Rheumatology International (2019) 39:697–705
https://doi.org/10.1007/s00296-018-4222-y

Rheumatology
INTERNATIONAL

IMAGING

To what extend is nail ultrasound discriminative between psoriasis, psoriatic arthritis and healthy subjects?

Esperanza Naredo[1] · Iustina Janta[2] · Ofelia Baniandrés-Rodríguez[3] · Lara Valor[4] · Michelle Hinojosa[5] · Natalia Bello[2] · Belén Serrano[2] · Jesús Garrido[6]

Received: 18 August 2018 / Accepted: 4 December 2018 / Published online: 10 December 2018

Abstract

To assess the discriminative utility of nail features detected by B-mode (BM) and color Doppler (CD) ultrasound (US) between patients with psoriasis (PsO) and psoriatic arthritis (PsA) and healthy controls. Sixty patients with PsA, 21 patients with PsO, and 20 healthy controls were prospectively included. All patients underwent a dermatologic assessment and PsA patients also a rheumatologic assessment. All patients and controls underwent a US assessment of the finger nails that included a BM score for nail plate integrity and four different CD scores based on the amount and location of CD signals in the nail bed/matrix. In addition, we measured the thickness of the nail bed (TNB) and nail plate (TNP). The BM score and the CD score based on the amount of signals in the nail bed in contact with the ventral plate discriminated between the control group (median, range 0.0, 0–4 and 2.0, 0–9, respectively) and the PsO/PsA group (median, range: 7.0, 0–31 and 5.14, 0–13, respectively) ($p < 0.05$) with or without clinical nail involvement. The CD scores based on the percentage of the nail bed/matrix occupied by Doppler signals did not discriminate between controls and PsO/PsA patients. TNB and TNP were significantly higher in psoriatic nails with or without clinical involvement than in control nails. In PsO/PsA patients, the BM score, TNB and TNP were significantly higher in clinically involved nail than in clinically non-involved nails. Our results showed discriminative utility of BM US and some CD US features for PsO/PsA nails.

Keywords Ultrasound · Nail · Psoriasis · Psoriatic arthritis · Doppler

Introduction

Psoriasis (PsO) is an immune-mediated skin disease highly prevalent worldwide (i.e., 2–3%) [1] with a reported prevalence of musculoskeletal (MSK) involvement, i.e., psoriatic arthritis (PsA) highly variable (i.e., 6–42%) [2].

Nail involvement is very common in the course of PsO, reported in up to 50% of the patients [3]. PsO patients with nail involvement have shown a higher probability to develop PsA [4]. Assessment of nail involvement in PsO is currently made by clinical physical examination [5, 6], which can detect superficial nail changes. However, the nail matrix and bed are not accessible for clinical assessment. MSK ultrasound (US) is playing an increasingly important role in the evaluation of PsA patients [7]. Recently, US is also becoming more used to evaluate nail involvement in PsO and PsA patients and a number of studies [8–17] have described some morpho-structural and vascular abnormalities characteristic of PsO nail. However, there are still a few studies dealing with the metric properties of B-mode (BM)

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00296-018-4222-y) contains supplementary material, which is available to authorized users.

✉ Esperanza Naredo
enaredo@ser.es

[1] Department of Rheumatology, Bone and Joint Research Unit, Hospital Universitario Fundación Jiménez Díaz, IIS Fundación Jiménez Díaz, and Universidad Autónoma de Madrid, Av. Reyes Católicos, 2, 28040 Madrid, Spain

[2] Department of Rheumatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain

[3] Department of Dermatology, Hospital General Universitario Gregorio Marañón, Madrid, Spain

[4] Rheumatology and Clinical Immunology Department, Universitätsklinikum Erlangen-Nürnberg, Erlangen, Germany

[5] Department of Internal Medicine and Rheumatology, Hospital Helios Klinikum Berlin-Buch, Berlin, Germany

[6] Department of Social Psychology and Methodology, Facultad de Psicología, Universidad Autónoma de Madrid, Madrid, Spain

and Doppler mode US in assessment of the nail in PsO and PsA patients [11–17].

The objectives of this cross-sectional, observational study were the following: (1) to test the discriminative ability of US-detected nail features, on both BM and Doppler mode between patients with PsO and PsA and healthy controls; (2) to assess the relation between US-detected nail features and skin and joint disease activity markers in patients with PsO and PsA.

Methods

Patients and controls

We included 60 patients (600 nails) with PsA diagnosed according to classification for psoriatic arthritis (CASPAR) criteria [18] and 21 patients (210 nails) with PsO diagnosed by an experienced dermatologist without MSK involvement, who consecutively attended the rheumatologic and dermatologic outpatient clinic, respectively. In addition, 20 healthy controls (200 nails) with neither MSK or dermatologic conditions nor family history of PsO/PsA were recruited from the hospital staff. Patients and controls with other conditions affecting nails or distal interphalangeal (DIP) joints (i.e., infections, micro-traumatic or traumatic lesions, osteoarthritis) were excluded.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee of the Hospital General Universitario Gregorio Marañón (Madrid, Spain) (protocol number 78/15, May 8th, 2015). Informed consent was obtained from all patients and controls before study enrolment.

