be gently removed before nail fold capillaroscopy
- Clean the hands and feet gently with soap and water
- Physically injured fingers to be avoided
- Nail-fold capillaroscopy to be performed under a cold light source to prevent vasodilation
- Adding excessive immersion fluid obstructs the field of vision
- At least 4 images to be taken from one finger
- Toe capillaroscopy is an unreliable tool
- 10–20 s video may be taken from the midline of the nail fold to capture blood flow
- To minimize reflections, contact angle and direction of the instrument may have to be changed

Capillaroscopic parameters

Nail-fold capillaroscopy evaluation depends on quantitative and qualitative parameters.[17] Quantitative parameters include mean capillary density and capillary limb width; while qualitative parameters include morphological or architectural alterations, neoangiogenesis, or presence/absence of a sub-papillary plexus [Figure 3].

Quantitative parameters

Mean capillary density

It is the average number of distal most capillary loops visualized per millimeter of proximal nail fold margin. A wide range of values for healthy subjects (7–14 capillaries/mm) have been reported.[24-29] Variations based on ethnic, demographic, or methodological factors are known [Table 2 and Figure 4].[30-32] In an Indian study, mean capillary density was reported as 8.7/mm[24] while more recently it was reported to be 7.6 capillaries/mm.[17]

Various methods have been used to calculate mean capillary density. Sebastian *et al*. considered distal most capillaries for this calculation, even if they were not at the same level. Major disadvantage of this approach is that a ramified capillary is counted multiple times giving a false high value.[33] Hofstee *et al*. suggested the "90-degree method," wherein a capillary is considered distal loop if the angle between the apex of that capillary and the apex of its two adjacent capillaries is greater than 90 degree.[34] A simplified protocol using calibration feature of USB dermatoscopes was devised by our team [Figure 5].[13,17] We mark the center of proximal nail fold with an ultra-thin marker pen and then take two images (at high magnification) on either side. Both images are analyzed with the calibration software of the USB dermatoscope, counting the distal most capillary loops visible over 2 mm length on either side of the marked point, giving the number of capillaries over 4 mm in an individual digit. The sum of number of capillaries of four fingers (right and left fourth and fifth finger) is added and the sum divided by 16 to give mean capillary density/mm.

Various authors have proposed capillary density scoring systems on the basis of calculated mean capillary density, [Table 3].[3,35,36] Hoerth *et al*. suggested a scoring system based on the age of the individual.[30]

Other quantitative parameters

Other reported quantitative parameters including mean capillary width, capillary length, arterial limb diameter, venous limb diameter, apex width, internal diameter and intercapillary distance [Table 4] require more sophisticated calibration tools.

Table 2: Important observations related to capillary density

- Capillary density is directly related to age. Younger children have fewer capilaries[30]
- Gender does not have a significant impact on mean capillary density[30]
- Mean capillary density can be difficult to calculate in darker skin individuals [Figure 4]
- Fingers have higher density than toes[31]
- Fourth and fifth fingers are preferred for counting capillaries[32]

Qualitative parameters

Homogenous and orderly capillaries arranged parallel, at regular inter-capillary distance are seen in normal individuals. Capillary disorganization refers to distortion of this regular pattern. Three morphological patterns described in healthy subjects are considered variations of normal [Table 5].[36] Tortuous loops are the most common aberrant findings in healthy subjects.[24,30] Various scoring systems for these alterations have been described [Table 6].[8,37]

Capillary dilatation

Dilated capillaries are seen as a local response to tissue hypoxia[9,23,38] and are one of the earliest microvascular alteration [Figure 6]. A dilated capillary is more than two times wider than surrounding normal capillaries. Giant capillaries (width>10 times the width of normal capillaries) are seen in later stages. The presence of even a single giant capillary suggests a microangiopathy.[23] Enlarged capillaries have been reported in 100% of systemic sclerosis patients, 56% of patients with mixed connective tissue disease and 86% of dermatomyositis patients.[23,39]

Micro-hemorrhages

Hemorrhages appear as extra-capillary brown aggregates of clotted blood in variable forms and sizes, enabling differentiation from extravasates and thrombosis. They indicate disease activity [Figure 6].[6] These could be focal (singularly placed micro-petechiae) or diffuse (multiple micro-petechiae in groups)

Capillary dropouts

Absence of a capillary loop from its dermal papilla is defined as a capillary dropout [Figure 5]. It is the earliest marker of development of avascular areas.

Avascular areas

It is an absence of two or more adjacent capillaries from the distal row [Figure 6].[40,41] It becomes larger and confluent in more advanced disease.[6] Avascular areas are often surrounded by capillaries with a disturbed distribution and orientation. Surrounding capillaries tend to get oriented toward the area of capillary loss probably as a compensatory mechanism.[6] Various scoring systems for avascular areas are summarized in Table 7. [8,28,42-44]

Tortuous capillaries

A capillary limb curled but not crossing over itself is known as a tortuous capillary [Figure 7]. Less than 5% of capillaries

