Dermatology Practical & Conceptual

Clinical and Ultrasonographic Assessment of Nail Psoriasis: A Comprehensive Study

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Key words: Nail Psoriasis, High Frequency Ultrasound, Psoriatic Arthritis, Psoriasis Diagnosis

Citation: Esposito M, Magnanimi LM, Antonetti P, et al. Clinical and Ultrasonographic Assessment of Nail Psoriasis: A Comprehensive Study. *Dermatol Pract Concept*. 2025;15(3):5318. DOI: https://doi.org/10.5826/dpc.1503a5318

Accepted: January 13, 2025; **Published:** July 2025

Funding: This work was supported by "Bando per il finanziamento dei progetti DISCAB anno 2023 (Progetto di ricerca codice 07_DG_2023_05)" from Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

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ABSTRACT

Introduction: In patients with plaque type psoriasis (PsO), the progression to psoriatic arthritis (PsA) exacerbates the disease's impact and increases disability risk. Nail psoriasis (NP) affects up to 90% of PsO patients, with a wide spectrum of clinical features, and is a significant predictor of enthesitis, often associated with early PsA stages.

Objective: This study aimed to clinically and ultrasonographically evaluate nail units in PsO patients, focusing on differences between those with/without PsA and those with/without onychopathy.

Methods: Sixty patients were enrolled (23/60 PsO and 37/60 PsO and PsA). PsO and PsA patients were evaluated and compared, as were patients with/without diagnosis of nail psoriasis in this cross-sectional single-center study. Nail abnormalities were evaluated by high frequency ultrasound (HFUS) using high frequency probes (27 MHz). After a descriptive assessment, the Nail Psoriasis Severity Index (NAPSI) and the Brown University Nail Enthesis Scale (BUNES) were used to clinically and ultrasonographically assess nails.

Results: HFUS evaluation identified a spectrum of nail and blood flow alterations. Nail disease was characterized by median NAPSI 16 (range 28), median BUNES morphometry 1.5 (range 0.9), and median BUNES power doppler (PD) 2.2 (range 4.03). Among the studied sample, 43/60 (71.7%)

presented nail psoriasis, with 69.7% presenting coexisting PsA as compared to PsO patients (30.3%) (P=0.04).

Conclusion: Our findings highlight the importance of close collaboration between dermatologists and rheumatologists in the evaluation of PsO patients, taking advantage of both clinical and ultrasonographic assessment of nail damage.

Introduction

Plaque-type psoriasis (PsO) is a chronic immune-mediated inflammatory disease characterized by consistent morbidity and quality of life impact. Progression to psoriatic arthritis (PsA) increases the impact of the disease and the risk of disability [1]. Nail involvement is estimated to be present in up to 90% of the patients affected by PsO, with a wide spectrum of clinical characteristics [2]. Nail psoriasis (NP) is an important predictor of enthesitis, which is associated with the early stages of PsA; for this reason, it is important for dermatologists to diagnose and treat NP early in order to prevent nail damage and potentially delay the onset and progression of joint disease [3]. Recent studies have explored the causal link between enthesitis and nail damage, revealing the importance of nail involvement in the transition from PsO to PsA, confirming that morphological changes of the nails are predominantly described in patients with PsA [4, 5, 6]. Mahmoud et al. [7] found that nail changes were associated with thicker extensor tendon and more erosions. Elliot et al. [8] confirmed a correlation between clinical and ultrasound (US) nail involvement with distal interphalangeal enthesitis and established a significant association between US nail changes and the Madrid Sonographic Enthesitis Index (MASEI), a clinical score of peripheral entheses.

Clinical signs related to nail bed apparatus involvement include onycholysis, "oil drop" discoloration, splinter hemorrhages, and subungual hyperkeratosis, while signs related to nail matrix disease involvement include pitting, leukonychia, red spots in lunula, and nail plate crumbling [2]. The severity of nail involvement can be assessed and monitored by the Nail Psoriasis Severity Index (NAPSI) [9]; however, it is not able to evaluate parameters such as nail bed and matrix thickness, nor can it evaluate and quantify blood microflow. In this regard, US imaging has the advantage of evaluating these parameters and identifying even subclinical nail involvement [2,10]. Moreover, US could be important to detect subclinical enthesitis in patients either with or without clinically detectable nail involvement, allowing treatment adjustment [6,11,12]. Indeed, US, especially high frequency ultrasonography (HFUS) with power doppler (PD), is able to reveal detailed information on both the structure of the nail, adjacent tissues, and the microvasculature [13].