Clinical assessment

Patient demographics and PsO/PsA features and treatment were recorded at study entry. All patients underwent a dermatologic assessment and PsA patients also a rheumatologic assessment. The dermatologic assessment was performed by the same dermatologist (OBR) for all patients and consisted of the evaluation of nail involvement in the hands according to the Nail Psoriasis Severity Index (NAPSI) (0–8 at nail level, 0–80 total NAPSI at patient level) [5] and skin involvement according to the Psoriasis Area and Severity Index (PASI) (0–72) [19]. The rheumatologic assessment was carried out by three rheumatologists (MH, NB, BS) for all PsO and PsA patients and consisted of tender joint count (TJC) (0–68) and swollen joint count (SJC) (0–66) for 68 and 66 joints, respectively, tender and swollen DIP counts (TDIPC and SDIPC, respectively) (0–10), and tenderness at 13 entheses [Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)] (0–13) [20]. For each PsA patient, C-reactive protein (CRP) level (normal 0–10 mg/l) and erythrocyte sedimentation rate (ESR) (normal 10–20 mm/h) were obtained from laboratory tests at study entry.

US assessment

For all patients and controls, a rheumatologist expert in MSKUS (4 years' experience) (IJ) performed a US longitudinal scanning of the 10 finger nails on BM and color Doppler (CD) mode, in the same day of the clinical evaluation for the PsO/PsA patients. A representative BM image and an image with maximal CD signal of each nail were recorded for further analysis.

Patients and controls waited 15–20 min in a room with a constant temperature (23 °C) before US scanning, which was performed in a darkened room using a real-time scanner (Esaote Mylab Twice, Genoa, Italy) equipped with a multifrequency (10–22 MHz) linear transducer. The BM and CD settings were optimized and standardized during the whole study as follows: BM frequency of 22 MHz, BM gain of 50%, Doppler frequency of 14.3 MHz, wall filter 3, and pulse repetition frequency of 1.0 KHz. Nail assessment was performed with the patients seated in front of the examiner, with the hands in neutral position over the examination table without pressing on the table with their fingers. A generous amount of gel was applied to avoid pressure over the nail structures.

Two rheumatologist ultrasonographers, the rheumatologists who acquired the US images (IJ) and a rheumatologist highly expert in MSKUS (20 years' experience) (EN) assessed together all acquired US images of the nails, in a random fashion, blinded to the subject group (i.e., PsA, PsO or healthy control) and clinical data, at least 1 month after the US scanning.

Based on the previous literature [8–10] and our own experience, we considered as normal US appearance of the nail plate a trilaminar structure composed of two hyperechoic layers, ventral and dorsal plates, separated by a hypoechoic line. The dorsal and ventral plates are sharp and homogeneous with similar thickness, although the dorsal plate can be a little thicker than the ventral plate. The ventral plate can show reverberation. In the root area, the two plates may sharpen. The nail bed appears as a hypoechoic band between the ventral plate and the bone of the distal phalanx, which extends proximally to the matrix area.

The following parameters were assessed on BM: (1) thickness (mm) of the nail bed (TNB) at the maximum distance from the cortex of the distal phalanx to the ventral plate (i.e., deep hyperechoic layer), according to Worstman et al. [8]; (2) thickness (mm) of the nail plate (TNP) from the dorsal (i.e., superficial hyperechoic layer) to the ventral plate (i.e., deep hyperechoic layer) at the maximum distance between both plates; and (3) dorsal and ventral plate

sharpness and integrity, which were scored using a novel 0–4 semiquantitative scoring system (BM-Sc) as follows: grade 0, normal trilaminar US appearance; grade 1, loss of sharpness and irregularities of the ventral plate at the level of the matrix; grade 2, loss of sharpness and irregularities of the whole ventral plate; grade 3, loss of sharpness and irregularities of both plates; grade 4, loss of the trilaminar US appearance, i.e., fusion of both plates with loss of the intermediate hypoechoic line. A global BM score (BM-GSc) (0–40) was calculated for each patient summing the BM-Sc from each nail.

On CD mode, we assessed the presence of Doppler signals at the nail bed and nail matrix together. We developed two scoring systems for CD assessment of each nail. For the first CD scoring system (CD-Sc1), we considered the matrix/bed area occupied by Doppler signals as follows: grade 0, no Doppler signal or isolated Doppler signals; grade 1, more than isolated signals but less than 50% of the nail matrix/bed area occupied by Doppler signals; grade 2, more than 50% of the nail matrix/bed area occupied by Doppler signals. For the second CD score (CD-Sc2), we considered the contact of Doppler signals in the nail bed with the ventral plate as follows: grade 0, without contact with the ventral plate; grade 1, focal contact with the ventral plate; grade 2, diffuse contact with the ventral plate. For each patient, two global CD scores (CD-GSc1 and CD-GSc2) (0–20) were calculated for each patient from the sum of CD-Sc1 and CD-Sc2, respectively, obtained for each nail. Additionally, we applied a previously described CD scoring system [13] used in the study by Arbault et al. [15], in which the nail matrix (CD-Sc3) and the nail bed (CD-Sc4) were scored separately as follows: 0, no signal; 1, confluent signal in $<25\%$ of the area; 2, confluent signal in 25–50% of the area; 3, confluent signal in $>50\%$ of the area. Thus, two additional global CD scores (CD-GSc3 and CD-GSc4) [0–30] were calculating for each patient from the sum of CD-Sc3 and CD-Sc4 obtained for each nail, respectively.