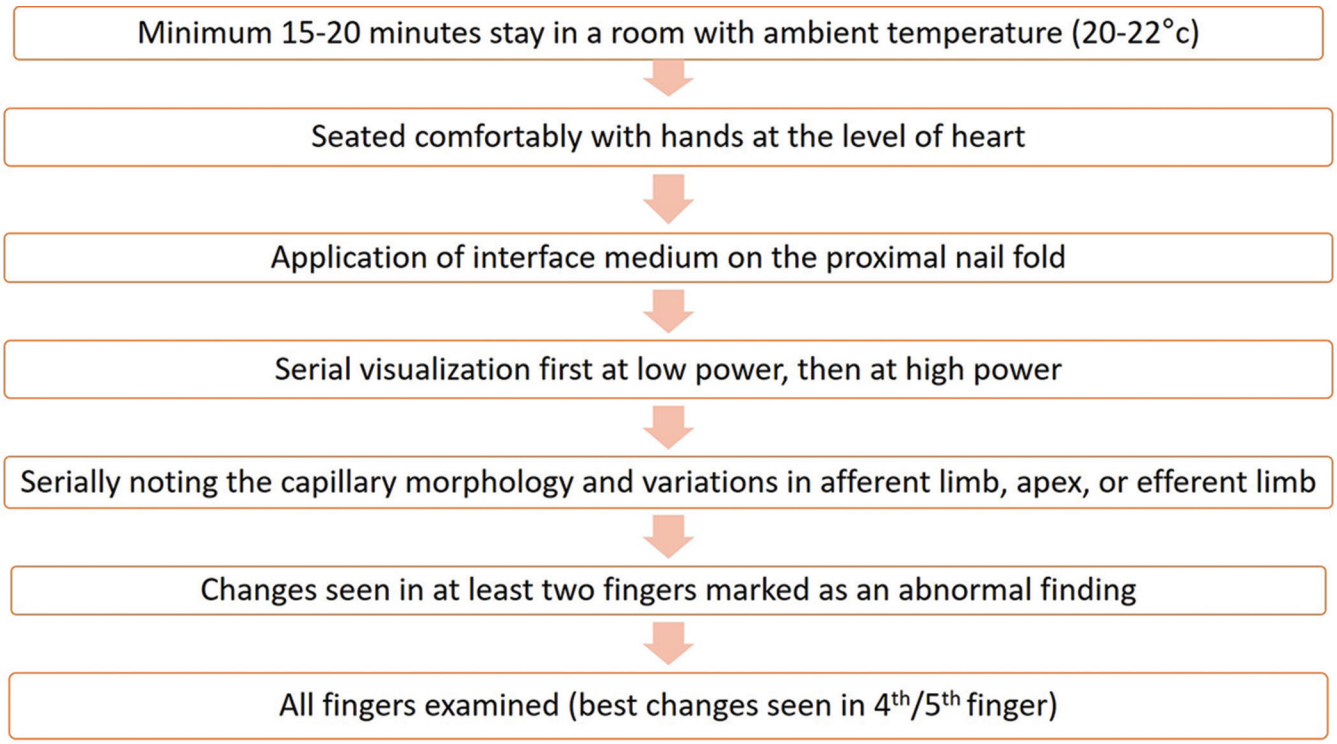

Figure 3a: Schematic representation of nail fold capillaroscopy procedure

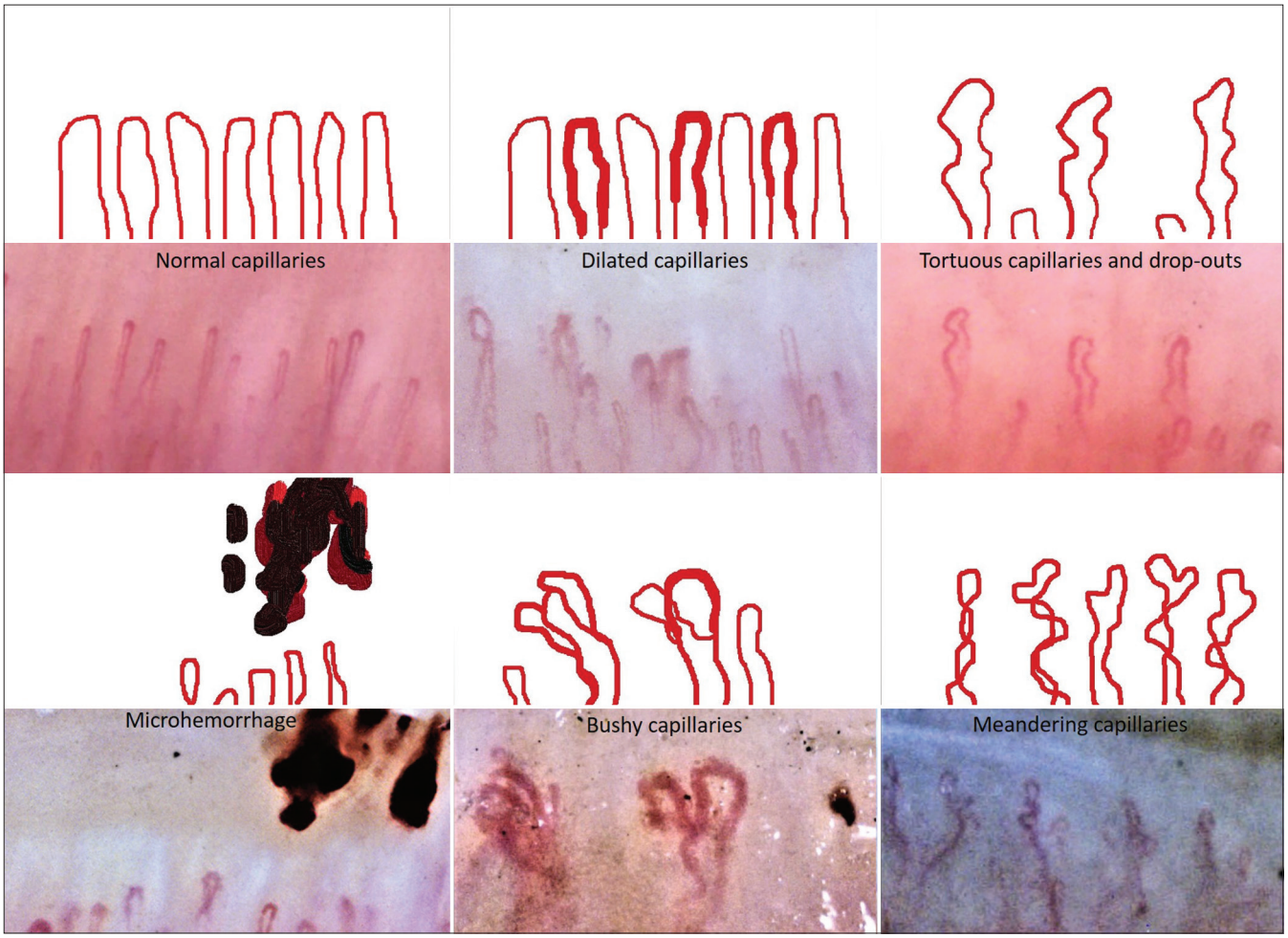

Figure 3b: Schematic representation of microvascular architectural abnormalities

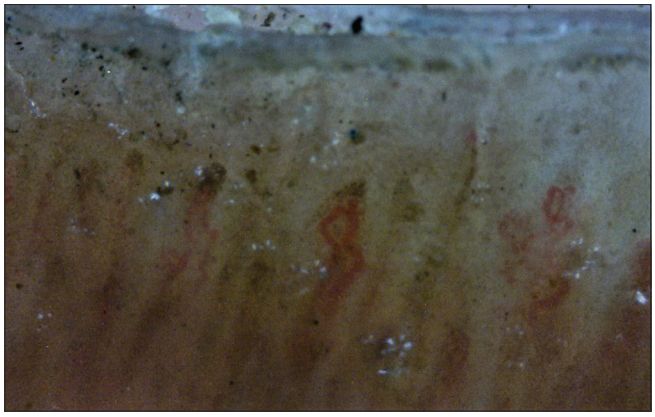

Figure 4: Nail-fold capillaroscopy in pigmented skin (Dinolite AM7515MZT, polarized ×180). The contrast with vessels may not be easy to visualize

showing this morphology is considered normal, while >10% is defined as an "increased tortuosity."[45,46]

Criss-cross forms

Also known as figure of eight forms, these capillaries have crossed arterial and venous limbs.[45] This is a normal variant and can be observed depending on the angle of observation.

Neoangiogenesis

It is new vessel formation seen as meandering, ramified or bushy capillaries.[6,9,45,47] **Bushy capillaries** are loops with limbs originating from small and multiple buds [Figures 7 and 8]; while, **meandering capillaries** have limbs crossed upon themselves or on other capillaries, several times over [Figure 9]. **Bizzare capillaries** have striking atypical morphology, not conforming to previously defined categories.

Dilated/prominent subpapillary plexus

This parameter is reflective of skin transparency, influenced by local conditions such as hyperkeratosis, pigmentation, injuries, or edema. It is the superficial cutaneous plexus located in the papillary dermis (subpapillary plexus) which gives rise to capillary loops [Figure 9]. It is visible in up to 26% of healthy individuals.[29] Blood flow in subpapillary plexus is sluggish as compared to capillary loops and an abnormally slow blood flow make it even more evident.[6]

Dystrophic capillary loops

Capillary loops which are not well developed, not of normal size and caliber or malformed are known as dystrophic. They have been described in very few studies.[48,49]

Indications for Nail-Fold Capillaroscopy

Based on the literature search, nail-fold capillaroscopy has been found to show conclusive or suggestive alterations in the following indications. Reflecting on the best available evidence for each indication, a level of evidence has been assigned based on the Grade Classification System. It is assigned as: **A** (experimental or observational study with better evidence); **B** (experimental or observational study with less evidence); **C** (case reports/uncontrolled studies); or **D** (opinion piece, consensus recommendation, or study on animal models).

Table 3: Capillary density scoring systems used in various studies

Reference	Points	Capillary density per mm
Lefford and Edwards[35]	0	>9 capillaries per mm
	1	>7–9 capillaries per mm
Ingegnoli *et al*.[36]	2	>4–7 capillaries per mm
	3	<4 capillaries per mm
Cutolo and Smith[3]	0	More than 9 capillaries
	1	<33% reduction of capillaries (7–9 capillaries)
	2	33–66% reduction of capillaries (4–6 capillaries)
	3	>66% reduction of capillaries (1–3 capillaries)

Table 4: Definition of various quantitative parameters assessed in nail-fold capillaroscopy

Parameter	Definition
Mean capillary density	Number of capillaries per mm length of the proximal nail fold
Capillary width	Width of the capillary loop at its widest section
Capillary length	Distance between the apex of capillary loop and the point where the capillary loop is no longer visible
Arterial and venous limb diameter	Width of the arterial and venous limb at their widest sections
Internal diameter	Distance between arterial and venous limbs measured at the level of capillary loop
Apex width	Maximum open space measured at the apex of a capillary
Intercapillary distance	Longest distance that exists between two adjacent capillary loops

Table 5: Three major morphological patterns described in healthy individuals[36]

Pattern	Definition
"Normal" Pattern	2–5 U-shaped capillary loops/mm and equal or less than 2 tortuous loops/mm
"Perfect Normal" Pattern	Equal to or greater than 5 U-shaped loops/mm
"Unusual Normal" Pattern	At least 1 meandering or bushy loop, or at least 1 microhemorrhage or with >4 crossed loops/mm

Rheumatological Indications

Rheumatological diseases are the primary indications for nail fold capillaroscopy. Over the years, study of nail fold capillaroscopy has been refined in these very disorders, to the extent that nail-fold capillaroscopy constitutes a part of the diagnostic criteria for Raynaud's phenomenon and systemic sclerosis.

Raynaud's phenomenon (Grade of recommendation - A)

Raynaud's phenomenon can occur both as a primary or a secondary phenomenon and nail-fold capillaroscopy helps distinguish these. Absence of abnormal capillaroscopic pattern is one of the diagnostic criteria for primary Raynaud's phenomenon [Table 8].[50] In fact, in patients with Primary Raynaud's phenomenon, if nail-fold capillaroscopy pattern is abnormal, they need to be closely followed up for the risk of developing a well-defined connective tissue diseases in future.[6,51-53] Secondary Raynaud's phenomenon accompanies various rheumatologic conditions such as systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis, Sjogren syndrome and dermatomyositis showing patterns accordingly.

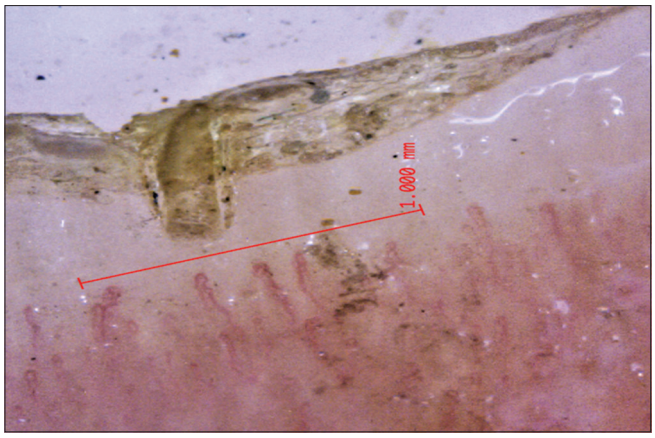

Figure 5: Nail-fold capillaroscopy image captured using the calibration software of the USB dermatoscope (Dinolite AM7515MZT, polarized ×180). The number of distal most capillaries can be counted over a millimeter. Area of capillary dropout can be seen where the distal most capillary loop is missing

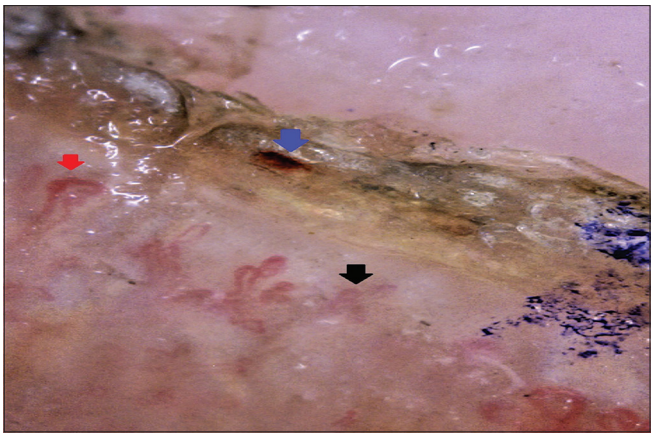

Figure 6: Nail-fold capillaroscopy image showing dilated capillaries (black arrow), giant capillary (red arrow) and microhemorrhages (blue arrow) (Dinolite AM7515MZT, polarized ×180)

