Original article

Novel application of optical coherence tomography and capillaroscopy in psoriatic arthritis in relationship to psoriasis and hand osteoarthritis

Jørgen Guldberg-Møller (b) ^{1,2}, Marius Henriksen¹, Karen Ellegaard¹, Merete Haedersdal³, Luna T. Lazar³, Lars Erik Kristensen¹ and Mette Mogensen³

Abstract

Objectives. Nailfold video capillaroscopy (NVC) and angiographic optical coherence tomography (OCTA) have potential in diagnosing PsA and differentiating it from psoriasis vulgaris (PsO) and hand OA. We aimed to assess the diagnostic properties of NVC and OCTA in patients with PsA compared with patients with PsO and hand OA based on nailfold capillary patterns.

Methods. Patients with DIP joint PsA and nail involvement (n = 50), PsO with nail involvement (n = 12) and OA (n = 13) were included in this cross-sectional study. Capillaries were evaluated semiquantitatively and qualitatively. Differences in capillary findings between groups were assessed using mixed linear models. Binary logistic regression analyses were performed to determine the probability for PsA diagnosis based on capillaroscopy findings.

Results. Below mean capillary density and reduced nailfold blood flow in OCTA images distinguished PsA from both PsO (P = 0.004 and P = 0.052, respectively) and OA (P = 0.024 and P < 0.001, respectively). Qualitative analysis revealed that glomerular capillaries were found in only 3% of PsA patients but in 13% of PsO patients (P = 0.003). Furthermore, crossed vessels were seen in only 55% of PsA patients and 71% of PsO patients (P = 0.043). NVC microhaemorrhage was dominant in PsA patients (13%) and significantly different from OA patients (P < 0.05). No capillary pattern was associated with an increased probability of the PsA diagnosis.

Conclusion. A pathognomonic pattern for PsA diagnosis was not identified; however, we demonstrated some characteristic capillaroscopy findings for PsA, such as decreased capillary density, reduced blood flow and fewer crossed vessels in OCTA and presence of NVC microhaemorrhages.

Key words: psoriatic arthritis, psoriasis, osteoarthritis, nailfold capillaroscopy, optical coherence tomography

Key messages

- In PsA, nail disease is linked to DIP joint enthesitis, which may identify the transition from psoriasis vulgaris.
- Capillary characteristics for PsA are decreased nailfold capillary density and flow in and microhaemorrhages.
- No single capillary pattern or nail blood flow rate proved diagnostic for PsA.

¹The Parker Institute, Bispebjerg and Frederiksberg University Hospitals, ²Department of Rheumatology, Slagelse Sygehus, Zealand University Hospitals, Slagelse and ³Department of Dermatology, University Hospitals of Copenhagen, Bispebjerg and Frederiksberg Copenhagen, Denmark

Submitted 15 April 2021; accepted 18 August 2021

Correspondence to: Jørgen Guldberg-Møller, The Parker Institute, Bispebjerg and Frederiksberg Hospital, Nordre Fasanvej 57, 2000 Frederiksberg, Copenhagen University Hospital, Denmark. E-mail: joergen.guldberg-moeller@regionh.dk

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted reuse, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Psoriasis vulgaris (PsO) is one of the most common chronic inflammatory skin diseases, affecting 3% of the population of the world, and approximately one-third of patients with PsO will transition to having PsA [1]. Over recent years, the incidence of PsA has been increasing, and it has a significant impact on patient health and society [2, 3].

In PsA, nail disease is intimately linked to the presence of DIP joint enthesitis and arthritis [4–6], and this clinical feature can help to identify the transition from PsO to PsA and differentiate it from seronegative rheumatoid arthritis (RA) but only to a lesser degree from hand OA. Dermatologists are in a unique position for early referral of potential PsA patients to rheumatological evaluation and treatment before extensive erosive arthritis occurs.

Nailfold video capillaroscopy (NVC) or, more commonly, dermoscopy are used in a dermatological setting, and a considerable effort has been made to find a distinct capillary pattern in relationship to nail changes seen both in PsO and PsA.

However, no uniform agreement on a consistent pattern in PsA nails has yet been found, and a rating scale for capillary abnormality in PsA does not exist, leaving it to the various studies to base their classifications on scales developed for other diseases. Capillaries in PsA have previously been described as meandering and with tight terminal convolutions [7], and significantly lower mean capillary length and mean capillary density were found in PsA compared with healthy individuals [8–12]. Interestingly, a study from 2013 [10] showed that capillaroscopic images of patients with RA and PsA differed, in that PsA patients had a higher number of tortuous capillaries and a lower density than RA patients.