Reliability of US scoring

Interobserver and intraobserver reliability for the novel BM and CD scoring systems (i.e., BM-Sc, CD-Sc1, and CD-Sc2) was tested using 50 BM images and 50 CD images, randomly chosen from the PsA, PsO and control nail US images, which were scored separately by the two investigator ultrasonographers 3 months and 6 months, respectively, after the first assessment of all patient and control US images.

Statistical analysis

Statistical analysis was performed using the IBM-SPSS 23 package. Quantitative variables were summarized as mean, standard deviation (SD), minimum and maximum or median and minimum and maximum, depending on their normal or non-normal distribution. Ordinal and nominal variables were summarized as frequencies and percentages. Comparisons between groups were analyzed with the Kruskal–Wallis or Mann–Whitney test for quantitative variables and with the Chi-square test or Fisher exact test for qualitative variables. Correlations between clinical and US variables were tested with the Spearman's coefficient. Interobserver and intraobserver reliability were analyzed using weighted kappa (kappa <0.4, low agreement; kappa 0.4–0.6, moderate agreement; kappa 0.6–0.8, good agreement; kappa >0.8, excellent agreement). A p value <0.05 was considered significant.

Results

Demographics and clinical features

There were no significant differences in gender distribution between groups: 29 (48.3%) women and 31 (51.7%) men in the PSA group, 12 (57.1%) women and 9 (42.9%) men in the PsO group, and 13 (65%) women and 7 (35%) men the healthy control group ($p=0.403$). The median (range) age was 53.0 (26–83) years for the PsA group, 56.0 (24–69) years for the PsO group, and 31.5 (23–60) years for the control group, the latter being significantly lower than the age of PSA/PsO patients ($p<0.001$). The median (range) duration of the skin diseases was 13.0 (0.5–63) years for the PsA group and 10.0 (0.5–48) years for the PsO group ($p=0.593$). The median (range) duration of PsA was 7.0 (0.5–35) years.

Clinical nail involvement (i.e., NAPSI >0) was significantly greater in PsO patients than in PsA patients. In the PsO group, 106 (50.5%) nails in 13 (61.9%) patients were involved vs 127 (21.2%) nails in 23 (38.3%) patients in the PsA group ($p<0.001$).

Twenty (33.3%) PsA patients were on synthetic disease-modifying antirheumatic drugs (DMARD), 20 (33.3%) PsA patients on biologic DMARD and 9 (15%) PsA patients on both synthetic and biologic DMARD. Two (9.5%) PsO were on synthetic DMARD and none on biologic DMARD. Most (15, 71.4%) PsO patients but only a few (2, 3.3%) PsA patients were on topical therapy or phototherapy.

The total NAPSI and PASI were significantly higher in PsO than in PsA patients: median (range) 5.0 (0–40) vs 0.0 (0–40) ($p=0.012$); and 3.0 (0–15.7) vs 0.0 (0–12.6) ($p<0.001$), respectively.

The median (range) TJC, SJC, TDIPC, SDIPC, and MASES for PsA patients were 1.0 (0–21), 0.0 (0–10), 0.0 (0–10), 0.0(0–10), and 0.0 (0–7), respectively. For the PsA group, the median (range) CRP was 0.30 (0.10–75) mg/l and the median (range) ESR 10.50 (2–82) mm/h.

Comparison of US variables between PsA, PsO and healthy controls

Supplementary Table 1 displays the distribution of scores for BM and CD in the control, PsO and PsA groups. In the control group, BM-Sc was 0 in most nails (92.5%), none of the nails showed BM-Sc > 2 and only 1 (0.5%) nail showed BM-Sc 2. A CD-Sc2 > 1 was not found in the control group nails and most nails (71.5%) were scored 0. However, there was a variable distribution of CD-Sc1, CD-Sc3 and CD-Sc4 grades among the nails of the healthy subjects.

Comparisons of TNB, TNP and BM and CD scores between controls, PsO and PsA groups at nail level and patient level are shown in Table 1. TNB and TNP were significantly higher in PsO and PsA nails than in controls and significantly higher in PsO as compared to PsA nails. From the US scores, only BM-Sc and CD-Sc2 at nail and patient levels were significantly higher in PsO and PsA nails/patients than in control nail/patients. CD-Sc1 was significantly higher in PsA nails than in control nails and PsO nails but without significant differences between control and PsO nails or at patient level. CD-Sc3 was also significantly higher in PsA nails than in PsO nails.

Table 2 displays the comparisons of TNB, TNP, BM score and CD scores between control and PsO + PsA groups at nail level and patient level. Again, TNB, TNP, BM-Sc and CD-Sc2 were significantly higher in the PsO/PsA group than in the control group both at nail and patient level. The remaining CD scores were not significantly different in controls and PsO/PsA patients.