As Raynaud's phenomenon may be an isolated complaint or may be the first symptom of connective tissue diseases; patients need to be regularly examined.[23,54-57] In studies with over ten-year follow-up, frequency of development of autoimmune connective tissue diseases increased from 5 to 19% in those with nail-fold capillaroscopy abnormalities.[46,56] In healthy individuals, the capillaroscopic patterns of a digit remains surprisingly constant over an extended period of time and abnormal findings have a positive predictive value of 47% for subsequent development of connective tissue diseases. Abnormal nail-fold capillaroscopy coupled with a positive anti-nuclear antibody or rheumatoid factor, increases the predictive value up to 55%.[57] Thus, in the presence of Raynaud's phenomenon, a follow-up nail-fold capillaroscopy analysis is recommended to be performed every six months.[6,9,38,58-60]

Systemic sclerosis (Grade of recommendation - A)

The "scleroderma pattern" in systemic sclerosis was first described by Maricq *et al*.[6,8,9,23,38,47,52,61] It is found in 83–93% cases with overt scleroderma.[38,52] Maricq *et al*. (1983) described two types of capillaroscopic changes in systemic sclerosis: "Active" pattern reflected by extensive and confluent avascular areas and neovascularization [Figure 10]; in contrast to "slow" capillaroscopic pattern represented by giant loops with minimal capillary loss.[6,52,62] Cutolo (2000) described three different capillaroscopic patterns on nail-fold videocapillaroscopy which are widely accepted and used [Table 9].[8]

Later, Maricq *et al*. defined "scleroderma-like" pattern in scleroderma spectrum disorders such as mixed connective tissue diseases, undifferentiated connective tissue disease, overlap syndromes and dermatomyositis with some of these showing similar parameters.[6,9,23,38,47,51,63-67] In 2013, the ACR-EULAR Classification criteria[68] were proposed which incorporated nail-fold capillaroscopy as an essential part of scoring and evaluating a patient with systemic sclerosis.

Various studies have explored correlation between nail-fold capillaroscopy changes, type of systemic sclerosis, severity of clinical activity and visceral involvement,[6,8,21,52,69-74] but the results are not uniform.[75-77] Severe capillary loss is reported more commonly in diffuse systemic sclerosis, while dilated capillaries without capillary loss were found more frequently in limited systemic sclerosis.[73] Anti-topoisomerase antibody (anti-Scl-70) correlate with "active" and "late" capillaroscopic changes and probably also accelerate their appearance. Positive anti-centromere antibody was observed more commonly with "early" phase capillaroscopic pattern and probably delayed the onset of "late" capillaroscopic changes.[21] Bredemeier *et al*. ascertained a relationship between loss of capillaries, skin involvement and activity of pulmonary disease as evaluated by high-resolution computed tomography in 91 systemic sclerosis patients.[78] Alterations of nail-fold capillaroscopy pattern during follow-up of patients with connective tissue diseases could also indicate visceral vascular involvement.[71,79] Structural abnormalities such as devascularization and distortion of architecture, which characterize late microvascular damage, are strong predictors of occurrence of digital ulcers.[80] Available evidence indicates a positive correlation between nail-fold capillaroscopy abnormalities and involvement of target organs.[80]

Dermatomyositis and polymyositis (Grade of recommendation - B)

Other than systemic sclerosis, the most consistent nail-fold capillaroscopy abnormalities are reported in dermatomyositis.[65,81] The pattern observed largely resembles systemic sclerosis, including the presence of two or more of the following characteristics in two or more nail folds, namely, capillary dilation, twisted enlarged capillaries, loss of capillaries, bushy capillaries, disorganization of capillary architecture and microhemorrhages [Figure 11].[10] Capillary dilation and loss of capillaries though reported in both dermatomyositis and polymyositis are more commonly and severely reported in dermatomyositis.[82] However, nail-fold capillaroscopy changes do not relate to the disease activity and severity.[82]

Systemic lupus erythematosus (Grade of recommendation - B)

Nail-fold capillaroscopy abnormalities are less commonly and less consistently found in systemic lupus erythematosus. The most frequently reported abnormalities include extremely

Table 6: Various capillary distributions and scoring systems

Study	Points	Capillary distribution/mm
Cheng *et al*.[37]	Stage A	
	0	Regular (100%)
	1	Slight irregularity
	Stage B	
	2	Disarranged (<50%)
	3	Disarranged (>50%)
	Stage C	
	4	Local avascularity
	5	Enlarged loop bordering avascularity
	6	Complete avascularity
Cutolo *et al*.[8]	0	Normal Distribution
	1	Mild disorganization (<33% alteration/mm)
	2	Moderate disorganization (33–66% alteration/mm)
	3	Severe disorganization (>66% alterations/mm)

Table 7: Various scoring systems for avascularity

Points	Avascularity/mm (Cutolo *et al*.,[8] Terreri *et al*.,[42] Kabasakal *et al*.,[29] Ingegnoli *et al*.[43])	Avascularity/mm (Hofstee *et al*.[44])
0	No avascular areas	-
1	Mild (1–2 avascular areas)	Mild (<2 consecutive capillary loss)
2	Moderate (>2 avascular area)	Moderate (2–4 consecutive capillary loss)
3	Severe (Large and confluent avascular areas)	Severe (>4 consecutive capillary loss; or >2 areas of >2 capillary loss)

long capillary loops (>750 μm), meandering capillaries and a prominent sub-papillary venous plexus [Figure 12].[82] When systemic lupus erythematosus is associated with Raynaud's phenomenon and/or Anti-U1RNP antibodies, avascular areas and enlarged capillary loops may be seen.[10] Nail-fold capillaroscopy changes have been found to correlate with disease activity and systemic manifestations in systemic lupus erythematosus.[10]

Anti-phospholipid syndrome (Grade of recommendation - B)

In patients with anticardiolipin antibodies (IgG or IgM), symmetrical microhemorrhages have been demonstrated on nail-fold capillaroscopy.[83] In a study from Brazil, significant alterations of nail-fold capillary morphology was demonstrated.[84]

Rheumatoid arthritis (Grade of recommendation - C)

Primary nail-fold capillaroscopy abnormalities reported in rheumatoid arthritis include elongated and tiny capillaries, tortuosity and prominent sub-papillary venous plexus, especially in those with positive anti-nuclear antibody [Figure 13].[85] Most common findings include increased capillary tortuosity, increased length and prominent subpapillary plexus.[45] Prominent subpapillary plexus was the most common finding in 62 rheumatoid arthritis patients, being seen in 69% cases.[86]

Primary Sjogren's syndrome (Grade of recommendation - B)

Nail-fold capillaroscopy abnormalities reported range from crossed capillaries, confluent hemorrhages or systemic sclerosis -type findings. Sjogren's syndrome patients with

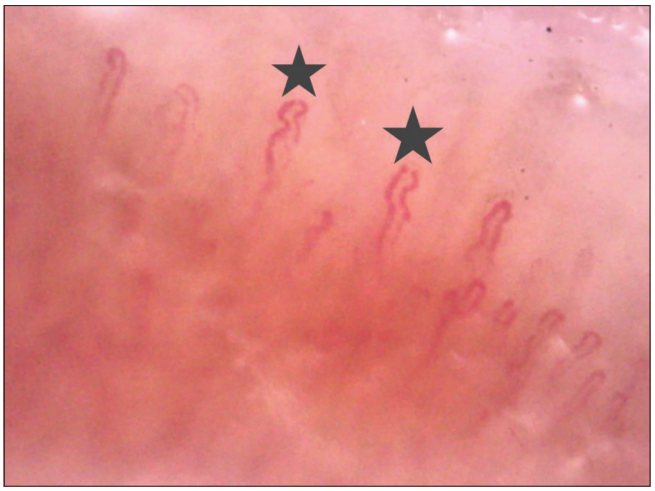

Figure 7: Nail fold capillaroscopy from a patient of dermatomyositis showing tortuous capillaries (star marked) in the centre of the image [Dinolite AM7515MZT, polarized, 180X]

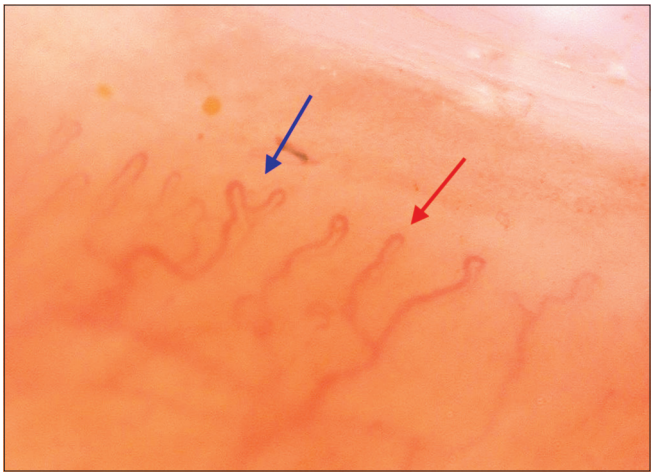

Figure 8: Nail fold capillaroscopy in a patient of systemic sclerosis showing a budding capillary (blue arrow) indicating neoangiogenesis and few dilated vessels (red arrows) [Dinolite AM7515MZT, polarized, 180X]

Raynaud's phenomenon have more frequent nail-fold capillaroscopy changes than patients without Raynaud's phenomenon.[87]

Others

Nail-fold capillaroscopy abnormalities have also been reported in mixed connective tissue diseases, undifferentiated connective tissue diseases, cryoglobulinemia and cryofibrinogenemia,[88] and fibromyalgia.[39]

Non-rheumatological Indications

This set of indications is becoming broader; however, only limited work has been done for most of these and precise nail-fold capillaroscopy parameters and changes are yet to be fully studied and defined.

