REVIEW ARTICLE

Capillaroscopy in healthy subjects of different age

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Summary

Introduction: Capillaroscopy is a non-invasive diagnostic tool used to detect morphological abnormalities in the microcirculation. The assessment of capillaroscopic findings in healthy subjects is likely the area where controversies are most difficult to resolve. This review focuses on capillary architecture in healthy individuals across different age groups.

Methods: A search was conducted in PubMed, MEDLINE, and Scopus using the following terms: capillaroscopy, healthy subjects, Raynaud's phenomenon, microcirculation, and microvascular abnormalities. A total of 10 relevant articles were identified.

Results: The shape of capillaries and the architecture of the nailfold microvascular network can vary significantly among healthy individuals. The most commonly observed abnormalities in this population include tortuosity, crossovers, homogeneously enlarged loops, neoangiogenic capillaries, and microbleeding. Less frequently, more unusual patterns, such as ramified, bushy, or glomerular loops may be observed. These atypical features require careful evaluation to avoid missing a potential underlying disease.

Conclusion: This review critically examines capillaroscopy findings in healthy individuals, taking into account typical nail care practices and age-related changes. These insights may assist clinicians in distinguishing physiological variations from early signs of microvascular damage.

Key words: capillaroscopy, healthy subjects, Raynaud's phenomenon, microcirculation, microvascular abnormalities.

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INTRODUCTION

Nailfold capillaroscopy (NFC) is a highly sensitive, inexpensive, simple, safe, noninvasive, and rapid diagnostic tool for detecting structural alterations in the microcirculation (1). It is particularly effective for distinguishing between primary and secondary Raynaud's phenomenon (RP) and serves as a useful tool for predicting scleroderma spectrum disorders in patients with RP (1, 2). The presence of a scleroderma pattern on NFC, either alone or in combination with anti-topoisomerase I or anti-centromere antibodies, has been shown to be a strong predictor of scleroderma development (3). In 2013, NFC was included in the classification criteria for systemic sclerosis established by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR), underscoring its diagnostic significance (4). Despite its widespread and effective use in a variety of pathological conditions, data on NFC findings in healthy individuals remain limited. To address this, a comprehensive literature search was conducted using PubMed, MEDLINE, and Scopus with the keywords: capillaroscopy, healthy subjects, Raynaud's phenomenon, microcirculation, and microvascular abnormalities. A total of 10 relevant articles were identified. The available literature indicates that capillaroscopic patterns in healthy individuals exhibit considerable variability, often making it difficult to distinguish between normal and pathological findings.

This review aims to summarize capillaroscopic features observed in healthy individuals across different age groups and may assist clinicians in differentiating physiological variations from early signs of microvascular disease.

ARCHITECTURE IN HEALTHY ADULT SUBJECTS

In healthy individuals, the capillary blood vessels at the finger nailfold typically exhibit a uniform arrangement, with their major axis oriented parallel to the skin surface. Individual capillary loops generally appear hairpin-shaped (also described as "reverse U-shaped" or resembling a "comb structure"), and their morphology is most clearly visible in the distal rows of the nailfold. The appearance of nailfold capillaries and the architecture of the microvascular network can vary widely, both between individuals and among different fingers of the same hand **(Figure 1)**.

The greatest variability in the nailfold capillary network within the same individual is generally observed between the second and fourth fingers (5). The best visibility is typically found in the fourth and fifth fingers of the non-dominant hand, as the skin in these areas tends to be more transparent than in other fingers (6).