To characterize vascular abnormalities in greater detail, angiographic optical coherence tomography (OCTA) has been introduced. OCTA depicts blood vessel architecture with a resolution of 7.5 μ m to a depth of 2 mm, which far exceeds the penetration of NVC [13]. Nailfold capillaroscopy performed using OCTA has shown dilated blood vessels with a haphazard architecture in PsO [14].

Based on these promising data from the literature, NVC and OCTA used in a clinical setting have the potential for early identification of patients with PsO and nail changes suspected to develop PsA based on nailfold capillary changes.

However, it remains unclear whether NVC or OCTA helps to diagnose PsA, especially when compared with related diagnoses, such as PsO and OA. Thus, we aimed to assess the differential diagnostic properties of NVC and OCTA in patients with PsA in comparison to patients with PsO and hand OA based on nailfold capillary patterns. We also aimed to establish the diagnostic value of NVC and OCTA in the diagnosis of PsA.

Methods

Study design

This cross-sectional study was approved by the local Ethics Committee of the Capital Region in Denmark on 25 May 2018 (Journal-no.: H-18006696) and the Danish Data Protection Agency on 4 June 2018 (VD-2018-149; med I-Suite no.: 6392), and written informed consent was obtained from all patients. Reporting of this study will follow the strengthening the reporting of observational studies in epidemiology (STROBE) guide-lines [15].

Population

Between 1 December 2017 and 1 June 2020, patients diagnosed with PsA according to the CASPAR criteria [16] and patients diagnosed with PsO by a dermatologist were enrolled from three rheumatology outpatient clinics located in the Capital Region of Denmark, the Zealand Region in Denmark and the Department of Dermatology at Bispebjerg and Frederiksberg Hospitals. A nail psoriasis severity index (NAPSI) score of at least five was required in both groups. Patients diagnosed with radiologically verified OA of the hand and no other known joint disease were recruited from the OA outpatient clinic at Bispebjerg and Frederiksberg Hospitals.

The recruitment process is shown in Fig. 1. For inclusion and exclusion criteria, see Supplementary Table S1, available at *Rheumatology Advances in Practice* online. The dominant hand was selected for the study, and data from the second to fifth fingers were retrieved for all patients.

Nailfold video capillaroscopy

NVC was performed with Optilia Digital Capillaroscopy System (VideoCap 9 Rheumatology, DS Medica, Milan, Italy) by a trained dermatologist (M.M.) with 7 years of experience. A semiquantitative validated rating scale by Cutolo et al. [17] developed for prognostic evaluation of nailfolds in patients with systemic sclerosis (SSc) was used to score each capillary abnormality, because no rating scale exists for capillaroscopy in PsA. In the Cutolo SSc scale, a capillary abnormality was defined as irregularly enlarged capillaries, giant capillaries, microhaemorrhages, capillary ramifications and capillary disorganization. A semiquantitative rating scale to score each capillary abnormality was adopted (0: no changes; 1: <33% of capillary alterations; 2: 33-66% of capillary alterations; 3: >66% of capillary alterations, per linear millimetre).

The normal range of capillaries was adopted from the literature: an average of nine capillaries per linear millimetre counted at the distal row of the nailfold. The number of capillaries was scored (0: >9 capillaries/mm; 1: 7-9 capillaries/mm; 2: 4-6 capillaries/mm; 3: 1-3 capillaries/mm).

Fig. 1 Flowchart of study participants



¹Reasons for declining further participation: no response after first examination day (PsA n = 1 and PsO = 1). ²Flow information not required owing to deformity (PsA n = 5 and OA n = 1). ³Software breakdowns (PsA n = 1). ⁴Nailbed hyperkeratosis (PsA n = 4, PsO n = 2 and OA n = 1). NVC: nailfold video capillaroscopy; OCTA: angiographic optical coherence tomography; PsO: skin psoriasis. Flow chart template modified from http://www.equator-network.org/ reporting-guidelines/stard/

Qualitative evaluation of capillary morphology in NVC images was based on EULAR guidelines on nailfold capillaroscopy [18]. The normal pattern was described as a single row of uniform capillary loops immediately above the cuticle. All other shapes were interpreted as abnormal shapes. Crossed capillaries were described as branches that intersect like the digit eight. Tortuosity was defined as when the afferent and efferent limb bend/undulate but do not cross, and the tip of the hairpin has an odd, not convex, shape. Ramified capillaries have lost their hairpin shape and demonstrate hyperplastic growth, forming tree-like morphologies as part of neoangiogenesis. Neoangiogenesis was defined as hyperplastic variants of abnormal vessels, either as ramifications or as glomerular vessels.

The following features were rated as either present (1) or absent (0): enlarged capillaries (diameter); elongated capillaries (length); presence of microhaemorrhages; ramified capillaries; tortuous/crossed capillaries; and glomerular capillaries (tight terminal convolutions).