Systemic diseases with microvascular changes

Diabetes mellitus (Grade of recommendation - A)

Capillary alterations have been described in diabetics, more often with poor metabolic control. Both morphological

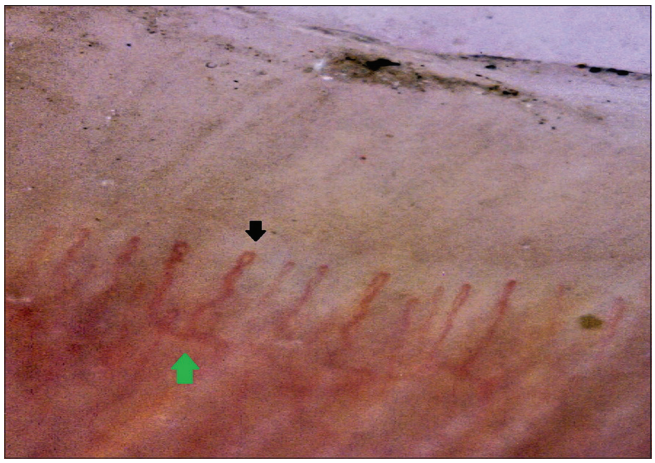

Figure 9: Multiple meandering capillaries (black arrows) (Dinolite AM7515MZT, polarized ×180). Subpapillary plexus can also be seen (green arrows)

Table 8: Le Roy and Medsger criteria for diagnosis of Primary Raynaud's Phenomenon[51]

a. Symmetrical involvement
b. Absence of tissue necrosis
c. Absence of digital ulceration and gangrene
d. Absence of a secondary cause (based on medical history and physical examination)
e. Normal Erythrocyte sedimentation rate
f. Negative test for antinuclear antibodies
g. Normal capillaroscopic pattern

Table 9: Three different patterns of capillaroscopy changes observed in SSc[8]

NVC Pattern	Features
"Early" NVC Pattern	• Appearance of few dilated and/or giant capillaries and a few hemorrhages • In this phase, the distribution is relatively preserved without loss of capillaries. These findings are of crucial importance for the early diagnosis of SSc
"Active" NVC Pattern	• Large numbers of giant capillaries and hemorrhages • In addition, a moderate loss of capillaries, slight derangement and diffuse pericapillary edema can be found
"Late" NVC Pattern	• Severe loss of capillaries with extensive avascular areas • Also includes bushy and ramified capillaries, or more than one capillary loop in a dermal papilla. These are the morphological substrates of defective neoangiogenesis

*NVC: Nail-fold videocapillaroscopy, SSc: Systemic sclerosis

and functional nail-fold capillaroscopy changes have been reported.[13,89-91] Studies have even reported a correlation between severity of microvascular changes and metabolic control.[90-92]

Diabetics have more tortuous and enlarged capillaries as compared to healthy controls. Nodular apical elongations are related to longer duration of disease. Frequency of enlarged capillaries and apical elongation is also higher in Type 2 diabetes with chronic complications. These findings were not influenced by the level of glycemic control[13]. Uniquely altered "angulated capillaries" have also been reported in Type 2 diabetics [Figure 14].[13] No difference in capillary density has been found;[93] in fact, regressional changes rather than proliferative changes are found. The degree of tortuosity is higher in patients with retinopathy.[94] Kaminska-Winciorek *et al.* showed an increased frequency of twisted capillaries in patients with both Type 1 and Type 2 disease.[92] A higher frequency of enlarged capillaries and nodular apical elongation were reported in Type 2 diabetes patients with chronic clinical complications.[95] Kaminska-Winciorek *et al*. and Barchetta *et al.* also concluded that the microvascular alterations in diabetics were not dependent on age or sex.[9,95] In decompensated Type 2 diabetes, a narrowing of arterial capillary segment and increase in rate of remodeling is found. This creates newer possibilities regarding the magnitude of microcirculatory changes in Type 2 diabetes, simultaneously evaluating the efficiency of treatment by monitoring the status of the microvasculature.[96]

Arterial hypertension (Grade of recommendation - B)

Only a limited evaluation of nail-fold microvasculature has been done in hypertensives, in contrast to studies about the retinal microvasculature.[23] Nail-fold capillaroscopy abnormalities in arterial hypertension include quantitative (decreased mean capillary density and loss of capillaries) and qualitative abnormalities (tortuosity, branching, enlarged capillary loops and microhemorrhages).[97] Features seen include capillary rarefaction, avascular areas, microhemorrhages, edema and dystrophic capillary loops.[47] Antonios *et al*. described decreased capillary density, increased looping and increased transcapillary filtration as hypertension related changes.[98] Using dynamic measurements, increased capillary pressure has also been recorded in untreated hypertensives.[99]

A decreased capillary density is seen in initial stages in experimental animal models of hypertension.[100] This has been documented in multiple microvascular beds, including muscle, skin, mesentery, bulbar conjunctiva, cremaster muscle and brain.[101] Capillary rarefaction in skin was first published in early 1990s.[102] Subsequently video microscopy revealed significantly fewer capillaries,[98] confirmed later by Serné *et al*.[103] and Debbabi *et al*.[104] isolated systolic hypertension predominantly affects macrovasculature while isolated diastolic hypertension affects microvasculature. Bonacci *et al*. showed significant correlation of retinal microvascular changes with mean capillary density in nailfolds.[48] Studies documenting increase in nail-fold capillary density with treatment;[104] as well as those contradicting this observation,[105] have been published.

Behcet's disease (Grade of recommendation - B)

Nail-fold capillaroscopy findings include enlarged capillaries, microhemorrhages and capillary loss.[106,107]

Dermatological diseases

Psoriasis (Grade of recommendation - B)

Changes in the microvasculature are known to play an important part in pathogenesis of psoriasis and psoriatic arthritis; hence, we expect changes in nail-fold capillaroscopy as well. However, nail-fold capillaroscopy findings in psoriasis are conflicting, possibly representing the polymorphous nature of the disease. Mean capillary density is reduced

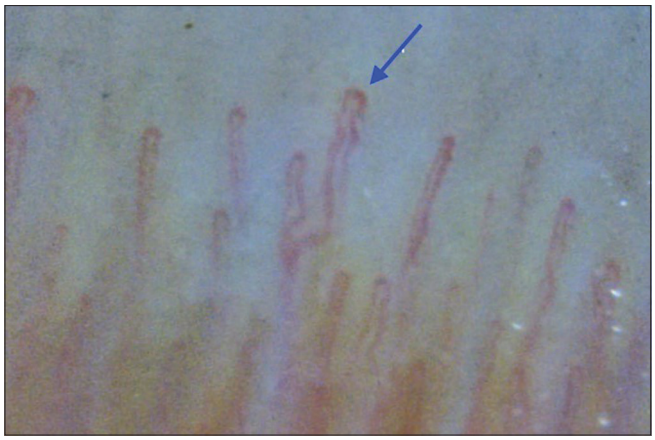

Figure 10a: Nail fold capillaroscopy from a patient with systemic sclerosis showing '**early pattern**', characterized by numerous dilated and tortuous vessels (blue arrow). [Dinolite AM7515MZT, polarized, 180X]

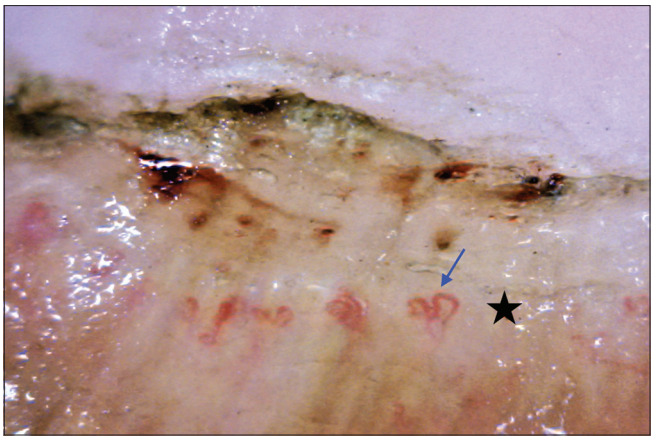

Figure 10b: Nail fold capillaroscopy from a pateint with systemic sclerosis showing an '**active pattern**' characterized by gross dilation, giant capillaries (blue arrow), avascular areas (black star), and microhemorrhages in various stages can be seen [Dinolite AM7515MZT, polarized, 180X]

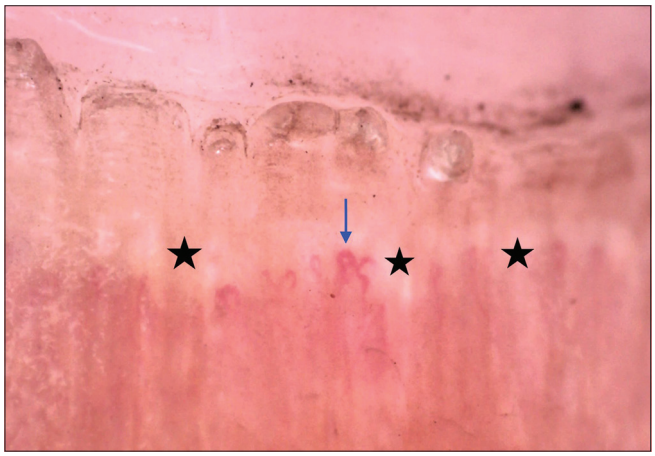

Figure 10c: Nail fold capillaroscopy from a patient with systemic sclerosis showing a 'late pattern' characterized by giant capillaries (blue arrow) and avascular areas (black star). [Dinolite AM7515MZT, polarized, 180X]