The integration of clinical and US evaluation of nails represents an innovative approach to diagnosing and monitoring NP and PsA. Traditional clinical assessment provides an evaluation of severity and extent of NP but can be insufficiently sensitive to detect early or subtle changes. On the other hand, HFUS allows a detailed assessment of structural and vascular changes in the nails, which may indicate early stage PsA. Therefore, combining both the assessments provides a more comprehensive clinical picture, improving sensitivity in the early diagnosis of PsA.

Objective

The aim of our study was to clinically and ultrasonographically evaluate the nail units of patients with a diagnosis of PsO, in particular to evaluate whether there were differences between PsO patients with/without PsA and with/without nail involvement.

Methods

Diagnosis and Clinical and HFUS Features

We performed a cross-sectional single-center study. PsO patients were selected from among those consecutively admitted to the Dermatology and/or Rheumatology Clinics of the University of l'Aquila, Italy, from June to December 2022. Diagnosis of PsO and PsA was performed by expert specialized clinicians. Two groups of patients were categorized: (i) patients affected by PsO without any musculoskeletal involvement (PsO group); (ii) patients affected by PsO and coexistent psoriatic inflammatory joint involvement (PsA group). The CASPAR criteria were used to diagnose PsA [14]. Inclusion criteria were voluntary adult patients (> 18 years) with a minimum disease duration of one year. Patients were excluded if treated with ongoing systemic immunomodulating therapies for PsO and/or PSA, insufficient wash-out period from previous systemic immunomodulating therapies, and/or other medical conditions potentially influencing nail and enthesis conditions. An adequate wash-out period was codified as the discontinuation for a time of at least three half-lives of the administered drugs. Clinical evaluation was based on the assessment of the Psoriasis Area and Severity Index (PASI) and body surface area (BSA), which

were used to measure PsO disease severity and extension and NAPSI for nail disease involvement [15,16,9].

For NAPSI score assessment, we considered the pathological nail that can develop from inflammation of the nail bed, nail matrix, or both. The Dermatology Life Quality Index (DLQI) was also used to assess patients' quality of life (QoL) [17]. The Psoriasis Epidemiology Screening Tool (PEST) was used to screen patients for the risk of PsA [18].

HFUS was carried out at the Radiology Department of the San Salvatore Hospital using high frequency probes (27 MHz), available on US machines (Esaote my Lab X8), having available a software implementation improving the quality of US imaging with color Doppler.

The US evaluation was performed by a radiologist with 10 years of US experience and five years of experience in musculoskeletal and nail pathology; the intra-operator reliability was high, as shown by an excellent intraclass correlation coefficient (ICC), while inter-operator evaluation was not performed.

The imaging parameters for Doppler US examinations were set to increase the detection of low-velocity, low-volume flows within the inside of the nail bed and tendon enthesis. The PD specifications have been standardized through a frequency ranging from 10.0 to 12.5 MHz and pulse repetition frequencies ranging from 0.9 to 1.0 kHz; color gain was set to avoid excessive color noise (color vs. echo priority ranging from 40 to 60% and color persistence adjusted to high values).

US assessment of nail abnormalities was performed by evaluating both hands in all subgroups of patients. All ten nails of the hands were studied. The longitudinal scan identify nail plate, composed of two hyperechoic lines representing the dorsal and ventral areas, with a virtual anechoic space between them; nail bed is characterized by a hypoechoic band between the superior hyperechoic nail plate and the inferior hyperechoic distal phalanx, while nail matrix is visualized as an isoechoic region under the proximal nailfold at the proximal portion of the nail bed.

