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REVIEW

Nailfold video capillaroscopy in psoriasis. An ongoing study and review of literature.

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Abstract

Background. Nailfold video capillaroscopy (NVC) has emerged as a valuable tool for assessing microvascular abnormalities in various autoimmune diseases, including psoriasis. This study comprises a literature review of NVC findings in psoriasis patients, followed by an ongoing prospective non-randomized, longitudinal cohort study with a cross-sectional component aimed at elucidating the relationship between NVC changes and clinical phenotypes of psoriasis, treatment strategies, and other relevant factors.

Methods. A systematic search of PubMed for articles published between 1978 and 2024, resulted in 7 relevant studies. Key aspects of NVC were reviewed. The ongoing study is a single-center, prospective longitudinal cohort study with a cross-sectional component conducted at a tertiary hospital, involving NVC assessment in biopsy-diagnosed psoriasis patients and control groups.

Results. The literature review revealed varied findings regarding capillary density, dimensions, morphology, and hemorrhages in psoriasis patients, indicating the complexity of microvascular changes associated with the disease. Preliminary findings from the ongoing study suggest various abnormalities, with no evidence of scleroderma pattern.

Conclusion. The systematic review highlights the need for further research to elucidate the role of NVC in monitoring disease progression and treatment response in psoriasis. Preliminary findings from the ongoing study suggest promising insights into NVC changes in psoriasis patients. Further analysis and validation of these findings are warranted.

Keywords: nailfold video capillaroscopy (NVC), psoriasis, psoriatic arthritis, microvascular abnormalities.

Introduction

Psoriasis (PsO) is a chronic autoimmune skin disorder characterized by inflammatory processes involving various components of the immune system. Although primarily recognized for its cutaneous manifestations, emerging new evidence suggests a potential association between PsO and systemic vascular abnormalities. Nailfold video capillaroscopy (NVC) has emerged out as a valuable tool for evaluating microvascular changes in various rheumatological and dermatological conditions. However, its practicality in PsO remains relatively underexplored. This ongoing study aims to investigate the application of NVC in PsO, providing insight on potential microvascular alterations and their clinical implications (especially in differential diagnosis and in aiding psoriatic arthritis diagnosis). Furthermore, we conducted a review of literature in order to synthesize existing evidence in reference to the role of NVC in PsO, shedding light on its diagnostic and prognostic value. By integrating clinical observations with current understanding of PsO pathophysiology, this paper strives to contribute to a thorough understanding of the vascular aspects of PsO and open the door for a different approach in clinical practice.

The European Alliance of Associations for Rheumatology (EULAR) Study Group on Microcirculation in Rheumatic Diseases has recently provided a consensus definition for assessing individual nailfold capillaries as either "normal" or "abnormal," applicable across various rheumatic conditions and capillaroscopic evaluations to ensure standardized interpretation.

In a typical normal capillary pattern, the distal row of nailfold capillaries exhibits some characteristics such as an open hairpin shape, uniform size (typically <20µm), regular arrangement in a parallel fashion, and a count ranging between 7 and 12. This morphological consistency is a notable feature. Any deviation from this pattern, such as a lack of convex tip or more than two crossings of the capillary limbs, is considered a "non-specific" abnormality.

It's worth noting that capillary wall rupture and

subsequent micro bleeding can occur even in healthy individuals, though the presence of giant capillaries or extensive avascularity (very low density) is not typical in a healthy population. In terms of interpretation, isolated or infrequent anomalies may simply reflect variations within the normal range. However, when anomalies are numerous or multiple types occur within an individual, it often suggests an underlying connective tissue disease, as shown by Andrade *et al.* [1].

REVIEW OF LITERATURE

Search strategy and process

A systematic literature search was performed using PubMed, last updated on March 16th, 2024, using a combination of keywords: "capillaroscopy [title]" AND "psoriasis [title]". This yielded a total of 9 articles (1978-2024). Articles written in a language other than English were excluded (1 article), as well as one ongoing article was excluded. Therefore, 7 articles in total remained valid for reviewing.