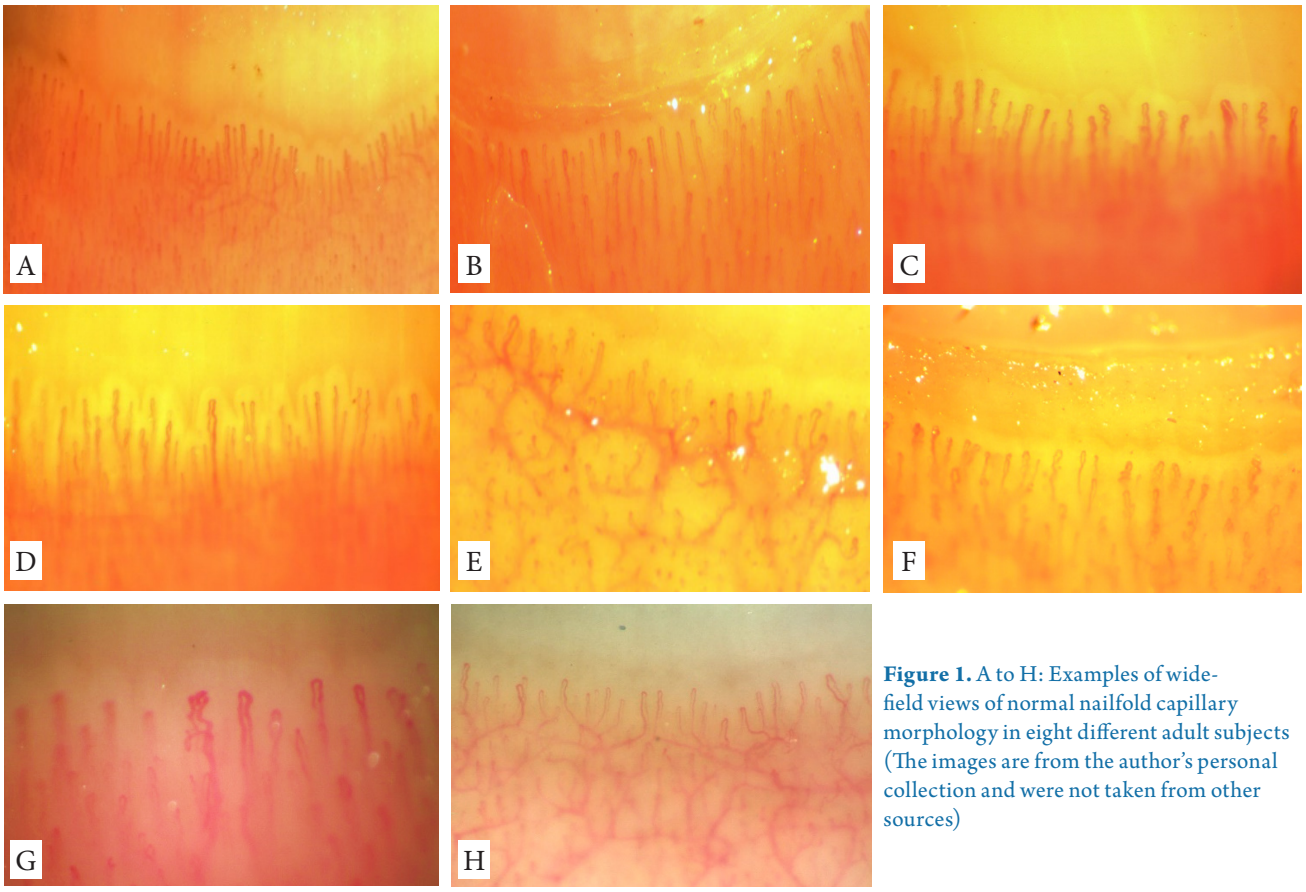

Figure 1. A to H: Examples of wide-field views of normal nailfold capillary morphology in eight different adult subjects (The images are from the author's personal collection and were not taken from other sources)

CAPILLARY DENSITY

Capillary density is a fundamental marker of the nailfold microvascular status in clinical capillaroscopy. Capillary density is also known as the "number of capillaries" and "capillaries number." It is most often determined from the number of capillaries in a 1 mm length of the distal row of each finger or toe (7). Capillary density in the toes (5-9 capillaries/mm) was lower compared to the fingers (7–11 capillaries/mm) and appears to vary in healthy adults in Europe (8). For example, German researchers reported a mean capillary density of 6.6 ± 0.97 (mean ± standard deviation), with a range of 5-9 capillaries per millimeter (8). In contrast, a Bulgarian group with an average capillary density of 10 ± 0.59 capillaries per millimeter observed a slightly higher capillary density than the German authors (7). Unlike fingers, capillaries in toes demonstrate greater variability. Clear differences can be seen when comparing the first and the second toe. While tortuous capillaries and parallel hairpin-shaped capillaries can be found in both toes, branching and elongation can be seen almost exclusively in the first toe, while capillary bundles are significantly more common in the second toe. The changes on toes could be due to recurrent microtraumas caused by heavy mechanical stress and shoes as well as external factors (nail polish or pedicure) (8).

Hoerth et al. (9) and Dolezalova et al. (10) have shown that capillary density is directly related to age; younger children have fewer capillaries compared to older children and adults. In countries with diverse ethnic populations, it is common to categorize patients as white or non-white. Terreri et al (11) demonstrated that capillary density increases progressively with age in both white and non-white groups. More recently, Smith et al. (12) concluded that normal capillary density in adults ranges from 7 to 12 capillaries per linear millimeter, with a mean of 7, as measured in the distal row of the nailfold. This finding is consistent with previous reports in the literature (13).