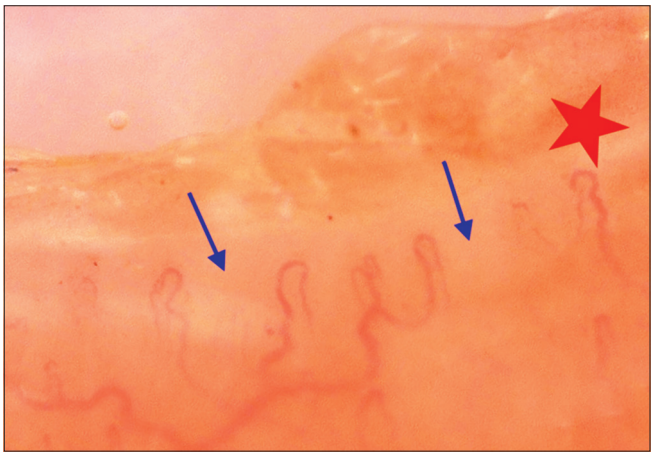

Figure 11: Nail fold capillaroscopy of a dermatomyositis patient showing dilated capillaries, and tortuous vessels (red star). Few capillary dropouts can be appreciated (blue arrows) [Dinolite AM7515MZT, polarized, 180X]

as compared to healthy individuals, while morphological changes in the form of coiled and folded capillaries have been reported. Bhushan *et al*. reported a significant decrease in capillary loop diameter in psoriasis patients with nail disease.[108] However, there was no difference in capillary dimensions as compared to normal controls. They also found no specific pattern of morphological changes in psoriasis. Ribeiro *et al.* reported decreased capillary density, increased avascular areas and morphologically abnormal capillaries as compared to controls. However, there was no association with disease duration or extent of skin involvement.[109]

Psoriatic arthritis (Grade of recommendation - B)

Nail-fold capillaroscopy is particularly helpful in differentiating psoriatic arthritis from rheumatoid arthritis. Psoriatic arthritis shows decreased capillary density, dilated, tortuous and disorganized capillaries along with hemorrhages [Figure 15]; while nail-fold capillaroscopy features of rheumatoid arthritis are discussed above and are inconsistent. A recent study evaluated nail-fold capillaroscopy in differentiating psoriatic arthritis sine psoriasis from rheumatoid arthritis.[110] It was found that psoriatic arthritis patients show a diffuse reddish background with/without dotted vessels; whereas, rheumatoid arthritis patients showed parallel dotted vessels, short linear vessels ("fish school") or irregular purple and ramified vessels. Both these types of features were however absent in normal controls.[110]

Alopecia areata (Grade of recommendation - C)

Gerkowicz *et al*. studied nail-fold capillaroscopy findings in alopecia areata and found abnormal images in 42% of patients with features being tortuous and branching capillaries, decreased density, enlargement of the efferent limb, or top part of the loop.[111]

Miscellaneous conditions

Nail-fold capillaroscopy abnormalities have also been reported in various diseases [Table 10][112-117] including acromegaly,[118] hyperthyroidism,[119] cardiac X syndrome,[120] mitral valve prolapse syndrome,[121] Crohn's disease,[122]

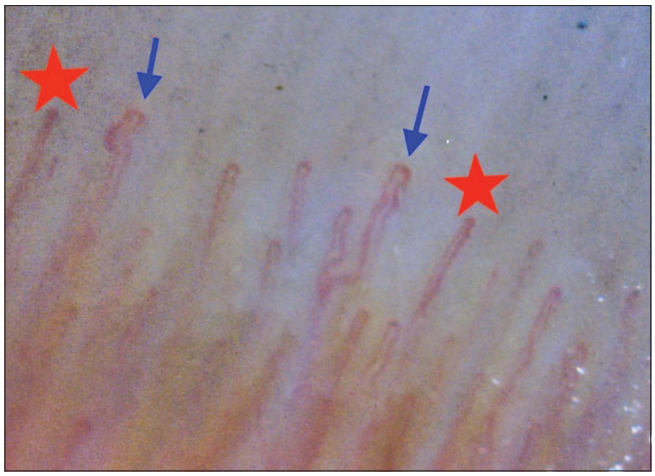

Figure 12: Nail fold capillaroscopy of a patient with systemic lupus erythematosus. Elongated capillaries (red star) with few dilated vessels and increased tortuosity (blue arrow) can be seen [Dinolite AM7515MZT, polarized 180X]

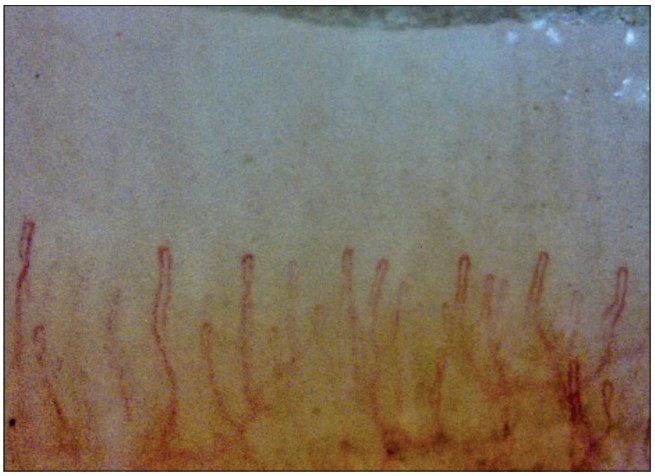

Figure 13: Nail-fold capillaroscopy in a patient with rheumatoid arthritis (Dinolite AM7515MZT, polarized x 180). Note the irregularly dilated, elongated and increasingly tortous capillaries with a prominent subpapillary venous plexus.

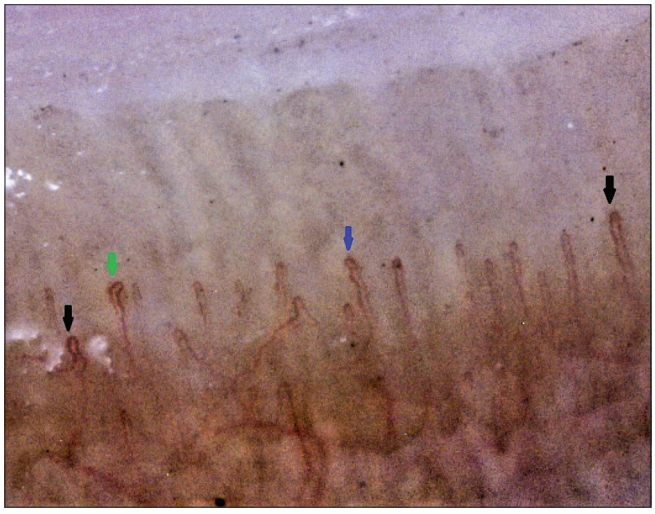

Figure 14: Nail-fold capillaroscopy in a patient with Type 2 Diabetes mellitus (Dinolite AM7515MZT, polarized ×180). Dilated capillaries (apical dilation) (black arrow), increased tortuosity (blue arrow) with "angulated capillaries" (green arrow) can be seen. There are capillary dropouts

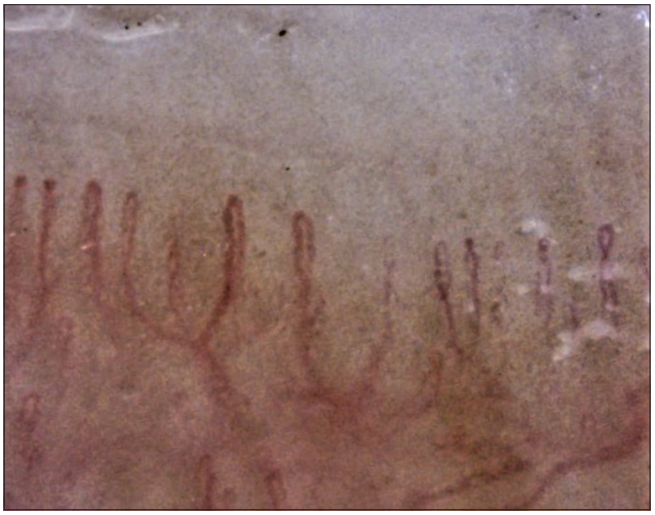

Figure 15: Nail-fold capillaroscopy in a patient with psoriatic arthritis (Dinolite AM7515MZT, polarized ×180). Multiple dilated and tortuous vessels can be seen. There is marked disorganization of the capillary architecture

peritoneal dialysis patients,[123] Familial Mediterranean fever,[124] Turner's syndrome,[125] and rosacea.[126]

Current limitations of nailfold capillaroscopy

Despite several advancements in the field of nailfold capillaroscopy, challenges remain with respect to its uniform applicability across ethnicities, type of devices used and standardization of nailfold capillaroscopy parameters. A limited visibility of nailfold capillaroscopy features is a unique constraint seen at times in patients with skin of colo. Despite the use of best devices, capillary visibility may be hindered by pigmented skin and in some cases even the trained eyes can not identify the nailfold capillaroscopy changes. Additionally, literature pertaining to the utility of nailfold capillaroscopy in assessing disease activity and correlating with other disease related parameters, is limited for disorders other than connective tissue diseases. More research is also needed regarding nailfold capillaroscopy changes in general dermatological conditions, especially where the micro-circulation may be affected.