Main findings

The forthcoming sections will encompass our research outcomes (summarized in Table 1) focused on four key aspects of nailfold video capillaroscopy: capillary density, dimensions, morphology, and hemorrhages. Additionally, we will dedicate a section to supplementary significant findings from the reviewed studies.

Density of capillaries

Several studies have investigated capillary density in patients with PsO and related conditions, some with conflicting results [2-12].

Bhushan *et al*. [2] found a significant reduction in capillary bed density only in PsO patients having distal interphalangeal (DIP) arthritis with/without nail changes, compared to healthy controls ($p<0.05$), with no differences in patients with PsO alone.

Similarly, Ribeiro *et al*. [3] reported a decrease in capillary density and areas of capillary dropout in psoriatic patients compared to healthy controls. Additionally, their findings indicated no significant variance in capillary density when comparing PsO patients with nail involvement to those without it. The presence of avascular zones was comparably frequent in both sets of patients ($p=0.047$). Moreover, the study did not reveal any statistically significant differences in capillary density, or the presence of avascular areas between patients with PsO who had arthritis and those who did not.

Guldberg-Møller *et al*. [4] observed below mean capillary density in patients with psoriatic arthritis (PsA) compared to PsO in NVC and compared to PsO and osteoarthritis (OA) in optical coherence tomography angiography (OCTA) images, indicating potential diagnostic utility in PsA. Sivasankari et al. [5] noted a mean capillary loop density between 7 and 9 capillaries/mm in 76% of PsO cases, and 20% between 4 and 6 capillaries/mm ($p<0.011$) while only 3.6% had avascular areas ($p>0.05$).

Bull *et al*. [6] found no significant reduction in density of capillaries in patients with PsO.

The systematic review by Lazar *et al*. [7] described that both PsO and PsA patient groups showed reduced capillary density compared to healthy controls. However, they identified certain inconsistencies, highlighting how abnormal morphology and branching could impact the outcomes, emphasizing the challenge of interpreting capillaroscopy, particularly due to its two-dimensional nature.

Avcı *et al*. [8] found in their evaluation (qualitative and semiquantitative) a decrease in capillary density in palmoplantar plaque psoriasis (PPP) and palmoplantar eczema (PPE) patients when compared to the healthy controls. In the evaluation, the mean score for decreased capillary density was significantly higher in PPE than in the PPP and control groups ($p<0.001$). Moreover, they found that avascular areas were more present in PPP and PPE compared to controls.

Dimensions of capillaries

Regarding capillary dimensions, the idea of much larger capillaries in psoriatic plaque skin when compared to healthy controls ($p<0.001$) emerged since 1992 when Bull *et al*. published their results [6].

Sivasankari *et al*. [5] showed that mean arterial limb diameter in PsO patients was 11.37 ± 2.434 μm; mean venous limb diameter was 15.89 ± 3.131 μm; top of the loop diameter was 14.41 ± 4.373 μm; length of the loop 152.51 ± 57.21 μm and only 3 patients had length of loop >300 μm.

Guldberg-Møller *et al*. [4] differentiated patients with PsA from those with PsO and OA. Given the importance of giant capillaries on NVC in Systemic Sclerosis, it is worth mentioning that in this study, giant capillaries were identified in 2% of the PsA patients; however, this finding was not statistically significant.

Lazar *et al*. [7], stated that there wasn't a clear or consistent finding across studies regarding changes in the diameter of capillaries. This suggests that while some studies might have explored this aspect, the evidence was not definitive enough to draw a solid conclusion about the diameter of capillaries.

Morphology

Studies have explored various morphological changes in psoriatic patients. Bhushan *et al*. [2] did not find significant differences in the number of twisted/tortuous capillaries between patient groups (PsO, PsO + arthritis, PsO + nail involvement, PsO + arthritis + nail involvement) compared to normal controls.

Ribeiro *et al*. [3] reported the presence of coiled capillary loops in 54.3% patients compared with 14% in healthy controls ($p < 0.0001$), indicating structural changes in the microvasculature associated with PsO.