MINOR MORPHOLOGICAL ABNORMALITIES

Andrade et al. (13), Fahrig et al. (14), and Gutierrez et al. (15) reported that the theoretical concept of a normal capillaroscopic appearance (typically characterized by U-shaped capillary loops arranged in a "comb-like" structure) often differs from what is observed in clinical practice. This discrepancy can lead to confusion when determining whether a capillaroscopic pattern is normal or pathological (15). Some features may be very common in healthy individuals, while others may be rare but not necessarily indicative of disease. Various factors, such as recent manicure, repetitive microtrauma, and skin transparency, can contribute to the substantial interindividual and intraindividual variability seen in normal capillaroscopic patterns (15). In addition, occupation type and a tendency toward onychophagia should be considered, as these factors may disrupt the architecture of nailfolds in healthy individuals. Repeated microtrauma can result in small scarred areas. Andrade et al. (13) reported instances of macroscopically visible nailfold scars that, microscopically, corresponded to moderate vascular deletion areas. In one case, this deletion area was surrounded by three ectatic loops. Notably, the capillaroscopic appearance of scar tissue resembles that seen in scleroderma, as both conditions are characterized by the replacement of normal tissue with fibrous tissue, although the intensity and extent differ. Ingegnoli et al. (16) emphasize that a more detailed characterization of capillary patterns in healthy individuals is essential for the early detection of potential pathological changes.

Andrade and colleagues (13) studied capillaroscopic findings in 800 healthy individuals and found that the open loop was most common (considered the typical normal loop), but slight variations were frequent: 24% of individuals exhibited other dominant morphological patterns. Morphological abnormalities were identified in 34% of the entire group; however, only a few altered capillaries were present in each individual. Therefore, caution should be exercised when interpreting these abnormalities. When isolated or infrequent, morphological abnormalities may represent normal variation. However, if they are numerous and/or accompanied by other changes, they may indicate microangiopathy. Megacapillaries are so rare in the normal population that their presence should be considered pathological (2, 17). Unusual structures such as branched, bushy, or glomerular loops **(Figure 2)** require careful evaluation to avoid missing an underlying disease (18). Additionally, sweat glands may sometimes be visualized and can lead to misinterpretation.

In a study of 100 healthy volunteers aged 5 to 58 years, nailfold capillaroscopy revealed capillary branching in 78%, meandering capillaries in 94%, tortuous loops in 64%, hemorrhagic extravasations in 25%, and apical dilatation of capillaries in 19%. Avascular fields, stasis, or reversal of blood flow were not observed (14). All these findings can be classified as non-specific and should ultimately be considered normal variants. The distinction between normal and abnormal NFC findings depends largely on the number of unusual features present. For example, an isolated branched capillary loop within an otherwise normal context should be regarded as unusual but not pathological, especially in the absence of clinically relevant symptoms. Approximately 40% of healthy subjects have completely normal capillaries, nearly half exhibit at least one minor abnormality, and only 5% show significant abnormalities (19) **(Figure 3)**.