Table 3 displays the comparisons of TNB, TNP, BM score and CD scores between control and PsO/PsA nails and patients with NAPSI > 0 and total NAPSI > 0, respectively. These comparisons showed similar results that those from the whole PsO/PsA population.

Table 4 shows the comparisons of TNB, TNP, BM score and CD scores between control and PsO/PsA nails and patients with NAPSI = 0 and total NAPSI = 0, respectively. Even in nails and patients without clinical involvement TNB, TNP, BM-Sc and CD-Sc2 were significantly higher in the PsO/PsA group than in the control group.

Comparisons of US variables between PsO/PsA nails clinically involved and not involved and PsO/PsA patients with and without nail involvement are displayed in Table 5. TNB, TNP and BM-Sc were significantly higher in involved nails than in not involved nails while all CD scores did not show significant differences between both clinically determined groups.

Table 6 shows US variables at nail level and patient level in PsO/PsA patients with and without treatment with either synthetic or biologic DMARD. There were no significant differences between both groups except for the CD-Sc1, which was significantly higher in patients with DMARD therapy.

Table 1 Comparisons of TNB, TNP, BM score and CD scores between control, PsO and PsA groups at nail level and patient level

US variables	Control group nails ($n = 200$)	PsO group nails ($n = 210$)	PsA group nails ($n = 600$)	p values*
TNB (mm), median (range)	1.6 (0.15–2.9)	1.9 (0.85–3.1)	1.8 (0.2–4.6)	$< 0.001^{A}$
TNP (mm), median (range)	0.12 (0.06–1.12)	0.15 (0.09–1.5)	0.15 (0.05–2)	$< 0.001^{A}$
BM-Sc, median (range)	0.0 (0–2)	0.0 (0–4)	0.0 (0–4)	$< 0.001^{A}$
CD-Sc1, median (range)	1.0 (0–2)	1.0 (0–2)	1.0 (0–2)	$< 0.001^{B}$
CD-Sc2, median (range)	0.0 (0–1)	0.0 (0–2)	0.0 (0–2)	$< 0.001^{C}$
CD-Sc3, median (range)	1.0 (0–3)	1.0 (0–3)	1.0 (0–3)	0.034^{D}
CD-Sc4, median (range)	1.0 (0–3)	1.0 (0–3)	1.0 (0–3)	0.075
US variables	Control group ($n = 20$)	PsO group ($n = 21$)	PsA group ($n = 60$)	p values*
BM-GSc, median (range)	0.0 (0–4)	7.5 (0–31)	6.0 (0–31)	$< 0.001^{C}$
CD-GSc1, median (range)	11.0 (0–18)	10.1 (0–17)	11.0 (1–20)	0.384
CD-GSc2, median (range)	2.0 (0–9)	5.5 (0–13)	5.0 (0–11)	0.027^{A}
CD-GSc3, median (range)	15.5 (0–26)	13.5 (4–27)	16.0 (3–30)	0.576
CD-GSc4, median (range)	15.5 (0–23)	13.0 (2–26)	15.0 (2–30)	0.562

US ultrasound, *PsO* psoriasis, *PsA* psoriatic arthritis, *TNB* nail bed thickness, *TNP* nail plate thickness, *BM* B-mode, *CD* color Doppler, *Sc* score, *Gsc* global score

*Kruskal–Wallis

[A]Mann–Whitney post hoc $p < 0.05$ differences between control and PsO groups, control and PsA groups, and PsO and PsA groups

[B] Mann–Whitney post hoc $p < 0.05$ differences between control and PsA groups, and PsO and PsA groups

[C]Mann–Whitney post hoc $p < 0.05$ differences between control and PsO groups, and control and PsA groups

[D] Mann–Whitney post hoc $p < 0.05$ differences between PsO and PsA groups

Table 2 Comparisons of TNB, TNP, BM score and CD scores between control group and PsO/PsA group at nail level and patient level

US variables	Control group nails ($n=200$)	PsO/PsA group nails ($n=810$)	p values
TNB (mm), median (range)	1.6 (0.15–2.9)	1.8 (0.20–4.6)	< 0.001
TNP (mm), median (range)	0.12 (0.06–1.12)	0.15 (0.05–2)	< 0.001
BM-Sc, median (range)	0.0 (0–2)	0.0 (0–4)	< 0.001
CD-Sc1, median (range)	1.0 (0–2)	1.0 (0–2)	0.320
CD-Sc2, median (range)	0.0 (0–1)	0.0 (0–2)	< 0.001
CD-Sc3, median (range)	1.0 (0–3)	1.0 (0–3)	0.197
CD-Sc4, median (range)	1.0 (0–3)	1.0 (0–3)	0.544
US variables	Control group ($n=20$)	PsO/PsA group ($n=81$)	p values
BM-GSc, median (range)	0.0 (0–4)	7.0 (0–31)	< 0.001
CD-GSc1, median (range)	11.0 (0–18)	10.93 (1–20)	0.220
CD-GSc2, median (range)	2.0 (0–9)	5.14 (0–13)	0.007
CD-GSc3, median (range)	15.5 (0–26)	16.41 (3–30)	0.197
CD-GSc4, median (range)	15.5 (0–23)	15.09 (2–30)	0.544