Guldberg-Møller *et al*. [4] described a pattern of tortuosity in nailfold morphology, suggesting distinct capillary patterns associated with different psoriatic conditions. There was a higher incidence of tortuous capillaries and a greater variety of capillary shapes, including “glomerular” capillaries, in patients with PsO

compared to those with PsA (p = 0.003), but less crossed vessels (p=0.043). The likelihood of diagnosing PsA based on capillary morphology alone was found to be indeterminate.

Sivasankari *et al*. [5] found that 84.5% of PsO cases had an 'inverse U' shape of capillaries, while the rest exhibited abnormal morphology, indicating variability in capillary morphology among psoriatic patients. They found tortuous loops in 17.3% of cases and ramifications in 9.1% of cases (p<0.001).

Avcı *et al*. [8] detected significantly more major morphological changes (mega, meandering, branching, bushy, bizarre, and disorganized polymorphic capillaries) in PPP patients compared to PPE and healthy control group (p < 0.001), suggesting distinct capillary morphology associated with other palmoplantar conditions.

In the systematic review of Lazar *et al*. [7], while numerous studies have shown a marked increase in abnormal capillary morphology in comparison to healthy controls, these alterations have not been distinct or consistent enough to serve as a definitive indicator for either PsO or PsA. Additionally, considerable methodological variations and diverse research strategies across studies make it challenging to categorize findings into specific capillary changes associated with PsO or PsA

Hemorrhages

In the study by Sivasankari *et al*. [7], they found that patients with PsO exhibited capillary abnormalities such as hemorrhages. They reported that the presence of hemorrhages was observed only in some cases of psoriatic patients (2.72%). However, the information wasn't of statistical relevance (p>0.05).

Guldberg-Møller *et al*. [4] investigated nailfold capillary changes in patients with PsA, PsO, and OA. They found that PsA patients exhibited a higher degree of microhemorrhages compared to OA patients (13% vs. 2%, p = 0.034). They found microhemorrhages in 7% of PsO cases, but with no statistical significance in comparison with the other groups.

The systematic review of Lazar *et al*. [7], displays microhemorrhages specifically in the context of PsA patients, noting their significantly greater prevalence compared to healthy controls. This observation was reported in a single study from those reviewed [9]. In contrast, no significant findings of microhemorrhages were reported in PsO patients when compared to healthy controls. They stated that the notable presence of microhemorrhages in PsA patients is attributed to the pathogenesis of arthritis, characterized by endothelial dysfunction and microvascular injury, which is believed to result from immune complex deposition and activation of the complement cascade [10]. This part of the systematic review emphasizes the distinct vascular changes associated with PsA, underscoring the role of microhemorrhages as a potential indicator of underlying pathophysiological processes specific to PsA, distinct from those observed in PsO patients.

Others

In this section, we present additional insights gleaned from our literature review on NVC in PsO patients, including observations on treatment options, disease severity, and VEGF levels.

- ***Treatment options***

Sivasankari *et al.* [5] studied patients undergoing different treatments, including topical medications, narrow-band ultraviolet B (NBUVB) therapy, methotrexate, and biological therapies. The diminished alterations in capillaries among treated patients might result from reduced levels of vasoactive substances or endothelial factors influencing the outcomes observed in NVC. Nonetheless, the statistical analysis did not show significant differences among the various treatment categories, likely due to the limited number of participants in each group.

The systematic review of Lazar *et al.* [7] mentioned the lack of substantial evidence supporting the use of NVC for monitoring treatment effects in PsO and PsA. This is in contrasted with conditions like Systemic Sclerosis (SSc), where NVC has demonstrated utility in treatment effect monitoring, indicating a need for further research to explore NVC's potential in this area for PsO and PsA.

- ***Disease Severity***

Sivasankari *et al.* [5] reported varying Psoriasis Area Severity Index (PASI) scores among patients. They did not find any statistically significant relationship between PASI score and NVC findings, indicating that disease severity may not directly correlate with nailfold capillary alterations in PsO. Likewise, in the study by Ribeiro *et al.* [3], the researchers found no significant association between the average capillary density per millimeter and the PASI score, nor between the average capillary density and the disease duration.