Table 10: Miscellaneous disease states and nail fold capillaroscopy changes

Disease state	Nail fold capillaroscopy findings
Kindler syndrome[112]	Reduced capillary density, neoangiogenesis, dilated and giant capillaries
Primary biliary cirrhosis[113]	Reduced capillary density, capillary loss, dilated capillary, giant capillary, neoangiogenesis and hemorrhages
Kawasaki disease[114]	Reduced capillary density, increase in limb diameter and increase in the inter-capillary distance
Henoch-Schonlein purpura[115,116]	Reduced capillary density, tortuosity, avascular areas, hemorrhages, increased length of capillaries and edema
Anti-synthetase syndrome[117]	Reduced capillary density, hemorrhage, ramified capillaries, Systemic sclerosis-like pattern

Conclusion

Medicine today lays emphasis on diagnosing and managing diseases early and in a quick and non-invasive manner; nail-fold capillaroscopy thus assumes a useful role. With increasing availability and usage of high-quality dermatoscopes, it seems possible that nail-fold capillaroscopy can find a place in early detection as well as long-term management of patients in the near future. Nail-fold capillaroscopy has an important role to play in aiding prognostication and prevention of grave complications.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

References

1. Cutolo M. Capillaroscopy in rheumatic diseases from the XVIII to the XXI centry. In: Cutolo M, editor. Atlas of Capillaroscopy in Rheumatic Diseases. Vol. 1. Milano: Elsevier; 2010. p. 3-5.
2. Müller-Ladner U. Raynaud's Phenomenon and Peripheral Ischemic Syndromes. 1st ed. Bremen: UNI-MED Verlag AG; 2008. p. 36-41.
3. Cutolo M, Smith V. Nailfold capillaroscopy. In: Varga J, editor. Scleroderma: From Pathogenesis to Comprehensive Management. New York: Springer Science Business Media, LLC; 2012. p. 331-46.
4. Grover C, Jakhar D. Onychoscopy: A practical guide. Indian J Dermatol Venereol Leprol 2017;83:536.
5. Grover C, Jakhar D. Diagnostic utility of onychoscopy: Review of literature. Indian J Dermatopathol Diagn Dermatol 2017;4:31.
6. Bollinger A, Fagrell B. Clinical Capillaroscopy-a Guide to Its Use in Clinical Research and Practice. Toronto: Hogrefe and Huber Publishers; 1990. p. 1-123.
7. Cortes S, Cutolo M. Capillaroscopic patterns in rheumatic diseases. Acta Reumatol Port 2007;32:29-36.
8. Cutolo M, Sulli A, Pizzorni C, Accardo S. Nailfoldvideocapillaroscopy assessment of microvascular damage in systemic sclerosis. J Rheumatol 2000;27:155-60.
9. Cutolo M, Sulli A, Secchi ME, Olivieri M, Pizzorni C. The contribution of capillaroscopy to the differential diagnosis of connective autoimmune diseases. Best Pract Res Clin Rheumatol 2007;21:1093-108.
10. Bergman R, Sharony L, Schapira D, Nahir MA, Balbir-Gurman A. The handheld dermatoscope as a nail-fold capillaroscopic instrument. Arch Dermatol 2003;139:1027-30.
11. Ureyen SB, Kara RO, Erturk Z, Yaldiz M. The microvascular and morphostructural changes of nails in psoriatic patients with nail disease; a link between ultrasound and videocapillaroscopy findings in the nailfold. Med Ultrason 2018;20:185-91.
12. Suchkova OV, Gurfinkel YI, Sasonko ML. Microcirculatory parameters in compensated and decompensated Type 2 diabetes mellitus. Ter Arkh 2017;89:28-35.
13. Jakhar D, Grover C, Singal A, Das GK, Madhu SV. Nail fold capillaroscopic changes in patients with Type 2 diabetes mellitus: An observational, comparative study. Indian J Med Spec 2020;11:28-33.
14. Triantafyllou A, Anyfanti P, Pyrpasopoulou A, Triantafyllou G, Aslanidis S, Douma S. Capillary rarefaction as an index for the microvascular assessment of hypertensive patients. Curr Hypertens Rep 2015;17:33.
15. Braverman IM. The cutaneous microcirculation. J Investig Dermatol Symp Proc 2000;5:3-9.
16. Bakst R, Merola JF, Franks AG Jr., Sanchez M. Raynaud's phenomenon: Pathogenesis and management. J Am Acad Dermatol 2008;59:633-53.
17. Jakhar D, Grover C, Singal A. Nailfold capillaroscopy with USB dermatoscope: A cross-sectional study in healthy adults. Indian J Dermatol Venereol Leprol 2020;86:33-8.
18. Beltrán E, Toll A, Pros A, Carbonell J, Pujol RM. Assessment of nailfold capillaroscopy by x 30 digital epiluminescence (dermoscopy) in patients with Raynaud phenomenon. Br J Dermatol 2007;156:892-8.
19. Anders HJ, Sigl T, Schattenkirchner M. Differentiation between primary and secondary Raynaud's phenomenon: A prospective study comparing nailfold capillaroscopy using an ophtalmoscope or stereomicroscope. Ann Rheum Dis 2001;60:407-9.
20. Sontheimer RD. A portable digital microphotography unit for rapid documentation of periungual nailfold capillary changes in autoimmune connective tissue diseases. J Rheumatol 2004;31:539-44.
21. Cutolo M, Sulli A, Smith V. How to perform and interpret capillaroscopy. Best Pract Res Clin Rheumatol 2013;27:237-48.
22. Cutolo M, Pizzorni C, Tuccio M, Burroni A, Craviotto C, Basso M, *et al*. Nailfold videocapillaroscopic patterns and serum autoantibodies in systemic sclerosis. Rheumatology (Oxford) 2004;43:719-26.
23. Cutolo M, Grassi W, Cerinic MM. Raynaud's phenomenon and the role of capillaroscopy. Arthritis Rheum 2003;48:3023-30.
24. Bhakuni DS, Vasdev V, Garg MK. Nailfold capillaroscopy by digital microscope in an Indian population with systemic sclerosis. Int J Rheum Dis 2012;15:95-101.
25. Dolezalova P, Young SP, Bacon PA, Southwood TR. Nailfold capillary microscopy in healthy children and in childhood rheumatic diseases: A prospective single blind observational study. Ann Rheum Dis 2003;62:444-9.
26. Cony M, Klene-Boudard C, Fontan I, Sanciaume C, Sarrat P, Taieb A, *et al*. Periungual capillaroscopy patterns in normal children. Arch Fr Pediatr 1992;49:171-4.
27. Martino F, Agolini D, Aprigliano D, Guido F, Placanica G, Giardini O. Nailfold capillaroscopy in normal children between 0 and 16 years of age. Minerva Pediatr 1997;49:197-201.
28. Ingegnoli F, Zeni S, Gerloni V, Fantini F. Capillaroscopic observations in childhood rheumatic diseases and healthy controls. Clin Exp Rheumatol 2005;23:905-11.
29. Kabasakal Y, Elvins DM, Ring EF, McHugh NJ. Quantitative nailfold capillaroscopy findings in a population with connective tissue disease and in normal healthy controls. Ann Rheum Dis 1996;55:507-12.
30. Hoerth C, Kundi M, Katzenschlager R, Hirschl M. Qualitative and quantitative assessment of nailfold capillaries by capillaroscopy in healthy volunteers. Vasa 2012;41:19-26.
31. Jung P, Trautinger F. Capillaroscopy of toes. J Dtsch Dermatol Ges 2013;11:855-66.
32. Tavakol ME, Fatemi A, Karbalaie A, Emrani Z, Erlandsson BE. Nailfold capillaroscopy in rheumatic diseases: Which parameters should be evaluated? Biomed Res Int 2015;2015:974530.
33. 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.
34. Hofstee HM, Noordegraaf AV, Voskuyl AE, Dijkmans BA, Postmus PE, Smulders YM, *et al*. Nailfold capillary density is associated with the presence and severity of pulmonary arterial hypertension in systemic sclerosis. Ann Rheum Dis 2009;68:191-5.
35. Lefford F, Edwards JC. Nailfold capillary microscopy in connective tissue disease: A quantitative morphological analysis. Ann Rheum Dis 1986;45:741-9.
36. Ingegnoli F, Gualtierotti R, Lubatti C, Bertolazzi C, Gutierrez M, Boracchi P, *et al*. Nailfold capillary patterns in healthy subjects: A real issue in capillaroscopy. Microvasc Res 2013;90:90-5.
37. Cheng C, Daskalakis C, Falkner B. Alterations in capillary morphology are found in mild blood pressure elevation. J Hypertens 2010;28:2258-66.
38. Cutolo M, Pizzorni C, Sulli A. Capillaroscopy. Best Pract Res Clin Rheumatol 2005;19:437-52.
39. Blockmans D, Beyens G, Verhaeghe R. Predictive value of nail fold capillaroscopy in the diagnosis of connective tissue diseases. Clin Rheumatol 1996;15:148-53.
40. Jones BF, Oral M, Morris CW, Ring EF. A proposed taxonomy for nailfold capillaries based on their morphology. IEEE Trans Med Imaging 2001;20:333-41.
41. Houtman PM, Kallenberg CG, Fidler V, Wouda AA. Diagnostic significance of nailfold capillary patterns in patients with Raynaud's