US ultrasound, *PsO* psoriasis, *PsA* psoriatic arthritis, *TNB* nail bed thickness, *TNP* nail plate thickness, *BM* B-mode, *CD* color Doppler, *Sc* score, *Gsc* global score

Table 3 Comparisons of TNB, TNP, BM score and CD scores between control and PsO/PsA nail and patients with NAPSI > 0 and total NAPSI > 0, respectively

US variables	Control group nails ($n=200$)	PsO/PsA group nails, NAPSI > 0 ($n=233$)	p values
TNB (mm), median (range)	1.6 (0.15–2.9)	1.9 (1–4.6)	< 0.001
TNP (mm), median (range)	0.12 (0.06–1.12)	0.18 (0–4)	< 0.001
BM-Sc, median (range)	0.0 (0–2)	1.0 (0–4)	< 0.001
CD-Sc1, median (range)	1.0 (0–2)	1.0 (0–2)	0.907
CD-Sc2, median (range)	0.0 (0–1)	1.0 (0–2)	< 0.001
CD-Sc3, median (range)	1.0 (0–3)	1.0 (0–3)	0.825
CD-Sc4, median (range)	1.0 (0–3)	1.0 (0–3)	0.244
US variables	Control group ($n=20$)	PsO/PsA group, total NAPSI > 0 ($n=36$)	p values
BM-GSc, median (range)	0.0 (0–4)	12.0 (0–31)	< 0.001
CD-GSc1, median (range)	11.0 (0–18)	10.5 (0–19)	0.952
CD-GSc2, median (range)	2.0 (0–9)	5.0 (0–13)	0.005
CD-GSc3, median (range)	15.5 (0–26)	15.5 (4–29)	0.879
CD-GSc4, median (range)	15.5 (0–23)	13.5 (2–28)	0.498

US ultrasound, *PsO* psoriasis, *PsA* psoriatic arthritis, *NAPSI* Nail Psoriasis Severity Index, *TNB* nail bed thickness, *TNP* nail plate thickness, *BM* B-mode, *CD* color Doppler, *Sc* score, *Gsc* global score

Representative US images of BM-Sc, CDSc1 and CD-Sc2 are shown in Supplementary Fig. 1a–e, Fig. 2a–c, and Fig. 3a–c, respectively.

Relation between clinical and US variables

In PsO/PsA patients, total NAPSI showed a significant moderate positive correlation with BM-GSc ($r=0.506$, $p<0.001$). Age showed a significant weak negative correlation with CD-GSc1 ($r=-0.243$, $p=0.029$), CD-GSc3 ($r=-0.341$, $p=0.002$), and CD-GSc4 ($r=-0.231$, $p=0.038$). There was a significant weak positive correlation between PsO duration and BM-GSc ($r=0.242$, $p=0.029$) and a significant weak negative correlation between PsO duration and CD-GSc1 ($r=-0.255$, $p=0.022$), CD-GSc3 ($r=-0.227$, $p=0.042$), and CD-GSc4 ($r=-0.272$, $p=0.014$).

In PsA patients, BM-GSc showed a significant weak positive correlation with CRP ($r=0.356$, $p=0.003$) and a significant weak negative correlation with TCJ ($r=-0.311$, $p=0.015$). No other significant correlations were found (data not shown).

Table 4 Comparisons of TNB, TNP, BM score and CD scores between control and PsO/PsA nails and patients with NAPSI = 0 and total NAPSI = 0, respectively

US variables	Control group nails ($n = 200$)	PsO/PsA group nails NAPSI = 0 ($n = 577$)	p values
TNB (mm), median (range)	1.6 (0.15–2.9)	1.8 (0.2–3.1)	< 0.001
TNP (mm), median (range)	0.12 (0.06–1.12)	0.15 (0.05–0.32)	< 0.001
BM-Sc, median (range)	0.0 (0–2)	0.0 (0–4)	< 0.001
CD-Sc1, median (range)	1.0 (0–2)	1.0 (0–2)	0.110
CD-Sc2, median (range)	0.0 (0–1)	0.0 (0–2)	< 0.001
CD-Sc3, median (range)	1.0 (0–3)	2.0 (0–3)	0.103
CD-Sc4, median (range)	1.0 (0–3)	1.0 (0.76, 0–3)	0.171
US variables	Control group ($n = 20$)	PsO/PsA group, total NAPSI = 0 ($n = 45$)	p values
BM-GSc, median (range)	0.0 (0–4)	4.0 (0–23)	< 0.001
CD-GSc1, median (range)	11.0 (0–18)	11.0 (1–20)	0.454
CD-GSc2, median (range)	2.0 (0–9)	5.0 (0–10)	0.032
CD-GSc3, median (range)	15.5 (0–26)	16.0 (3–30)	0.540
CD-GSc4, median (range)	15.5 (0–23)	15.0 (2–30)	0.716