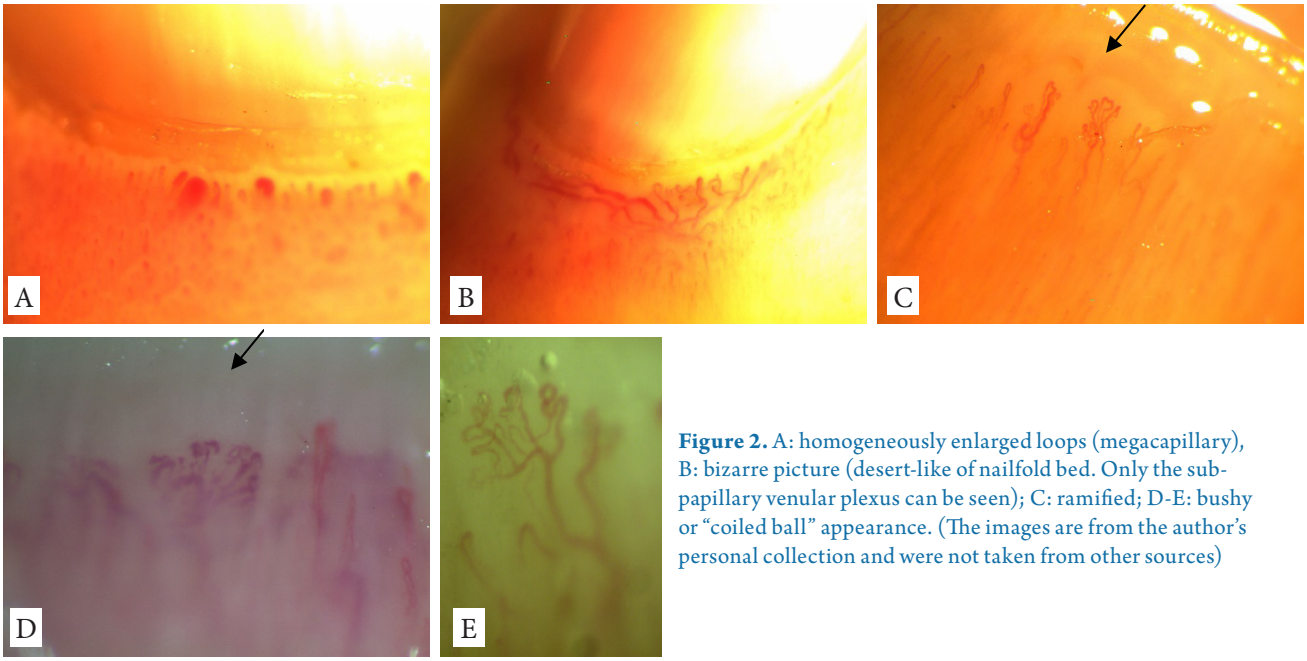

Figure 2. A: homogeneously enlarged loops (megacapillary), B: bizarre picture (desert-like of nailfold bed. Only the subpapillary venular plexus can be seen); C: ramified; D-E: bushy or "coiled ball" appearance. (The images are from the author's personal collection and were not taken from other sources)

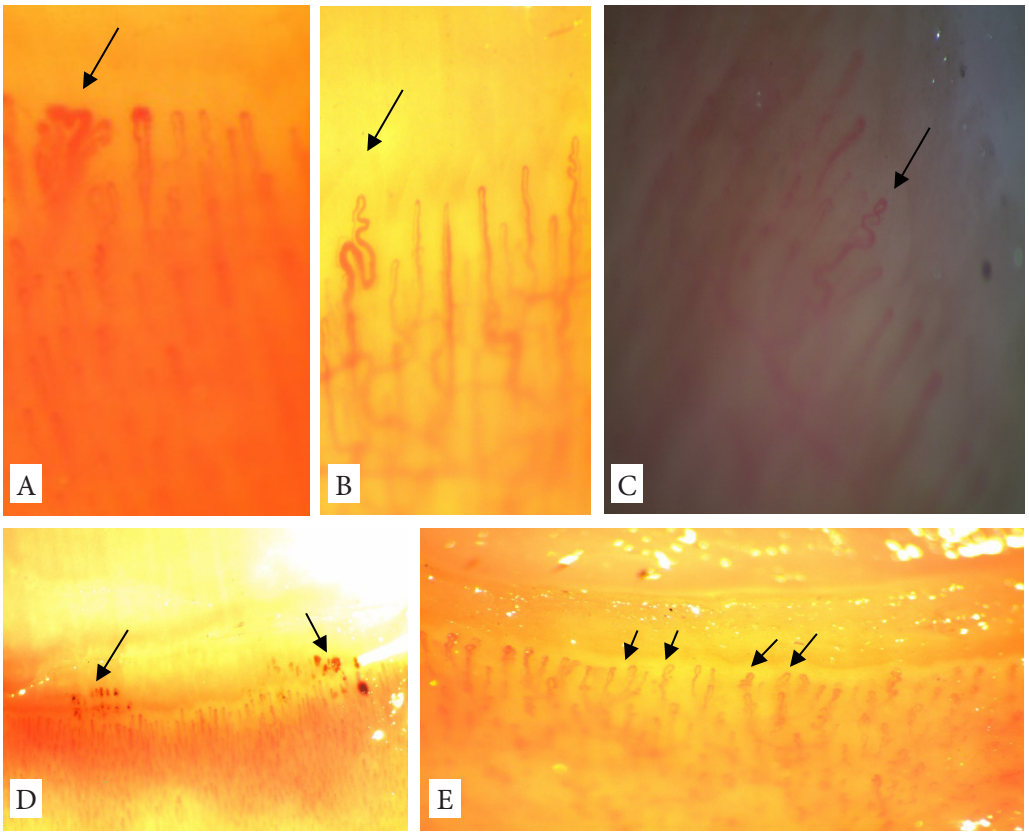

Figure 3. Minor abnormality in healthy subjects. A: capillary branching; B: meandering, C: tortuous lops, D: hemorrhagic extravasations, E: apical dilatation (The images are from the author's personal collection and were not taken from other sources).