Evaluation of all NVC images at the end of the study was performed on inherent VIDEOCAP computer software by M.M., who was blinded to the patient by assigning a participant number.

Optical coherence tomography angiography

OCT images were acquired using a swept-source laser OCT system with a central laser wavelength of 1310 nm (VivoSight Dx, Michelson Diagnostics, Maidstone, UK; CE 0459, FDA K080788). The OCT provides cross-sectional and horizontal visualization of the skin at a penetration depth of 1–2 mm and has a resolution of <7.5 μ m. The field of view is 6 mm \times 6 mm.

Angiographic OCT (OCTA) enables the visualization of microvasculature by detecting the motion of red blood cells by repeatedly scanning the same locations. OCTA images were analysed, and vessel flow was calculated using an integrated software tool (Michelson Diagnostics) and represented by an arbitrary number, because OCTA does not measure flow in metres per second. In each OCTA scan, the angiographic OCT data were captured from 0.05 mm below the top of the epidermis to a depth of 1.8 mm in the entire three-dimensional block, measuring 6 mm \times 6 mm in length and width.

Nails and nailbeds were scanned and scored by a trained dermatologist (M.M.) with 12 years of experience. The data analysis of blood flow in OCTA images was performed as a batch analysis by Michelson Diagnostics, blinded to the identity of each dataset.

Statistics

The distribution of NVC and OCT findings was calculated using descriptive statistics. Differences in distributions of the findings between diagnoses were calculated using Pearson χ^2 test. Continuous variables were compared between diagnoses using independent samples t-tests. Binary logistic regression analyses were performed to determine the association between nailfold patterns in NVC and OCTA and PsA diagnosis. In all analyses, $P \leq 0.05$ was considered significant. No imputation was carried out for missing data. The analyses were conducted using the statistical program IBM SPSS Statistics v.25.

Results

We included 50 patients with PsA, 12 with PsO and 13 with OA. Demographics and clinical characteristics of the three groups are shown in Table 1.

Patients with PsA and PsO were younger than OA patients and had a higher BMI than OA patients. Only a tiny fraction of PsA patients were without DMARD treatment compared with the PsO group. According to the

NAPSI total score, the PsO group had the most severe nail changes of the three groups expressed as the highest prevalence of nail crumbling, oil spot changes and onychorrhexis. The PsA group presented the highest prevalence of nail pitting and onycholysis. The only nail changes seen in the OA group were onychorrhexis, leuconychia and splinter haemorrhages, all of which are common nail changes in healthy individuals.

Nailfold capillary changes in PsA, PsO and OA

The distribution of nailfold capillary changes in PsA, PsO and OA, according to NVC and OCTA, are shown in Table 2. The Cutolo NVC scoring system differentiated PsA patients from PsO patients by below mean capillary density (P = 0.019). A higher degree of microhaemorrhages and a lower degree of capillary ramifications significantly differentiated PsA patients from OA (P = 0.034 and P = 0.020, respectively).

Below mean capillary density in OCTA images of the nailfold distinguished PsA from both PsO (P < 0.001) and OA (P = 0.012). A difference between PsA and OA patients was not found in NVC. This was also reflected in a lower OCTA blood flow found in the PsA patients (mean 6.00) than in both PsO (mean 6.94) and OA