US ultrasound, *PsO* psoriasis, *PsA* psoriatic arthritis, *NAPSI* Nail Psoriasis Severity Index, *TNB* nail bed thickness, *TNP* nail plate thickness, *BM* B-mode, *CD* color Doppler, *Sc* score, *Gsc* global score

Table 5 Comparisons of US variables between PsO/PsA nails and patients with NAPSI > 0 and total NAPSI > 0 and those with NAPSI = 0 and total NAPSI = 0, respectively

US variables	PsO/PsA group nails NAPSI > 0 ($n = 233$)	PsO/PsA group nails NAPSI = 0 ($n = 577$)	p values
TNB (mm), median (range)	1.9 (1–4.6)	1.8 (0.2–3.1)	< 0.001
TNP (mm), median (range)	0.18 (0–4)	0.15 (0.05–0.32)	< 0.001
BM-Sc, median (range)	1.0 (0–4)	0.0 (0–4)	< 0.001
CD-Sc1, median (range)	1.0 (0–2)	1.0 (0–2)	0.102
CD-Sc2, median (range)	1.0 (0–2)	0.0 (0–2)	0.167
CD-Sc3, median (range)	1.0 (0–3)	2.0 (0–3)	0.097
CD-Sc4, median (range)	1.0 (0–3)	1.0 (0.76, 0–3)	0.002
US variables	PsO/PsA group, total NAPSI > 0 ($n = 36$)	PsO/PsA group, total NAPSI = 0 ($n = 45$)	p values
BM-GSc, median (range)	12.0 (0–31)	4.0 (0–23)	< 0.001
CD-GSc1, median (range)	10.5 (0–19)	11.0 (1–20)	0.323
CD-GSc2, median (range)	5.0 (0–13)	5.0 (0–10)	0.136
CD-GSc3, median (range)	15.5 (4–29)	16.0 (3–30)	0.445
CD-GSc4, median (range)	13.5 (2–28)	15.0 (2–30)	0.085

US ultrasound, *PsO* psoriasis, *PsA* psoriatic arthritis, *NAPSI* Nail Psoriasis Severity Index, *TNB* nail bed thickness, *TNP* nail plate thickness, *BM* B-mode, *CD* color Doppler, *Sc* score, *Gsc* global score

Reliability of US scoring

The interobserver and intraobserver reliability for BM-Sc, CD-Sc1 and CD-Sc2 were good or excellent with interobserver kappa values between the two rheumatologist ultrasonographers of 0.828, 0.869 and 0.858, respectively, and intraobserver kappa values of 0.855, 0.768 and 0.846, respectively, for the first ultrasonographer and 0.757, 0.829 0.925, respectively, for the second ultrasonographer.

Table 6 Comparisons of US variables in patients with and without DMARD therapy

US variables	PsO/PsA group nails with DMARD ($n=510$)	PsO/PsA group nails without DMARD ($n=300$)	p values
TNB (mm), median (range)	1.8 (0.2–4.6)	1.8 (0.85–2.7)	0.873
TNP (mm), median (range)	0.16 (0.05–2)	00.15 (0.09–1.50)	0.115
BM-Sc, median (range)	0.0 (0–4)	0.0 (0–4)	0.608
CD-Sc1, median (range)	1.0 (0–2)	1.0 (0–2)	0.001
CD-Sc2, median (range)	0.0 (0–2)	0.0 (0–2)	0.690
CD-Sc3, median (range)	2.0 (0–3)	1.0 (0–3)	0.092
CD-Sc4, median (range)	1.0 (0–3)	1.0 (0–3)	0.173
US variables	PsO/PsA group with DMARD ($n=51$)	PsO/PsA group without DMARD ($n=30$)	p values
BM-GSc, median (range)	7.0 (0–31)	7.0 (0–31)	0.814
CD-GSc1, median (range)	11.0 (1–19)	10.5 (0–20)	0.221
CD-GSc2, median (range)	5.0 (0–11)	6.0 (0–13)	0.768
CD-GSc3, median (range)	16.0 (3–29)	15.5 (4–30)	0.521
CD-GSc4, median (range)	15.0 (2–28)	14.0 (2–30)	0.450

US ultrasound, *PsO* psoriasis, *PsA* psoriatic arthritis, *DMARD* disease-modifying antirheumatic drugs, *TNB* nail bed thickness, *TNP* nail plate thickness, *BM* B-mode, *CD* color Doppler, *Sc* score, *Gsc* global score

Discussion

Although a few case–control studies comparing US characteristics of psoriatic nails with non-psoriatic nails have been published [9, 11, 12, 14, 16], our study provided the largest population of PsA and PsO patients where a wide spectrum of US parameters of the nail were assessed with US.

In accordance with previously published data [9, 11, 12, 14], our results showed that the nail bed thickness and the plate thickness were significantly higher in nails from psoriatic, either PsO or PsA patients than in nails from healthy individuals. In addition, and also as previously described [12], although these measures were significantly higher in clinically involved nails than in clinically non-involved nails of PsO/PsA patients, they were also significantly higher in nails without clinical involvement from PsO/PsA patients as compared to controls. Normal cut-off points for nail bed thickness with variable numbers [eg, < 3 mm; < 2.5 mm; < 2 mm] have been calculated in a few studies [9, 10, 13, 14] which, as our study, were not designed for this purpose because of their insufficient sample size.