SUBPAPILLARY VENULAR PLEXUS

The subpapillary venular plexus (SPVP) appears as a large, interconnected network of vessels located distal to the proximal rows **(Figure 4)**. The SPVP was clearly visible in only 26% of subjects (18, 20). Its visibility depends on the degree of skin transparency, which tends to be greater in children than in adults and higher in Caucasian compared to non-Caucasian individuals. Additionally, visibility is influenced by local conditions such as hyperkeratosis, skin pigmentation, injury, and/or edema. Visibility is generally considered good in ring fingers, where the SPVP is frequently assessed; it is also usually visible in the fifth finger. Building on Maricq's observations of a higher plexus visibility score (PVS) on the left hand (20), Andrade and colleagues confirmed a statistically higher PVS on the left hand compared to the right (13). Increased SPVP visibility has been reported in patients with systemic lupus erythematosus (21, 22), in children, and in individuals aged 70 years and older (21). In these cases, the enlargement and congestion of venules and capillaries appear to be related to the permanent opening of arteriovenous anastomoses (21). No other differences between hands have been observed.

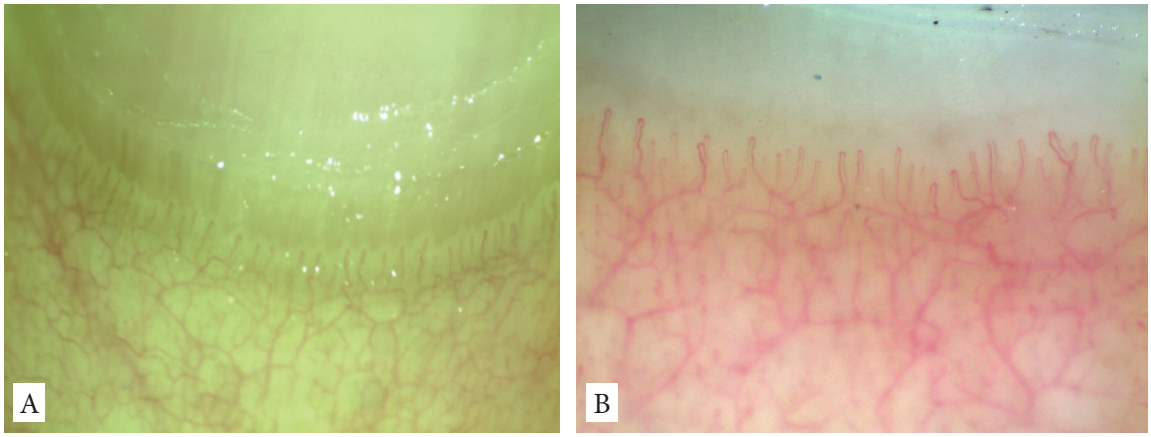

Figure 4. A-B: Examples of normal capillaries and clearly visible subpapillary venular plexus (The images are from the author's personal collection and were not taken from other sources)

AGE-RELATED CHANGES IN CAPILLARY MORPHOLOGY

Capillaries in children

In younger children, capillary morphology is generally less uniform than in adults (10, 23). The characteristic hairpin shape is usually apparent from the second year of life and the capillary structure then develops throughout childhood (10). Children may have a lower density of capillary loops and a higher frequency of bizarre capillary shapes (10) **(Figure 5)**.

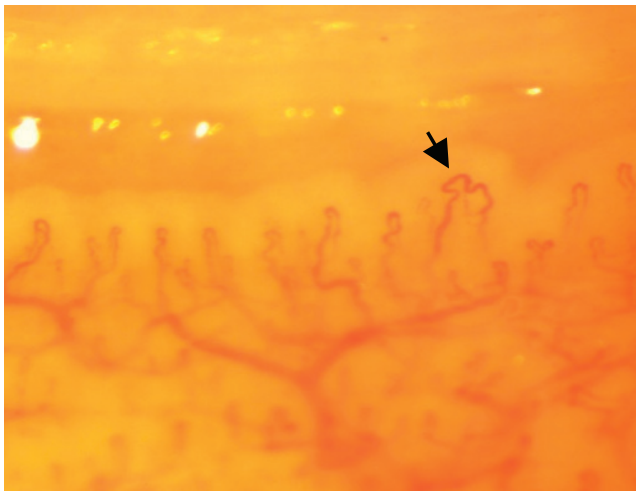

Figure 5. Nailfold capillaroscopy in a 7-year-old child showing low loop density and a bizarre capillary (black arrow) (The image is from the author's personal collection and were not taken from other sources)