The study of Avcı *et al*. [8] points to a possible link between capillary changes and disease severity or progression, given the correlation between major morphological changes and the modified Palmoplantar Psoriasis Area and Severity Index (m-PPPASI) which was of statistical significance (p < 0.05).

- ***VEGF levels***

Avcı *et al.* [8] found no significant relationship between serum VEGF level and clinical severity or capillaroscopic findings, suggesting VEGF may not be directly associated with microvascular alterations in palmoplantar psoriasis and eczema. However, it's important to acknowledge the limitations of the study, emphasizing the need for further research involving a larger patient cohort.

Moreover, the systematic review of Lazar *et al.* [7] mentions one study that found a significant correlation between higher levels of Vascular Endothelial Growth Factor (VEGF) and changes observed in capillaroscopy, suggesting an association with underlying disease mechanisms [11].

Discussion

The discussions on capillary density, dimensions,

morphology, hemorrhages, and their clinical relevance in PsO and PsA present a nuanced understanding of microvascular changes and their diagnostic implications. Notably, the study by Bhushan *et al.* [2] and Ribeiro *et al.* [3] illustrate the variability in capillary density in psoriatic conditions, highlighting a significant reduction in patients with DIP arthritis with/without nail changes compared to controls, without notable differences in PsO alone. This inconsistency is echoed in findings by Guldberg-Møller *et al.* [4], which suggest diagnostic potential in distinguishing PsA from PsO through capillary density in nailfold capillaroscopy and optical coherence tomography angiography (OCTA). Such discrepancies underscore the complex relationship between psoriatic disease manifestations and microvascular alterations.

The dimension of capillaries, as reported by Bull *et al.* [6] and further explored in Sivasankari *et al.* [5], adds another layer of complexity, with observations of larger capillaries in psoriatic skin and variations in arterial and venous limb diameters. The presence of giant capillaries, although not statistically significant, introduces systemic sclerosis (SSc) into the differential diagnosis but remains inconclusive due to the low prevalence and non-fulfillment of scleroderma criteria.

Morphologically, studies document a wide array of capillary changes, from the twisted and tortuous capillaries without significant deviation from control in Bhushan *et al.* [2], to the presence of coiled loops and dropout areas noted by Ribeiro *et al.* [3]. Guldberg-Møller *et al.* [4] observations of tortuosity and variety in capillary shapes suggest potential markers for differentiating PsO and PsA. However, the indeterminate diagnostic utility of capillary morphology alone for PsA, as highlighted in their study, calls for cautious interpretation.

Hemorrhages, although more prevalent in PsA patients as per Guldberg-Møller *et al.* [4] and supported by Zaric *et al.* [9], in the systematic review by Lazar *et al.* [7], point to the specific pathophysiological processes underlying PsA, distinguishing it from PsO. The limited observation of hemorrhages in PsO, contrasted with their significance in PsA, highlights endothelial dysfunction and microvascular injury as pivotal elements in the disease's progression.

In terms of treatment implications, Sivasankari *et al.* [5] examination of various therapeutic approaches was unable to exhibit significant correlations due to sample size limitations. The absence of conclusive evidence for NVC's utility in monitoring treatment effects in PsO and PsA, as noted by Lazar *et al.* [7], further emphasizes the need for extensive research in this domain.

The relationship between disease severity and capillary changes remains elusive, with no significant correlation found between PASI scores, disease duration, and capillary density or morphology. The potential link between VEGF levels and capillary alterations, while intriguing, necessitates further investigation to clarify its clinical significance.

Collectively, these studies illustrate the intricate interplay between microvascular changes and psoriatic disease, challenging the clinical utility of capillaroscopy in diagnosing PsA and PsO. Despite the methodological disparities and limitations, the body of evidence emphasizes the critical need for standardization in capillaroscopic evaluation and its integration into a holistic diagnostic and therapeutic framework for PsO and PsA.