phenomenon. An analysis of patterns discriminating patients with and without connective tissue disease. J Rheumatol 1986;13:556-63.
42. Terreri MT, Andrade LE, Puccinelli ML, Hilário MO, Goldenberg J. Nail fold capillaroscopy: Normal findings in childrenand adolescents. Semin Arthritis Rheum 1999;29:36-42.
43. Ingegnoli F, Gualtierotti R, Lubatti C, Zahalkova L, Meani L, Boracchi P, *et al*. Feasibility of different capillaroscopic measures for identifying nailfold microvascular alterations. Semin Arthritis Rheum 2009;38:289-95.
44. Hofstee HM, Serné EH, Roberts C, Hesselstrand R, Scheja A, Moore TL, *et al*. A multicentre study on the reliability of qualitative and quantitative nail-fold videocapillaroscopy assessment. Rheumatology (Oxford) 2012;51:749-55.
45. Redisch W. Capillaroscopic observations in rheumatic diseases. Ann Rheum Dis 1970;29:244-53.
46. Pavlov-Dolijanović S, Damjanov N, Ostojić P, Susić G, Stojanović R, Gacic D, *et al*. The prognostic value of nailfold capillary changes for the development of connective tissue disease in children and adolescents with primary raynaud phenomenon: A follow-up study of 250 patients. Pediatr Dermatol 2006;23:437-42.
47. Maricq HR, LeRoy EC, D'Angelo WA, Medsger TA Jr., Rodnan GP, Sharp GC, *et al*. Diagnostic potential of *in vivo* capillary microscopy in scleroderma and related disorders. Arthritis Rheum 1980;23:183-9.
48. Bonacci E, Santacrocea N. Nail fold capillaroscopy in the study of microcirculation in elderly hypertensive patients. Arch Gerontol Geriatr 1996;5:79-83.
49. Wu PC, Huang MN, Kuo YM, Hsieh SC, Yu CL, Yu CL, *et al*. Clinical applicability of quantitative nailfold capillaroscopy in differential diagnosis of connective tissue diseases with Raynaud's phenomenon. J Formos Med Assoc 2013;112:482-8.
50. LeRoy EC, Medsger TA Jr. Raynaud's phenomenon: A proposal for classification. Clin Exp Rheumatol 1992;10:485-8.
51. Nagy Z, Czirjac L. Nailfold digital capillaroscopy in 447 patients with connective tissue disease and Raynaud's disease. J Eur Acad Dermatol Venerol 2004;18:62-8.
52. Maricq HR, Harper FE, Khan MM, Tan EM, LeRoy EC. Microvascular abnormalities as possible predictors of disease subsets in Raynaud phenomenon and early connective tissue disease. Clin Exp Rheumatol 1983;1:195-205.
53. Bukhari M, Hollis S, Moore T, Jayson MI, Herrick AL. Quantitation of microcirculatory abnormalities in patients with primary Raynaud's phenomenon and systemic sclerosis by videocapillaroscopy. Rheumatology (Oxford) 2000;39:506-12.
54. Seibold JR, Steen VD. Systemic sclerosis. In: Klippel JH, Dieppe PA. Rheumatology. London: Mosby; 1994. p. 6.8-11.
55. Steven AO. Raynaud's phenomenon. In: Sterling JB, editor. Secrets of Rheumatology. Moscow: Binom; 2001. p. 614-9.
56. Ziegler S, Brunner E, Eigenbauer E, Minar E. Long-term outcome of primary Raynaud's phenomenon and its conversion to connective tissue disease: A 12 year prospective patient analysis. Scand J Rheumatol 2003;32:343-7.
57. Kirou KA, Crow MK. Raynaud's phenomenon. In: Paget SA, Gibofsky A, Beary JF, Pellicci P, editors. Manual of Rheumatology and Outpatient Orthopedic Disorders: Diagnosis and Therapy. 4th ed. Philadelphia, PA: Lippincot Williams and Willkins; 2000. p. 82-7.
58. Block JA, Sequeira W. Raynaud's phenomenon. Lancet 2001;357:2042-8.
59. Ingegnoli F, Boracchi P, Gualtierotti R. Prognostic model based on nailfold capillaroscopy for identifying Raynaud's phenomenon patients at high risk for the development of a scleroderma spectrum disorder. Arthritis Rheum 2008;58:2174-82.
60. Kallenberg CG, Wouda AA, Hoet MH, van Venrooij WJ. Development of connective tissue disease in patients presenting with Raynaud's phenomenon: A six year follow up with emphasis on the predictive value of antinuclear antibodies as detecting by immunoblotting. Ann Rheum Dis 1988;47:634-41.
61. Maricq HR, Valter I. A working classification of scleroderma spectrum disorders: A proposal and the results of testing on a sample of patients. Clin Exp Rheumatol 2004;22 Suppl 33:S5-13.
62. Silver RM, Thomas A, Medsger TA Jr., Bolster MB. Systemic sclerosis and scleroderma variants: Clinical aspects. In: Koopman WJ, editor. Arthritis and Allied Conditions. 15th ed. Philadelphia, PA: Lippincot Williams and Wilkins; 2005. p. 1633-80.
63. Maricq HR. Comparison of quantitative and semiquantitative estimates of nailfold capillary abnormalities in scleroderma spectrum disorders. Microvasc Res 1986;32:271-6.
64. de Holanda Mafaldo Diógenes A, Bonfá E, Fuller R, Caleiro MT. Capillaroscopy is a dynamic process in mixed connective tissue disease. Lupus 2007;16:254-8.
65. Ganczarczyk ML, Lee P, Armstrong SK. Nailfold capillary microscopy in polymyositis and dermatomyositis. Arthritis Rheum 1988;31:116-9.
66. Smolen JS, Steiner G. Mixed connective tissue disease: To be or not to be? Arthritis Rheum 1998;41:768-77.
67. Targoff IN. Humoral immunity in polymyositis/dermatomyositis. J Invest Dermatol 1993;100:116S-23S.
68. van den Hoogen F, Khanna D, Fransen J, Johnson SR, Baron M, Tyndall A. 2013 classification criteria for systemic sclerosis: An American college of rheumatology/European league against rheumatism collaborative initiative. Arthritis Rheum 2013;65:2737-47.
69. Caramaschi P, Volpe A, Canestrini S, Bambara LM, Faccini G, Carletto A, *et al*. Correlation between homocysteine plasma levels and nailfoldvideocapillaroscopic patterns in systemic sclerosis. Clin Rheumatol 2007;26:902-7.
70. Caramaschi P, Canestrini S, Marinelli N, Volpe A, Pieropan S, Ferrari M, *et al*. Scleroderma patients nail fold videocapillaroscopic patterns are associated with disease subset and disease severity. Rheumatology (Oxford) 2007;46:1566-9.
71. Cutolo M, Sulli A, Secchi ME, Paolino S, Pizzorni C. Nailfold capillaroscopy is useful for the diagnosis and follow-up of autoimmune rheumatic diseases. A future tool for the analysis of microvascular heart involvement? Rheumatology (Oxford) 2006;45:43-6.
72. Kim H, Seo SH, Kwok SK, Ju JH, Yoon CH, Park KS, *et al*. Nailfold capillaroscopic abnormality in systemic sclerosis: Relationship with clinical manifestation. Ann Rheum Dis 2006;65 Suppl 2:396.
73. Ostojic P, Damjanov N. Different clinical features in patients with limited and diffuse cutaneous systemic sclerosis. Clin Rheumatol 2006;25:453-7.
74. Sato LT, Kayser C, Andrade LE. Nailfold capillaroscopy abnormalities correlate with cutaneous and visceral involvement in systemic sclerosis patients. Acta Reumatol Port 2009;34:219-27.
75. Lovy M, MacCarter D, Steigerwald JC. Relationship between nailfold capillary abnormalities and organ involvement in systemic sclerosis. Arthritis Rheum 1985;28:496-501.
76. Ushiama O, Ushiyama K, Yamada T, Koarada S, Tada Y, Suzuki N, *et al*. Retinal findings in systemic sclerosis: A comparison with nailfold capillaroscopic patterns. Ann Rheum Dis 2003;62:204-7.
77. Lee P, Leung FY, Alderdice C, Armstrong SK. Nailfold capillary microscopy in the connective tissue diseases: A semiquantitative assessment. J Rheumatol 1983;10:930-8.
78. Bredemeier M, Xavier RM, Capobianco KG, Restelli VG, Rohde LE, Pinotti AF, *et al*. Nailfold capillary microscopy can suggest pulmonary disease activity in systemic sclerosis. J Rheumatol 2004;31:286-94.
79. Matucci-Cerinic M, Steen V, Nash P, Hachulla E. The complexity of managing systemic sclerosis: Screening and diagnosis. Rheumatology (Oxford) 2009;48 Suppl 3:iii8-13.
80. Kayser C, Bredemeier M, Caleiro MT, Capobianco K, Fernandes TM, de Araújo Fontenele SM, *et al*. Position article and guidelines 2018 recommendations of the Brazilian society of rheumatology for the indication, interpretation and performance of nailfold capillaroscopy. Adv Rheumatol 2019;59:5.
81. Klyscz T, Bogenschutz O, Junger M, Rassner G. Microangiopathic changes and functional disorders of nail fold capillaries in dermatomyositis. Hautarzt 1996;47:289-93.
82. Granier F, Vayssairat M, Priollet P, Housset E. Nailfold capillary microscopy in mixed connective tissue disease. Arthritis Rheum 1986;29:189-95.
83. Sulli A, Pizzorni C, Cutolo M. Nailfold videocapillaroscopy abnormalities in patients with antiphospholipid antibodies. J Rheumatol 2000;27:1574-6.
84. Vaz JL, Dancour MA, Bottino DA, Bouskela E. Nailfold videocapillaroscopy in primary antiphospholipid syndrome (PAPS). Rheumatology 2004;43:1025-7.
85. Altomonte L, Zoli A, Galossi A, Mirone L, Tulli A, Martone FR, *et al*. Microvascular capillaroscopic abnormalities in rheumatoid arthritis patients. Clin Exp Rheumatol 1995;13:83-6.