TABLE 1 Demographics and characteristics of PsA, PsO and OA patients

Descriptives	PsA (<i>n</i> = 50)	PsO (<i>n</i> = 12)	Hand OA (<i>n</i> = 13)
Sociodemography/treatment			
Females, n (%)	21 (42)	5 (41)	13 (100)
Age, mean (s.d.), years	54.4 (12.0)	55.3 (18.0)	69.5 (8.9)
Disease duration, months	60 [19; 120]	25 [12; 96]	78 [12; 99]
Height, mean (s.d.), cm	172.8 (10.0)	173.3 (10.0)	160.2 (6.7)
weight, mean (s.p.), kg	85.7 (16.8)	82.6 (16.3)	62.7 (10.7)
BMI, mean (s.d.), m/kg ²	28.8 (6.6)	27.5 (5.3)	24.3 (2.5)
PASI (if BSA >1) (0–72)	1.9 [0.8; 4.0]	1.8 [0.0; 6.1]	0.0 [0.0; 0.0]
Treated with csDMARDs, n (%)	30 (60)	3 (25)	1 (7)
Treated with bDMARDs, n (%)	4 (8)	5 (42)	0
Treated with both bDMARDs and csDMARDs, n (%)	7 (14)	0	0
No treatment, <i>n</i> (%)	9 (18)	4 (33)	12 (93)
Nail characteristics			
NAPSI total score finger 2 (0–8)	3.0 [2.0; 4.0]	3.5 [2.0; 5.0]	0.0 [0.0; 0.0]
NAPSI total score finger 3 (0–8)	3.0 [2.0; 4.0]	4.0 [2.3; 4.8]	0.0 [0.0; 0.0]
NAPSI total score finger 4 (0–8)	2.0 [1.0; 4.0]	3.5 [2.0; 5.8]	0.0 [0.0; 0.0]
NAPSI total score finger 5 (0–8)	2.0 [1.0; 4.0]	2.0 [1.0; 3.0]	0.0 [0.0; 0.0]
Nail pitting, <i>n/n</i> -total (%)	83/200 (42)	8/48 (17)	0/52 (0)
Nail leuconychia, <i>n/n-</i> total (%)	9/200 (5)	3/48 (6)	2/52 (4)
Nail crumbling, <i>n/n</i> -total (%)	17/200 (9)	12/48 (25)	0/52 (0)
Nail lunula red spots, <i>n/n</i> -total (%)	5/200 (3)	0/48 (0)	0/52 (0)
Nail onychorrhexis, <i>n/n</i> -total (%)	17/200 (9)	6/48 (13)	3/52 (6)
Nail oil spot change, <i>n/n</i> -total (%)	29/200 (15)	11/48 (23)	0/52 (0)
Nail onycholysis, <i>n/n</i> -total (%)	109/200 (55)	23/48 (48)	0/52 (0)
Nail subungual hyperkeratosis, <i>n/n</i> -total (%)	7/200 (4)	4/48 (8)	0/52 (0)
Nail splinter haemorrhage, <i>n/n</i> -total (%)	17/200 (9)	5/48 (10)	1/52 (2)

Data are presented as median [25th–75th percentiles] unless otherwise stated. bDMARDs: biological DMARDs; csDMARDs: conventional DMARDs; NAPSI: nail psoriasis severity index; PASI: Psoriasis Area Severity Index; BSA: Body surface area; PsO: psoriasis vulgaris.

TABLE 2 The distribution of nailfold video capillaroscopy and angiographic optical coherence tomography capillary morphology between PsA, PsO and OA

NVC rating	PsA (<i>n</i> = 188)	PsO (n = 42)	OA (n = 48)	PsA <i>vs</i> PsO <i>P</i> -value	PsA <i>vs</i> OA <i>P</i> -value
NVC ad modum Cutolo					
Below mean capillary density, n (%)	95 (51)	14 (31)	24 (51)	0.019	1.000
Capillary disorganization, n (%)	84 (45)	24 (57)	23 (48)	0.172	0.746
OCTA rating	PsA (n = 193)	PsO(n = 48)	OA ($n = 52$)	PsA vs PsO P-value	PsA vs OA P-value
Capillary morphology	PsA (n = 192)	PsO (n = 48)	OA (n = 52)	PsA vs PsO P-value	PsA vs OA P-value
Irregularly enlarged capillaries, n (%)	42 (22)	14 (33)	12 (25)	0.163	0.703
Giant capillary, <i>n</i> (%)	3 (2)	0	0	0.631	0.610
Microhaemorrhages, n (%)	24 (13)	3 (7)	1 (2)	0.429	0.034
Capillary ramifications, n (%)	27 (14)	10 (24)	14 (29)	0.162	0.020
OCTA ad modum Cutolo					
Below mean capillary density, n (%)	103 (53)	10 (21)	17 (33)	<0.001	0.012
Irregularly enlarged capillaries, n (%)	66 (34)	27 (56)	10 (19)	0.005	0.062
Giant capillary, <i>n</i> (%)	0	0	0	-	-
Microhaemorrhages, n (%)	0	0	0	-	-
Capillary ramifications, n (%)	0	0	0	-	-
Capillary disorganization, n (%)	108 (55)	22 (46)	25 (49)	0.263	0.529
OCT					
Nail thickness ^a , mean (s.p.), mm	0.62 (0.13)	0.73 (0.39)	0.59 (0.08)	0.876	0.020
OCTA blood flow percentage, mean (s.p.)	6.00 (2.94)	6.94 (3.08)	7.88 (3.30)	0.052	<0.001
Qualitative evaluation of NVC morphology					
Tortuous/crossed capillaries, n (%)	105 (55)	34 (71)	29 (56)	0.050	1.000
Enlarged capillary diameter, n (%)	33 (17)	10 (21)	9 (17)	0.674	1.000
Ramified capillaries, n (%)	24 (13)	7 (15)	10 (19)	0.810	0.258
Microhaemorrhages, n (%)	32 (17)	3 (6)	4 (8)	0.106	0.125
Elongated capillaries, n (%)	11 (6)	2 (4)	2 (4)	0.747	0.741
Different capillary shapes, glomerular, n (%)	5 (3)	6 (13)	1 (2)	0.010	1.000