Recently, Torrente-Segarra et al. (24) recommended performing NFC in children suspected of having connective tissue diseases who test positive for antinuclear antibodies, regardless of whether they present with complete or incomplete RP. Pavlov-Dolijanovic et al. (25) reported that children with primary RP, as well as most children and adolescents who later developed systemic lupus erythematosus, juvenile idiopathic arthritis, or undifferentiated connective tissue disease, exhibited either normal capillary findings or nonspecific capillary changes. In contrast, 61% of children and adolescents who eventually developed scleroderma spectrum disorders, including systemic sclerosis, dermatomyositis, and sclerodermatomyositis showed scleroderma type capillary changes up to six months before the full clinical manifestation of the disease.

Capillaries in the elderly

Ingegnoli et al. (16) found that general morphological characteristics tend to remain constant over time in healthy adult subjects, with no marked differences observed between age groups. In contrast, the study by Andrade et al. (13) observed a trend toward more frequent morphological anomalies and dominant morphological patterns other than the open type in individuals over 40. However, their sample included only a few individuals over 60. Other authors have reported an increase in tortuosity and the frequency of capillary anomalies in the elderly (26). Additionally, elderly subjects show a higher frequency of increased loop diameters, more frequent apical capillary dilatations, greater tortuosity, and a tendency toward micro-aneurysms, which are characteristic of "senile microangiopathy" (27). A longer history of local trauma, along with age-related progressive reductions in cardiac output and increased peripheral resistance, may also explain the higher frequency of microvascular abnormalities in the elderly (27). Consequently, defining normal morphological patterns in this population is more complex than in younger adults and children, as selecting an appropriate, truly healthy reference group presents a significant challenge.

FACTORS THAT CAN AFFECT NAILFOLD CAPILLAROSCOPIC FINDINGS

Sex and Race

Terreri et al. (11) reported that general visibility during NFC was adequate in 98% of individuals examined, with only 2% not adequately assessable. However, visual challenges, such as difficulty recognizing micro-petechiae

and the capillary plexus, counting the number of loops per millimeter, and evaluating the morphology of distal row loops, were noted in approximately one-third of cases, particularly among nonwhite individuals. Differences based on race and sex have been reported in the literature. Racial variations revealed that plexus visibility was higher among white subjects. Skin pigmentation may influence capillaroscopic visibility due to the strong absorption of illuminating light by heavily pigmented tissues, as observed in non-Caucasian individuals. This can lead to challenges in interpreting NFC findings, and in some cases, reduced visibility may be misinterpreted as decreased capillary density or abnormal morphological of loops (5).

The influence of gender was minimal. Plexus visibility scores were slightly higher in men, while the number of loops per millimeter was slightly higher in white women with good overall visibility. Vascular deletion areas and ectatic loops were more frequently observed in women, possibly due to the effects of manicures (11). Additionally, NFC images are generally more easily obtained in females than in males, likely due to differences in skin elasticity and transparency. Women typically have a less dry cutaneous surface and thinner digital skin consistency (5). In contrast, acquiring high-quality capillaroscopy images in men can sometimes be challenging, particularly in those who frequently use their hands for heavy work (28).

Constitutional type

Constitutional body type can also influence the quality of capillaroscopic images. For example, images from obese individuals with puffy, edematous fingers may be less well-defined and potentially difficult to interpret. Conversely, very thin, healthy individuals with slender fingers can also pose challenges, as the resulting capillaroscopic images may appear pale, and loop morphology may seem irregular or poorly defined (5, 29).

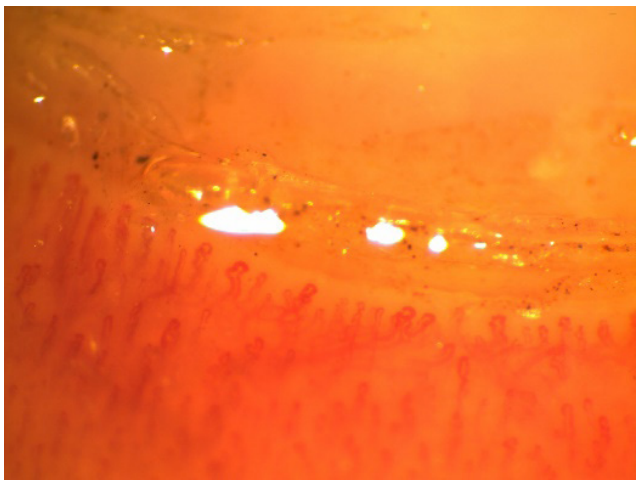

Figure 6. Nailfold capillaroscopy of a manual worker showing shorter and sometimes dilated capillary loops (The image is from the author's personal collection and were not taken from other sources)