86. Lambova SN, Müller-Ladner U. Capillaroscopic pattern in inflammatory arthritis. Microvasc Res 2012;83:318-22.
87. Tektonidou M, Kaskani E, Skopouli FN, Moutsopoulos HM. Microvascular abnormalities in Sjogren's syndrome: Nailfold capillaroscopy. Rheumatology 1999;38:826-30.
88. Lin KM, Cheng TT, Chen CJ. Clinical applications of nailfold capillaroscopy in different rheumatic diseases. J Intern Med Taiwan 2009;20:238-47.
89. TibiriçáE, Rodrigues E, Cobas RA, Gomes MB. Endothelial function in patients with type 1 diabetes evaluated by skin capillary recruitment. Microvasc Res 2007;73:107-12.
90. Hosking SP, Bhatia R, Crock PA, Wright I, Squance ML, Reeves G. Non-invasive detection of microvascular changes in a paediatric and adolescent population with Type 1 diabetes: A pilot cross-sectional study. BMC Endocr Disord 2013;13:41.
91. Kuryliszyn-Moskal A, Dubicki A, Zarzycki W, Zonnenberg A, Górska M. Microvascular abnormalities in capillaroscopy correlate with higher serum IL-18 and sE-selectin levels in patients with Type 1 diabetes complicated by microangiopathy. Folia Histochem Cytobiol 2011;49:104-10.
92. Kaminska-Winciorek G, Deja G, Polańska J, Jarosz-Chobot P. Diabetic microangiopathy in capillaroscopic examination of juveniles with diabetes Type 1. Postepy Hig Med Dosw (Online) 2012;66:51-9.
93. Moura EG, Bouskela E, Torres-Filho IP, Breitenbach MM. Nail fold capillaroscopy in diabetes mellitus: Morphological abnormalities and relationship with microangiopathy. Braz J Med Biol Res 1987;20:777-801.
94. Chang CH, Tsai RK, Wu WC, Kuo SL, Yu HS. Use of dynamic capillaroscopy for studying cutaneous microcirculation in patients with diabetes mellitus. Microvasc Res 1997;53:121-7.
95. Pazos-Moura CC, Moura EG, Bouskela E, Torres-Filho IP, Breitenbach MM. Nailfold capillaroscopy in diabetes mellitus: Morphological abnormalities and relationship with microangiopathy. Braz J Med Biol Res 1987;20:777-80.
96. Barchetta I, Riccieri V, Vasile M, Stefanantoni K, Comberiati P, Taverniti L, *et al*. High prevalence of capillary abnormalities in patients with diabetes and association with retinopathy. Diabet Med 2011;28:1039-44.
97. Gasser P, Bhuler FR. Nailfold microcirculation in normotensive and essential hypertensive subjects, as assessed by video-microscopy. J Hypertens 1992;10:83-6.
98. Antonios TF, Singer DR, Markandu ND, Mortimer PS, Macgregor GA. Structural skin capillary rarefaction in essential hypertension. Hypertension 1999;33:998-1001.
99. Williams SA, Booell M, Macgregor GA, Smaje LH, Wasserman SM, Toom JE. Capillary hypertension and abnormal pressure dynamics in patients with essential hypertension. Clin Sci 1990;79:5-8.
100. Sokolova IA, Manukhina EB, Blinkov SM, Koshelev VB, Pinelis VG, Rodionov IM. Rarefication of the arterioles and capillary network in the brain of rats with different forms of hypertension. Microvasc Res 1985;30:1-9.
101. Chen II, Prewitt RL, Dowell RF. Microvascular rarefaction in spontaneously hypertensive rat cremaster muscle. Am J Physiol Circ Physiol 1981;241:H306-10.
102. Prasad A, Dunnill GS, Mortimer PS, MacGregor GA. Capillary rarefaction in the forearm skin in essential hypertension. J Hypertens 1995;13:265-8.
103. Serné EH, Gans RO, Ter Maaten JC, Tangelder GJ, Donker AJ, Stehouwer CD. Impaired skin capillary recruitment in essential hypertension is caused by both functional and structural capillary rarefaction. Hypertension 2001;38:238-42.
104. Debbabi H, Uzan L, Mourad JJ, Safar M, Levy BI, Tibiriçà E. Increased skin capillary density in treated essential hypertensive patients. Am J Hypertens 2006;19:477-83.
105. de Araújo Penna GL, de Freitas Garbero R, Neves MF, Oigman W, Bottino DA. Treatment of hypertension does not normalizes capillery rarefaction. Clinics 2008;63:613-8.
106. Movasat A, Shahram F, Carreira PE, Nadji A, Akhlaghi M, Naderi N, *et al*. Nailfold capillaroscopy in Behçet's disease, analysis of 128 patients. Clin Rheumatol 2009;28:603-5.
107. Aytekin S, Yuksel EP, Aydin F, Senturk N, Ozden MG, Canturk T, *et al*. Nailfold capillaroscopy in Behçet disease, performed using videodermoscopy. Clin Exp Dermatol 2014;39:443-7.
108. Bhushan M, Moore T, Herrick AL, Griffiths CE. Nailfold video capillaroscopy in psoriasis. Br J Dermatol 2000;142:1171-6.
109. Ribeiro CF, Siqueira EB, Holler AP, Fabrício L, Skare TL. Periungual capillaroscopy in psoriasis. An Bras Dermatol 2012;87:550-3.
110. Errichetti E, Zabotti A, Stinco G, Quartuccio L, Sacco S, de Marchi G, *et al*. Dermoscopy of nail fold and elbow in the differential diagnosis of early psoriatic arthritis sine psoriasis and early rheumatoid arthritis. J Dermatol 2016;43:1217-20.
111. Gerkowicz A, Krasowska D, Pietrzak A, Michalak-Stoma A, Bartosińska J, Juszkiewicz-Borowiec M, *et al*. Videocapillaroscopic alterations in alopecia areata. Biomed Res Int 2013;2013:160203.
112. Dobrev HP, Vutova NI. Nailfold capillaroscopic changes in kindler syndrome. Intractable Rare Dis Res 2015;4:214-6.
113. Monoe K, Takahashi A, Abe K, Kanno Y, Watanabe H, Ohira H. Evaluation of nail fold capillaroscopy findings in patients with primary biliary cirrhosis. Hepatol Res 2014;44:E129-36.
114. Huang MY, Huang JJ, Huang TY, Gupta-Malhotra M, Syu FK. Deterioration of cutaneous microcirculatory status of Kawa-Saki disease. Clin Rheumatol 2012;31:847-52.
115. Zampetti A, Rigante D, Bersani G, Rendeli C, Feliciani C, Stabile A. Longitudinal study of microvascular involvement by nailfold capillaroscopy in children with Henoch-Schönlein purpura. Clin Rheumatol 2009;28:1101-5.
116. Martino F, Agolini D, Tsalikova E, Bederti O, Principessa L, Martino E, *et al*. Nailfold capillaroscopy in Henoch-Schonlein purpura: A follow-up study of 31 cases. J Pediatr 2002;141:145.
117. Sebastiani M, Triantafyllias K, Manfredi A, González-Gay MA, Palmou-Fontana N, Cassone G, *et al*. Nailfold capillaroscopy characteristics of antisynthetase syndrome and possible clinical associations: Results of a multicenter international study. J Rheumatol 2019;46:279-84.
118. Schiavon F, Maffei P, Martini C, de Carlo E, Fais C, Todesco S, *et al*. Morphology study of microcirculation in acromegaly by capillaroscopy. J Clin Endocrinol Metab 1999;84:3151-5.
119. Pazos-Moura CC, Moura EG, Breitenbach MM, Bouskela E. Nailfold capillaroscopy in hypothyroidism and hyperthyroidism: Blood flow velocity during rest and postocclusive reactive hyperemia. Angiology 1998;49:471-6.
120. Pasqui AL, Puccetti L, di Renzo M, Bruni F, Camarri A, Palazzuoli A, *et al*. Structural and functional abnormality of systemic microvessels in cardiac syndrome X. Nutr Metab Cardiovasc Dis 2005;15:56-64.
121. Martinez R, Dragagna G, Saponaro A, Russo R, Santoro L, Leopardi N, *et al*. Microcirculatory changes in mitral prolapse as an expression of a systemic change in the connective tissue. Cardiologia 1992;37:285-90.
122. Jouanny P, Schmidt C, Wahl D, de Korwin JD, Schmitt J. Nailbed capillaroscopy in Crohn's disease. Rev Med Interne 1991;12:377-9.
123. Schumann L, Korten G, Holdt B, Holtz M. Microcirculation of the fingernail fold in CAPD patients: Preliminary observations. Perit Dial Int 1996;16:412-6.
124. Dinc A, Melikoglu M, Korkmaz C, Fresko I, Ozdogan H, Yazici H. Nailfold capillary abnormalities in patients with familial Mediterranean fever. Clin Exp Rheumatol 2001;19 Suppl 24:S42-4.
125. Coelho SC, Ramos AD, Pinheiro VS, Solberg PF, de Faria JP, Naliato EC. Nailfold video capillaroscopy in Turner syndrome: A descriptive study. J Vasc Bras 2007;6:325-31.
126. Fonseca GP, Brenner FM, de Souza Muller C, Wojcik AL. Nailfold capillaroscopy as a diagnostic and prognostic method in rosacea. An Bras Dermatol 2011;86:87-90.