Data are presented as a percentage of capillary finding within the group unless otherwise stated. Differences between PsA and the other groups are presented as a two-sided *P*-value; values of P < 0.05 are considered significant. ^aOne patient from the PsO group was excluded from this analysis because a nail thickness of >2.0 mm exceeded the maximum penetration depth of the OCT laser, thus representing an outlier. NVC: nailfold video capillaroscopy; OA: hand OA; OCTA: angiographic optical coherence tomography; PsO: psoriasis vulgaris.

(mean 7.88) patients, significant only for the OA patients (P < 0.001), but borderline significant compared with PsO (P = 0.052). Irregularly enlarged capillaries in OCTA images differed significantly in PsA and PsO patients, with fewer enlarged capillaries in PsA (P = 0.005).

OCT mean nail thickness was significantly greater in the PsA group than in the OA group, but no differences were found compared with PsO.

The qualitative analysis of nailfold morphology in NVC images revealed a pattern of neoangiogenesis and tortuosity that we described as glomerular vessels owing to their resemblance to glomerular kidney vessels, shown in Fig. 2. Fewer glomerular capillaries were characteristic for PsA, found in only 3% of PsA patients compared with 13% of PsO patients (P = 0.010). Furthermore, significantly less tortuosity was found in PsA patients, seen in 55% of PsA and 71% of PsO patients (P = 0.050). No capillary abnormalities other than glomerular vessels were detected in the different capillary shapes category (Table 2).

It was impossible to evaluate giant capillaries, microhaemorrhages or capillary ramification using OCTA in either group owing to the lower resolution. OCTA images and clinical photographs showing the nail and nailfold in PsA, PsO and OA patients are shown in Fig. 3, and OCTA images show less normal nailfold capillaries in the PsA patients.

Odds ratios for PsA diagnosis based on capillary patterns and flows in NVC and OCT

Table 3 show the odds ratios for having a PsA diagnosis based on NVC capillary pattern and flows in NVC and OCT compared with PsO or OA, or in PsA compared with PsO and OA grouped. No capillary pattern or blood flow percentage was significantly associated with an increased or decreased probability of having the PsA diagnosis.

Discussion

In this diagnostic cross-sectional study, we showed different capillary patterns dependent on the underlying diagnosis. We produced both semiquantitative and qualitative results using a validated rating scale by



Fig. 2 Qualitative nailfold video capillaroscopy morphology in patients with PsA, psoriasis vulgaris and hand OA

(A) Ramified capillaries (white ring) in PsA. (B) Elongated capillaries in PsA. (C) Elongated capillaries with microhaemorrhages (white arrow) in PsA. (D) Microhaemorrhages (white arrows) in PsA. (E) Glomerular and dilated capillaries in OA (white ring). (F) Glomerular and dilated capillaries in psoriasis vulgaris (white rings). (G) Crossed/tortuous capillaries in PsA. (H) Capillary ramifications in OA (white ring). Dilated capillaries are defined to have a diameter of 20–50 µm.

Cutolo *et al.* [17] and a qualitative evaluation of all NVC images, respectively. This provides accurate and versatile results despite the lack of a scale suited for PsA. Although patients with PsO demonstrated the most nail changes in our cohort, PsA patients were significantly differentiated from PsO and OA patients by below mean capillary density in OCTA images and by the presence of NVC microhaemorrhages and lower blood flow shown in OCTA (Table 2).

A below mean capillary density in PsA has not been demonstrated previously by OCTA, but several studies have found that the mean NVC capillary density was significantly lower in PsA patients than in healthy controls [8–11]. We could not replicate the finding in OA patients. A possible explanation is that the field of view was much smaller in NVC than in OCTA, and capillary ramifications were prominent in OA patients, which might have influenced the capillary count in NVC.

The lower OCTA blood flows in PsA patients compared with OA patients and, to some degree, PsO patients could represent a continuum of microvascular changes resulting from an increased inflammatory load. A higher US-measured nailfold vessel resistive index [19], NVC decreased blood flow velocity [20], capillary shortening and decreased maximum length/width [21] and lower capillary density [22] have previously been shown in patients with PsO disease compared with healthy controls. An explanation for a decreased blood flow has been proposed by Espinoza et al. [23]: blood flow is slowed down by immune complex deposition and complement cascade activation causing vascular damage, endothelial cell swelling, inflammatory cell infiltration and marked thickening of the blood vessel. Therefore, capillary density might be reduced in patients suffering from PsA and PsO owing to changes in the normal angiogenesis. The neoangiogenetic morphology Fig. 3 Optical coherence tomography of the nail and nailbed in PsA, psoriasis vulgaris, and OA



*: nail plate; ¤: cuticle; white arrow: proximal nailfold; §: 1 mm field.