Tabel 1 – *Summary of study findings*

No.	Author	Density	Arterial Limb Diameter	Venous Limb Diameter	Morphology	Clinical Severity Correlation
1	Bull *et al*., 1992 [6]	No increase in density in PsO	Capillaries in psoriatic plaque skin were larger than in healthy control ($p<0.001$)		-	-
2	M.Bhushan *et al*., 2000 [2]	There was a significant ($p<0.05$) decrease in capillary loop density in patients with either: -PsO plus nail disease -PsO plus nail and DIP joint disease when compared with controls	No difference in capillary dimensions between patients with PsO and/or nail changes when compared with normal controls. In patients with psoriatic arthritis affecting the DIP joints, there was a statistically significant ($p<0.05$) decrease in arterial and venous capillary limb diameters, and this was also seen in those with arthritis associated with nail changes		No significant difference between groups and healthy controls	-
3	Ribeiro *et al*., 2012 [3]	Patients with PsO had: -lower capillary density ($p=0.0005$), -increased avascular areas (45% vs 18%, $p=0.0035$) compared to healthy controls The presence of avascular areas was more common in PsO + nail involvement ($p=0.047$).	-	-	Increased number of morphologically abnormal capillaries (54.3% vs 14%, $p<0.0001$)	No correlation between capillary density per millimeter and PASI score or duration of the disease.

4	M. Sivasankari *et al*., 2020 [5]	Mean capillary loop density: 76%: 7-9 capillaries/mm 20%: 4 -6 capillaries/mm 3.6%: avascular areas (p>0.05)	Mean arterial limb diameter was 11.37 ± 2.434 µm	Mean venous limb diameter was 15.89 ± 3.131 µm top of the loop diameter 14.41 ± 4.373µm	15.5% bizarre morphology (p<0.001). Widespread disease and PsA had more irregular and haphazard distribution of capillaries (p<0.001).	No statistically significant relationship between NVC and PASI.
5	Guldberg-Møller *et al*., 2021 [4]	Reduced mean capillary density in PsA compared to PsO (p=0.004)	-	-	Less glomerular capillaries (p=0.003) and more crossed vessels (p=0.043) in PsA compared to PsO	No single capillary feature was significantly associated with PsA diagnosis.
6	Avcı *et al*., 2023 [8]	Qualitative: Decreased capillary density Increased avascular areas In both PPP and PPE compared to control Semiquantitative: decreased capillary density was significantly higher in PPE than in the PPP and control groups (p<0.001).	-	-	Major morphological changes* and disorganized capillaries in PPP higher than PPE and control (p<0.001). Minor morphological changes* higher in PPE than PPP and control (p=0.011) Disorganized capillaries in PPP patients were significantly higher than in the PPE and control groups (P < 0.001).	Major morphological change and m-PPPASI scores were correlated in PPP patients (p<0.05). No significant correlation between VEGF, clinical severity and capillaroscopy findings.

'-' = Not Reported, PsA – Psoriatic Arthritis, PsO – Psoriasis, DIP - Distal Interphalangeal, PASI - Psoriasis Area and Severity Index, m-PPPASI - Modified PASI, NVC – Nailfold videocapillaroscopy, PPP - Palmoplantar Pustulosis, PPE - Palmoplantar Erythroderma, VEGF - Vascular Endothelial Growth Factor

**Major morphological changes (mega, meandering, branching, bushy, bizarre, and disorganized polymorphic capillary); Minor morphological changes (tortuous, crossed and enlarged capillary)*

ONGOING STUDY – Nailfold video capillaroscopy in psoriasis patients

Introduction

Understanding nailfold capillary changes in patients diagnosed with PsO is crucial in interpreting NVC (especially when performed in patients with other autoimmune diseases). Considering all the non-specific changes described in literature and the scarcity of studies on this matter, our aim is to conduct a prospective longitudinal cohort study with a cross-sectional component to describe the intricate relationship between NVC and PsO phenotypes (including lesion distribution and nail involvement), taking into account clinical severity (measured by PASI score), disease duration and treatment strategies (topical therapies, methotrexate, biologics), but also demographic factors, lifestyle habits (smoking and alcohol consumption), occupational exposures to toxic environments, comorbidities and familial predisposition (particularly autoimmune diseases and conditions associated with hypoxemia). We hope such insights can facilitate the diagnostic and differential diagnostic process and, by regularly monitoring these patients, to asses NVC utility in evaluating therapeutic response.