We developed a BM score and two CD scores (i.e., CD-Sc1 and CD-Sc2) that showed high inter- and intraobserver reliability, similar to that reported for other scoring systems used in psoriatic nail [13, 15]. Our novel BM score of nail plate integrity discriminated between the control group and the PsO/PsA group with or without clinical involvement, which was confirmed at nail level and at patient level. In fact, loss of integrity of the ventral plate beyond the matrix area or involvement of both ventral and dorsal plate was found almost exclusively on nails from PsO/PsA patients. Our results were consistent with those from previous studies [9, 10, 14–16] that have shown characteristic BM structural abnormalities at the psoriatic nail plate on which we based our score.

Regarding CD scores, our results were of particular interest. We tested four CD scoring systems at nail level and at patient level. The first one was a simplified version of the score developed by Gutierrez et al. [13] in which we evaluated the percentage of the nail bed and nail matrix together (as they are a continuous structure from an anatomical and US perspective) occupied by CD signals. In the second one, following Wortsman's descriptions [8], we scored the amount of CD signals in the nail bed in contact with the ventral plate. The third and fourth scores consisted of the score by Gutierrez et al. [13] applied separately for the nail matrix and the nail bed as used in the study by Arbault et al. [15]. Of them, only the grade of contact of CD signals with the ventral plate of the nail, showed discriminative utility between control nails and patients and PsO/PsA nails and patients, respectively, with or without clinical nail involvement. Of particular note was that, independently of the amount of CD signals in the nail bed, we did not find extensive contact between them and the ventral plate in any control nail. Unlike the BM score, this CD score did not show significant differences between clinically involved and clinically non-involved nails of PsO/PsA patients.

In contrast with previous studies [9, 14, 16], the CD scores based on the percentage of the nail bed/matrix occupied by Doppler signals, although in general were higher in PsA nails than in control nails, did not consistently discriminate between control nails and nails from PsO/PsA patients since the amount of CD-detected blood flow in the nail bed/matrix was highly variable among healthy subjects.

Marina et al. [16] found significantly increased CD signals scored according to Gutierrez et al. [13] in the nail bed of 23 PsO patients as compared to 11 healthy controls. They included PsO patients with moderate to severe skin disease (i.e., PASI > 10) while they excluded patients in systemic or topical therapy. Conversely, most of our patients were on DMARD or topical treatment/phototherapy and showed low PASI-measured skin disease activity. Thus, although we found neither relevant differences in the CD scores between DMARD-treated and non-DMARD-treated patients nor significant correlations between CD scores and PASI, it is possible that a low disease activity and/or the effect of either systemic or topical therapy may have reduced CD-detected nail bed flow in our patients. Nevertheless, it is of particular attention that using the same scoring system (i.e., CD-Sc4), while Marina et al. [16] did not find grade 2 and 3 in controls, we found these scores in almost 50% of the control nails for which we have no explanation except the hypothesis that either their different machine settings (i.e., 6.5–13 MHz BM frequency, CD frequency not provided) or the difference in age between their controls (46.09 ± 11.8 years) and ours (37.7 ± 10.6 years) may have influenced. Gutierrez et al. [9] and Sandobal et al. [14] also reported increased power Doppler-detected blood flow in the nail bed of PsO patients as compared to controls but these authors did not provide definition for increased Doppler signal in the nail bed neither did they use any scoring system for that in these studies. On the contrary, our results were consistent with those from the study by Aydin et al. [17]. This study [17] also showed no differences in the presence of power Doppler signal in the nail bed between psoriatic nails and healthy controls. In fact, these authors [17] found more power Doppler-scored nail vascularity in nails of healthy controls as compared to psoriatic nails. Thus, the discriminative capacity of the amount of Doppler-detected nail bed blood flow for PsO/PsA needs further clarification.

Among all potential correlations between clinical and US parameters, only the total NAPSI and the global B score showed a consistent positive correlation. Thus, it seems that US parameters of the nail are independent of markers of skin and joint disease activity, and that Doppler scores are not related with clinical score of nail involvement.

Some limitations in our study should be noted. The PsA/PsO population was very heterogeneous regarding skin and joint disease duration. In particular, the greater clinical nail involvement in PsO patients than in PsA patients could explain that BM abnormalities were more severe in PsO than in PsA nails. In addition, the control population was relatively small and younger than the PsA/PsO population. Both facts may have biased the results. Furthermore, we tested reliability only for the novel scores as the other measures and scores have been already successfully tested in previous studies [13, 15].

In conclusion, we propose measurement of nail bed and plate thickness, BM-scored nail plate abnormalities and CD-scored contact of Doppler signal with the nail ventral plate as US discriminative markers in the psoriatic nail. Further studies on their diagnostic utility in early disease, their responsiveness, and their added value in PsO and PsA management are warranted.