Capillary parameter	Groups	Odds ratio (95% CI)	<i>P</i> -value
NVC microhaemorrhages	PsA vs PsO	1.54 (0.17, 13.92)	0.701
	PsA vs OA	0.27 (0.01, 6.72)	0.424
	PsA vs PsO + OA	2.12 (0.27, 16.72)	0.473
NVC glomerular	PsA vs PsO	0.33 (0.02, 5.84)	0.447
	PsA vs OA	0.81 (0.11, 61.71)	0.923
	PsA vs PsO + OA	0.49 (0.03, 7.68)	0.611
NVC crossed capillaries	PsA vs PsO	0.61 (0.15, 2.45)	0.480
	PsA vs OA	1.04 (0.26, 4.18)	0.960
	PsA vs PsO + OA	0.77 (0.24, 2.46)	0.652
OCTA below mean capillary	PsA vs PsO	2.92 (0.68, 12.50)	0.148
density	PsA vs OA	0.51 (0.27, 2.06)	0.343
	PsA vs PsO + OA	2.41 (0.73, 7.88)	0.147
OCTA Irregularly enlarged	PsA vs PsO	0.50 (0.13, 1.96)	0.318
	PsA vs OA	0.56 (0.11, 2.71)	0.465
	PsA vs PsO + OA	0.89 (0.27, 2.97)	0.849
OCTA blood flow	PsA vs PsO	0.92 (0.72, 1.17)	0.494
percentage	PsA vs OA	0.19 (0.93, 1.46)	0.186
	PsA vs PsO + OA	0.88 (0.71, 1.08)	0.219

TABLE 3 The odds ratio for having PsA diagnosis according to capillary morphology and blood flow

Values are presented as the odds ratio and corresponding 95% CI of capillary haemorrhages, glomerular or crossed capillaries in NVC and below mean capillary density and irregularly enlarged capillaries in OCTA or blood flow percentage compared with PsO, OA or PsO and OA grouped. NVC: nailfold video capillaroscopy; OA: hand OA; OCTA: angiographic optical coherence tomography; PsO: psoriasis vulgaris.

might then be compensation for decreased capillary density. Given that inflammation in PsA is more widespread than in PsO, the changes in OCTA flow could be more pronounced in PsA, as reflected in our findings.

However, the finding is not aligned with the study by Aldahan *et al.* [14], who found increased OCT blood flow in patients with PsO compared with healthy controls. Differences might be explained by differences in sample sizes in their study and our OCT analysis, being 32 vs 293 nails, respectively. In their study, they also described 'dilated vessels with a haphazard architecture in the psoriatic nails' but did not quantify the distribution of the finding systematically. The finding might resemble the OCTA irregularly enlarged capillaries, which was a significant finding in our PsO group.

The presence of NVC microhaemorrhages in PsA patients compared with OA patients has not been shown before. In SSc, nailfold microhaemorrhages may reflect an active inflammatory phase in autoimmune disorders [24]. Whether this is the case in PsA in our cohort cannot be interpreted from our data, because the finding was rare in all three groups. Future studies with more participants could investigate the hypothesis that the presence of NVC microhaemorrhages could be linked to disease activity in PsA or PsO. Importantly, nailfold microhaemorrhages are also common in manual workers [25].

The PsO group was characterized by a high prevalence of NVC crossed and glomerular capillaries and OCTA irregularly enlarged capillaries (Table 2). Crossed or tortuous capillaries, also termed tight terminal convolutions [11, 26], very similar to what we describe here as glomerular vessels, have previously been associated with PsO and linked to decreased blood flow in the nailfold [19, 20]. Capillary tortuosity has been suggested as a marker in differentiating between PsO/PsA and RA and healthy controls [10]. In our data, the OA group presented the same degree of tortuous capillaries as the PsA group; hence, a distinction between PsO/PsA and OA based on this finding might be difficult. However, the finding is in good alignment with Fioravanti *et al.* [27], who found NVC tortuous loops to be of significant prevalence in erosive OA compared with nodal OA and healthy controls.

The OA group was differentiated from PsA by significantly more NVC capillary ramifications, which could be attributed to a higher age in this group but are also seen in 47% of healthy individuals [28]. Also, onychorrhexis occurs in most older people and is expected in the OA group simply owing to age.