Specifically, our main goal is to describe NVC changes in PsO patients and their significance when compared to control groups (healthy controls, psoriatic arthritis group, other autoimmune diseases group); our secondary objective is to asses NVC utility in therapeutic response, by follow-up NVC evaluation at a 6-month interval.

Through these objectives, the study endeavors to provide a comprehensive understanding of the relationship between NVC changes and various factors in PsO patients, thereby contributing to enhanced disease management and patient care, but also facilitate rheumatologist when interpreting NVC in suspected autoimmune diseases in patients with comorbid PsO.

Materials and methods

This is a single center, prospective non-randomized, longitudinal cohort study with a cross-sectional component, conducted in a tertiary hospital (Colentina Clinical Hospital, Bucharest), involving the internal medicine, in collaboration with the dermatology departments. NVC is performed using Smart G-Scope

Capillaroscope (200x magnification) and interpreted according to EULAR criteria for normal/abnormal nailfold video capillaroscopy.

We initiated the collection of data from biopsy diagnosed PsO patients who have been admitted to our hospital, process which is currently underway as we work towards creating a substantial database. We also started collecting data for all our control groups (healthy controls, psoriatic arthritis group, other autoimmune diseases group). We will describe the NVC findings in PsO patients, but also perform statistical analysis regarding NVC differences between groups and the influence of therapy and other variables over a recurrent 6-month follow-up period. The exact study design, number of patients and both qualitative and quantitative results will be published and made available to the public.

Limited preliminary results

Highlighting the ongoing nature of this study, acknowledging that the statistical analysis will be released at a later time, we will mention some qualitative, descriptive findings of NVC in PsO patients; we found that 36% have at least 1 area of lowered density (4-6/mm) and 9% with at least 1 area of further lowered density (0-3/mm); all patients have both normal and dilated capillaries (<50um), 18% having at least 1 giant capillary (≥50um); all patients have abnormal capillary morphologies with at least one of each of the following: three times crossing, not convex tip, ramified capillary; 90% of patients have at least one hemorrhage in the nail bed (this result might be biased due to trauma induced microvascular bleeding). We mention that none of them could be classified as having a scleroderma pattern. Also, none of them had any other autoimmune condition associated.

The preliminary results point to promising findings in PsO patients which, from a rheumatologist point of view, can become valuable in interpreting NVC changes especially in patients with PsO who have clinical suspicion of another autoimmune disease. Likewise, these findings can facilitate PsO patient management (diagnosis, therapeutic response).

Conclusions

Understanding nailfold capillary changes in patients diagnosed with psoriasis is of paramount importance, especially when considering the broader context of autoimmune diseases. The collected findings from the studies we reviewed highlight the intricate relationship between psoriasis and microvascular alterations evident in nailfold capillaroscopy findings. While establishing a diagnosis of psoriasis solely on capillary morphology is unlikely, the presence of microvascular alterations opens avenues for future research. Overall, this review emphasizes the importance of continued research in elucidating the role of nailfold capillaroscopy and microvascular involvement in psoriasis, with potential implications for diagnosis, disease monitoring, prognosis and targeted treatment strategies.

Building upon the foundation laid by the review of literature, our ongoing study extends the examination of nailfold capillaroscopy findings in psoriasis patients. Preliminary qualitative findings from NVC assessments in psoriasis patients highlight notable observations, including abnormal capillary morphologies, hemorrhages in the nail bed, and the absence of a scleroderma pattern or association with other autoimmune conditions. These findings provide valuable insights into the microvascular alterations in psoriasis and lay the groundwork for further quantitative analysis and interpretation. The results of our study will be later published, hoping to contribute to a broader understanding of psoriasis and its implications.

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