Author contributions Study design: EN. Acquisition of data: IJ, OBR, LV, MH, NB, BS, and EN. Analysis and interpretation of data: EN and JG. Manuscript drafting: EN, IJ, and JG. Manuscript revision and approval: IJ, OBR, LV, MH, NB, BS, JG, and EN.

Funding This work was supported by UCB Pharma through a publication Grant, and underwent courtesy review by UCB Pharma.

Compliance with ethical standards

Conflict of interest Esperanza Naredo, Iustina Janta, Ofelia Baniandres-Rodriguez, Lara Valor, Michelle Hinojosa, Natalia Bello, Belén Serrano, and Jesús Garrido declare that they have no conflict of interest relating to the topic.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Langley RG, Krueger GG, Griffiths CE (2005) Psoriasis: epidemiology, clinical features, and quality of life. Ann Rheum Dis 64(Suppl 2):ii18–i23
2. Gladman DD, Antoni C, Mease P, Clegg DO, Nash P (2005) Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Ann Rheum Dis 64(Suppl 2):ii14–i7
3. Sánchez-Regaña M. Umbert P (2008) Diagnosis and management of nail psoriasis. Actas Dermosifiliogr 99:34–43
4. Wilson FC, Icen M, Crowson CS, McEvoy MT, Gabriel SE, Kremers HM (2009) Incidence and clinical predictors of psoriatic arthritis in patients with psoriasis: a population-based study. Arthritis Rheum 61:233–239
5. Rich P, Scher RK (2003) Nail Psoriasis Severity Index: a useful tool for evaluation of nail psoriasis. J Am Acad Dermatol 49:206–212
6. Cassell SE, Bieber JD, Rich P, Tutuncu ZN, Lee SJ, Kalunian KC, Wu CW, Kavanaugh A (2007) The modified Nail Psoriasis Severity Index: validation of an instrument to assess psoriatic nail involvement in patients with psoriatic arthritis. J Rheumatol 34:123–129
7. Østergaard M, Eder L, Christiansen SN, Kaeley GS (2016) Imaging in the diagnosis and management of peripheral psoriatic arthritis-The clinical utility of magnetic resonance imaging and ultrasonography. Best Pract Res Clin Rheumatol 30:624–637
8. Wortsman X, Jemec GB (2006) Ultrasound Imaging of nails. Dermatol Clin 24:323–328

9. Gutierrez M, Wortsman X, Filippucci E, De Angelis R, Filosa G, Grassi W (2009) High-frequency sonography in the evaluation of psoriasis nail and skin involvement. Ultrasound Med 28:1569–1574
10. Gutierrez M, Filippucci E, De Angelis R, Filosa G, Kane D, Grassi W (2010) A sonographic spectrum of psoriatic arthritis: "the five targets". Clin Rheumatol 29:133–142
11. Aydin SZ, Castillo-Gallego C, Ash ZR, Marzo-Ortega H, Emery P, Wakefield RJ, Wittmann M, McGonagle D (2012) Ultrasonographic assessment of nail in psoriatic disease shows a link between onychopathy and distal interphalangeal joint extensor tendon enthesopathy. Dermatology 225:231–235
12. Gisondi P, Idolazzi L, Girolomoni G (2012) Ultrasonography reveals nail thickening in patients with chronic plaque psoriasis. Arch Dermatol Res 304:727–732
13. Gutierrez M, Di Geso L, Salaffi F, Bertolazzi C, Tardella M, Filosa G, Filippucci E, Grassi W (2012) Development of a preliminary US power Doppler composite score for monitoring treatment in PsA. Rheumatology 51:1261–1268
14. Sandobal C, Carbó E, Iribas J, Roverano S, Paira S (2014) Ultrasound Nail Imaging on Patients With Psoriasis and Psoriatic Arthritis Compared With Rheumatoid Arthritis and Control Subjects. J Clin Rheumatol 20:21–24
15. Arbault A, Devilliers H, Laroche D, Cayot A, Vabres P, Maillefert JF, Ornetti P (2016) Reliability, validity and feasibility of nail ultrasonography in psoriatic arthritis. Joint Bone Spine 83:539–544
16. Marina ME, Solomon C, Bolboaca SD, Bocsa C, Mihu CM, Tătaru AD (2016) High-frequency sonography in the evaluation of nail psoriasis. Med Ultrason 18:312–317
17. Aydin SZ, Castillo-Gallego C, Ash ZR, Marzo-Ortega H, Wakefield R, McGonagle D (2017) Vascularity of nail bed by ultrasound to discriminate psoriasis, psoriatic arthritis and healthy controls. Clin Exp Rheumatol 35:872
18. Taylor W, Gladman D, Helliwell P, Marchesoni A, Mease P, Mielants H, CASPAR Study Group (2006) Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 54:2665–2673
19. Langley RG, Ellis CN (2004) Evaluating psoriasis with psoriasis area and severity index, psoriasis global assessment, and lattice system physician's global assessment. J Am Acad Dermatol 51:563–569
20. Heuft-Dorenbosch L, Spoorenberg A, van Tubergen A, Landewé R, van ver Tempel H, Mielants H, Dougados M, van der Heijde D (2003) Assessment of enthesitis in ankylosing spondylitis. Ann Rheum Dis 62:127–132