NVC and OCTA capillary disorganization, NVC capillary ramifications, enlarged diameter and elongated capillaries were distributed almost evenly among the three groups. This explains why none of these features was diagnostic (Table 3).

Strengths

This is the first study to examine OCTA capillary patterns and blood flow of the nailfold in PsA. The study benefits from consecutively enrolled patients treated with various DMARDs in a dermatological and rheumatological setting, strengthening the external validity of the study. The internal validity has been increased by NVC and OCTA image evaluation blinded to patient identity. OCTA can easily quantify blood flow in three-dimensional OCT and thereby supplement NVC data with data from a larger area. We experienced that OCTA imaged nailfold capillaries in cases where NVC imaging was hampered by hyperkeratosis. In contrast, in optimal conditions the resolution and magnification of superficial capillaries were superior in NVC in evaluating capillary morphology. OCTA flow calculation has been done anonymized by a computer program.

Limitations

Evaluation of capillary morphology in NVC was impaired in some of our subjects because of nailfold hyperkeratosis, a common finding in patients with PsA and PsO. In OCTA, a similar ragged and indurated skin surface impaired the flow calculation because of a steep angle at the proximal nailfold. Capillary blood flow is very temperature dependent, which might have affected OCTA blood flow measurements and NVC capillary morphology because patients did not, in all cases, have time to acclimate in a warm room before imaging procedures. Co-morbidity, such as diabetes mellitus, glaucoma and essential hypertension, is associated with NVC capillary change [29] and has not been registered systematically in this study. One patient diagnosed with PsO and one with OA had diabetic nephropathy but only a slight reduction in kidney function, and one patient with PsO had reduced kidney function from essential hypertension. The impact of this co-morbidity seems limited for our results.

Conclusion

Although several of our findings proved distinctive features in both NVC and OCTA images of the nailfold, no single capillary feature was associated with either an increased or a decreased probability of PsA diagnosis. Thus, we did not demonstrate a unique pathognomonic pattern for PsA but outlined some characteristic features of PsA, such as below mean capillary density and low blood flow in OCTA and the presence of NVC microhaemorrhages. Also, we identified abnormalities visualized only by OCTA, such as below mean capillary density and more irregularly enlarged capillaries, thus highlighting the potential of this device to supplement dermatological and rheumatological diagnosis of hand arthritis and hand OA patients. These findings are novel and might help to guide the clinician in reaching a diagnosis. Further morphological and functional studies are needed to understand the significance of the abnormalities of the microvascular environment in the nailfold.

Acknowledgements

A huge thanks to Line Rustad at the Parker Institute for organizing the flow of participants.

The data analysis of blood flow in angiographic OCT images was kindly performed as a batch analysis by CEO Jon Holmes, Michelson Diagnostics Ltd, Kent, UK.

Funding: This work was supported by an investigatorinitiated grant from Novartis, the research foundation of Bispebjerg and Frederiksberg Hospitals, Denmark, Innovation Fund Denmark [ShapeOCT 4107-00011A], the OAK Foundation [Core grant OCAY-13-309] and a grant from Minister Erna Hamiltons Foundation for Science and Art [J.nr. 13-2020].

Disclosure statement: J.G.-M. has received speaking fees from AbbVie, NOVARTIS, Eli-Lilly and BK Ultrasound outside the present work. L.E.K. has received fees for speaking and/or consultancy from Pfizer, AbbVie, Amgen, UCB, Celgene, BMS, Biogen, Sanofi, MSD, Novartis, Eli Lilly and Janssen Pharmaceuticals outside the present work. The remaining authors have declared no conflicts of interests.

Data availability statement

The dataset will be available from the corresponding author to the extent possible under the Danish national law.

Supplementary data

Supplementary data are available at *Rheumatology Advances in Practice* online.

References

- 1 Gladman DD, Antoni C, Mease P *et al.* Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis 2005;64(Suppl 2): ii14–7.
- 2 Kristensen LE, Jørgensen TS, Christensen R *et al.* Societal costs and patients' experience of health inequities before and after diagnosis of psoriatic arthritis: a Danish cohort study. Ann Rheum Dis 2017;76: 1495–501.
- 3 Egeberg A, Kristensen LE, Thyssen JP et al. Incidence and prevalence of psoriatic arthritis in Denmark: a nationwide register linkage study. Ann Rheum Dis 2017; 76:1591–7.
- 4 McGonagle D. Enthesitis: an autoinflammatory lesion linking nail and joint involvement in psoriatic disease. J Eur Acad Dermatol Venereol 2009;23(Suppl 1):9–13. [Internet]. [cited 2017 Jun 26] Available from: http://doi. wiley.com/10.1111/j.1468-3083.2009.03363.x
- 5 McGonagle D, Tan AL, Benjamin M. The nail as a musculoskeletal appendage – implications for an improved understanding of the link between psoriasis and arthritis. Dermatology 2009;218:97–102.
- 6 Tan AL, Grainger AJ, Tanner SF, Emery P, McGonagle D. A high-resolution magnetic resonance imaging study of distal interphalangeal joint arthropathy in psoriatic arthritis and osteoarthritis: are they the same? Arthritis Rheum 2006;54:1328–33.