Kind of employment

Various types of occupational activities can influence peripheral circulation and thereby affect the capillaroscopic image. Activities such as playing the guitar (30), drumming (31), archery (32), and gardening are among the more common non-pathological causes of NFC abnormalities (21). Sirufo et al. (33) documented significant capillaroscopic differences between volleyball players and healthy controls, including both males and females in each group. These findings should not be misinterpreted as indicative of an underlying disease. The capillaroscopist should be aware that loop architecture in individual digits may become disorganized due to trauma or occupational exposure. In manual workers who are frequently subjected to repeated local microtrauma, the capillaroscopic pattern may exhibit irregular distribution, morphological heterogeneity, and shortened capillaries **(Figure 6)**.

Tortuosity is relatively common in healthy individuals and is often associated with microtraumas to the

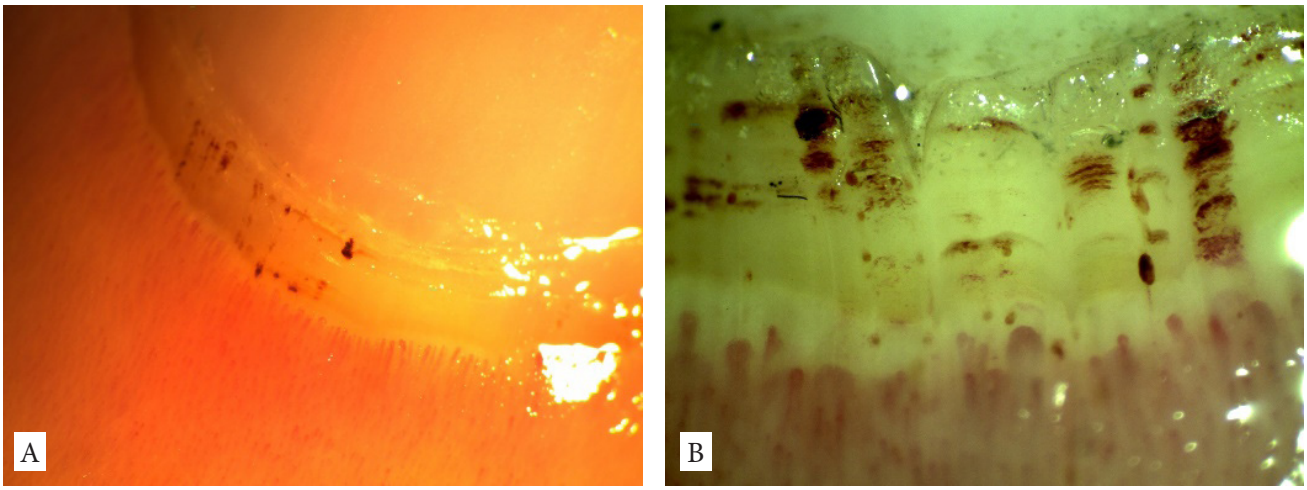

Figure 7. A: Microhaemorrhages due to traumatic endothelial injury, B: Microhaemorrhages due to endogenous endothelial injury. (The images are from the author's personal collection and were not taken from other sources)

nailfold. When micropetechiae appear in clusters, they likely reflect exogenous or trauma induced endothelial injury, which typically presents with a focal distribution. These abnormalities are considered to result from external factors and are not indicative of vascular disease. In contrast, when micropetechiae are scattered across the nailfold and observed on multiple fingers, they are more likely due to endogenous endothelial injury, suggesting a diffuse capillary involvement **(Figure 7)**.

Contact with chemical substances such as toluene, benzene, or exposure to radiation (34) can alter the endothelium, leading to lumen occlusion and subsequent tissue damage. As such, NFC is a valuable tool for monitoring individuals exposed to these occupational hazards. Employment-related NFC abnormalities may also occur in individuals who use vibratory tools for extended periods. Therefore, it has been suggested that NFC be incorporated into medical surveillance programs for exposed workers (21).

Habits

A recent manicure can significantly alter the capillaroscopic pattern, particularly if it has been aggressive or deep, resulting in distorted images. Individuals who have undergone a vigorous manicure often exhibit frequent, misleading microhemorrhages, as well as an irregular distribution and shape of capillary loops. These loops may appear shortened, with varying degrees of enlargement and tortuosity (5, 21), **(Figure 8)**.