- 7 Redisch W, Messina EJ, Hughes G, McEwen C. Capillaroscopic observations in rheumatic diseases. Ann Rheum Dis 1970;29:244–53.
- 8 Lambova SN, Müller-Ladner U. Capillaroscopic pattern in inflammatory arthritis. Microvasc Res 2012;83:318–22.
- 9 Bhushan M, Moore T, Herrick AL, Griffiths CE. Nailfold video capillaroscopy in psoriasis. Br J Dermatol 2000; 142:1171–6.
- 10 Graceffa D, Amorosi B, Maiani E *et al.* Capillaroscopy in psoriatic and rheumatoid arthritis: a useful tool for differential diagnosis. Arthritis 2013;2013:957480.
- 11 Zaric D, Worm AM, Stahl D, Clemmensen OJ. Capillary microscopy of the nailfold in psoriatic and rheumatoid arthritis. Scand J Rheumatol 1981;10: 249–52.
- 12 Grassi W, Core P, Carlino G, Cervini C. Nailfold capillary permeability in psoriatic arthritis. Scand J Rheumatol 1992;21:226–30.
- 13 Ulrich M, Themstrup L, De Carvalho N *et al.* Dynamic optical coherence tomography in dermatology. Dermatology 2016;232:298–311.
- 14 Aldahan AS, Chen LL, Fertig RM *et al.* Vascular features of nail psoriasis using dynamic optical coherence tomography. Ski Appendage Disord 2016;2:102–8.
- 15 von Elm E, Altman DG, Egger M et al.; STROBE Initiative. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg 2014;12:1495–9.
- 16 Taylor W, Gladman D, Helliwell P et al.; CASPAR Study Group. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006;54:2665–73.
- 17 Cutolo M, Sulli A, Pizzorni C, Accardo S. Nailfold videocapillaroscopy assessment of microvascular damage in systemic sclerosis. J Rheumatol 2000;27:155–60.
- 18 Smith V, Herrick AL, Ingegnoli F et al.; EULAR Study Group on Microcirculation in Rheumatic Diseases and the Scleroderma Clinical Trials Consortium Group on Capillaroscopy. Standardisation of nailfold capillaroscopy for the assessment of patients with Raynaud's phenomenon and systemic sclerosis. Autoimmun Rev 2020;19:102458.

- 19 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.
- 20 Long F, He F, Wang J *et al.* Nailfold capillary abnormalities: a possible cause for nail psoriasis? Br J Dermatol 2021;184:178–80.
- 21 Ohtsuka T, Yamakage A, Miyachi Y. Statistical definition of nailfold capillary pattern in patients with psoriasis. Int J Dermatol 1994;33:779–82.
- 22 Ribeiro CF, Siqueira EBD, Holler AP, Fabrício L, Skare TL. Periungual capillaroscopy in psoriasis. An Bras Dermatol 2012;87:550–3.
- 23 Espinoza LR, Vasey FB, Espinoza CG, Bocanegra TS, Germain BF. Vascular changes in psoriatic synovium. a light and electron microscopic study. Arthritis Rheum 1982;25:677–84.
- 24 McBride JD, Sontheimer RD. Proximal nailfold microhemorrhage events are manifested as distal cuticular (eponychial) hemosiderin-containing deposits (CEHD) (syn. Maricq sign) and can aid in the diagnosis of dermatomyositis and systemic sclerosis. Dermatol Online J 2016;22:13030/qt8sr306pb.
- 25 Cortes S, Cutolo M. Capillarosecopic patterns in rheumatic diseases. Acta Reumatol Port 2007;32: 29–36.
- 26 Zaric D, Clemmensen OJ, Worm AM, Stahl D. Capillary microscopy of the nail fold in patients with psoriasis and psoriatic arthritis. Dermatology 1982; 164:10-4.
- 27 Fioravanti A, Tofi C, Cerase A, Priolo F, Marcolongo R. Capillaroscopic findings in erosive and nodal osteoarthritis of the hands. Clin Rheumatol 2001;20: 174–6.
- 28 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.
- 29 Ciaffi J, Ajasllari N, Mancarella L *et al.* Nailfold capillaroscopy in common non-rheumatic conditions: a systematic review and applications for clinical practice. Microvasc Res 2020;131:104036.