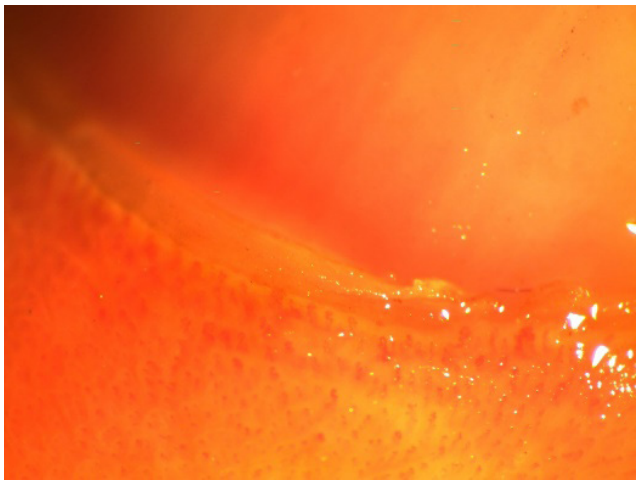

Figure 8. High degree of shape heterogeneity (shortened and tortuous loops, "decapitacion" of the demal papilla) induced by manicures (The image is from the author's personal collection and were not taken from other sources).

Less frequently, neoangiogenesis may also be observed, typically in association with repeated injuries. Additionally, the presence of nail polish can cause misleading reflections that obscure the nailfold area, potentially masking capillaroscopic abnormalities (5).

CONCLUSION

In conclusion, there is a growing consensus among experts that the range of normal nailfold videocapillaroscopy findings are quite broad. This article may serve as a useful starting point to help clinicians better understand various aspects of normal capillary morphology. It is essential to clearly define which capillary parameters should be considered part of a "normal" capillaroscopic pattern (tortuosity, crossovers, homogeneously enlarged loops, shortened capillaries, subpapillary venular plexus visibility). Clinicians must also recognize that certain atypical capillary loop features (ramified, bushy, or glomerular loops), excluding giant capillaries, can occasionally be observed in healthy individuals and do not necessarily indicate an underlying pathological condition. Various capillary morphological findings can be present in normal individuals but their presence in a greater number of fingers should be considered to be pathological.

Based on current evidence, NFC is recognized as a valuable biomarker in rheumatology. It enables the accurate assessment of primary and secondary Raynaud's phenomenon, aids in the early detection of systemic autoimmune diseases, and offers a means to monitor therapeutic responses to various pharmacological interventions. By doing so, NFC contributes to the prevention of irreversible vasculopathy and the accumulation of long-term organ damage. Future prospective studies of healthy individuals are needed to further clarify the limits of normal capillaroscopic findings.

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Ethical approval: N/A

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KAPILAROSKOPIJA KOD ZDRAVIH OSOBA RAZLIČITOG UZRASTA

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Sažetak

Uvod: Kapilaroskopija je neinvazivni dijagnostički alat koji se koristi za otkrivanje morfoloških abnormalnosti u mikrocirkulaciji. Procena kapilaroskopskih nalaza kod zdravih ispitanika je verovatno oblast u kojoj je kontroverze najteže rešiti. Ovaj pregled se fokusira na kapilarnu arhitekturu kod zdravih osoba različitih starosnih grupa.

Metode: Pretraga je sprovedena u PubMed-u, MEDLINE-u i Scopus-u koristeći sledeće termine: kapilaroskopija, zdravi ispitanici, Rejnoov fenomen, mikrocirkulacija i mikrovaskularne abnormalnosti. Identifikovano je ukupno 10 relevantnih članaka.

Rezultati: Oblik kapilara i arhitektura mikrovaskularne mreže ruba nokatne ploče mogu se značajno razlikovati kod zdravih osoba. Najčešće primećene abnormalnosti u ovoj populaciji uključuju izvijuganost, izukrštanost, homogeno uvećanje petlje, neoangiogenezu i mikrokrvarenje. Ređe se mogu primetiti neobičniji obrasci, kao što su razgranate, žbunaste ili glomerularne petlje. Ove atipične karakteristike zahtevaju pažljivu procenu kako bi se izbeglo previđanje potencijalne osnovne bolesti.

Zaključak: Ovaj pregled kritički ispituje nalaze kapilaroskopije kod zdravih osoba, uzimajući u obzir tipične prakse nege noktiju i promene povezane sa starenjem. Ovi uvidi mogu pomoći kliničarima u razlikovanju fizioloških varijacija od ranih znakova mikrovaskularnog oštećenja.

Ključne reči: kapilaroskopija, zdrave osobe, Raynaud's fenomen, mikrocirkulacija, mikrovaskularne abnormalnosti

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