The Brown University Nail Enthesis Scale (BUNES) was used to evaluate different nail structures and PD activity [19]. Morphologic normal findings were indicated with a score of 0 for each area scanned (nail plate, matrix, and bed). Nail plate changes, abnormal or thickened nail beds (2.0–3.0 mm) and/or matrix were scored as 1. Nail bed and matrix PD findings were assessed as 0=no signal, 1=confluent signal in <25% of the area, 2=confluent signal in >25% and <50%, or 3=confluent signal >50%. A mean score of BUNES morphometry of 1.5 and a mean score of BUNES PD of 3 were used as thresholds to identify pathologic nail involvement.

Statistical Analysis

Statistics first provided a descriptive assessment of registered clinical features of our cohort of patients. Collected continuous variables are presented as median and interquartile range (IQR) considering their distribution. Dichotomic variables are expressed as number and percentage. Clinical characteristics were compared, according to the presence of onychopathy or PsA, by non-parametric t-test for continuous variables and chi-squared test for categorical ones, as appropriate. In addition, possible correlations between values of NAPSI and other continuous variables were estimated by Spearman's rank correlation coefficient. Point biserial correlation was used to estimate possible correlation between NAPSI and dichotomic variables. Due to the relatively simple study design, few retrieved missing data were managed by the exclusion of these from analyses. Two-sided p-values of ≤0.05 were considered as being statistically significant. The Statistics Package for Social Sciences (SPSS for Windows, version 22.0, SPSS Inc., Chicago, IL, USA) was used for all analyses.

Results

A total of 60 PsO patients were studied (Table 1): 22 males (36.7%), 38 females (63.3%); the median age was 53 years (range 18.75), median disease duration was 10 years (range 18),

Table 1. Clinical and Ultrasonographic Findings in Patients Studied.

Characteristics of Patients		No. of Samples N = 60
Sex	Males (%)	22 (36.7)
	Females (%)	38 (63.3)
Age	Median age (IQR)	53 (18.75)
BMI	Median BMI (IQR)	26.05 (6.46)
Disease duration	Median Disease duration (IQR)	10 (18)
NAPSI	Median NAPSI (IQR)	16 (28)
BUNES Morphometry	Median BUNES M (IQR)	1.5 (0.9)
BUNES PD	Median BUNES PD (IQR)	2.2 (4.0324)
BSA	Median BSA (IQR)	5.0 (10.125)
PASI	Median PASI (IQR)	4.4 (9.6)
PGA	Median PGA (IQR)	1.0 (1)
NRS Itch	Median Itch NRS (IQR)	5.0 (7.250)
DLQI	Median DLQI (IQR)	5.0 (7)
PEST 0_5	Median PEST 0_5 (IQR)	3.0 (3)

Abbreviations: BMI: body mass index; BSA: body surface area; BUNES PD: Brown University Nail Enthesis Scale power Doppler; DLQI: Dermatology Life Quality Index; IQR: interquartile range; NAPSI: Nail Psoriasis Severity Index; NRS: numeric rating scale; PASI: Psoriasis Area and Severity Index; PEST: Psoriasis Epidemiology Screening Tool; PGA: Physician Global Assessment score.

and median PASI score at evaluation was 4.4 (range 9.6). Among PsO patients, there were patients with inverse or genital psoriasis (18.3%) and patients with palmoplantar psoriasis (11.6%). Among the sample, 37/60 (61.6%) presented PsA, while 43/60 (71.6%) received a diagnosis of nail psoriasis. Among patients with onychopathy, 69.7 % were affected with PsA. Clinical observation of nail abnormalities revealed signs related to nail bed apparatus involvement: onycholysis (37.2%), oil drop discoloration (18.6%), splinter hemorrhages (48.8%), subungual hyperkeratosis (44.2%), and signs related to nail matrix disease involvement: pitting (46.5%), leukonychia (18.6%), red spots in lunula (9.3%), and crumbling (46.5%). Median NAPSI score was 16 (range 28).

Demographic and clinical differences between PsO and PsA patients are described in Table 2.

HFUS Nail Features

Descriptively, HFUS evaluation identified different morphological and vascular nail findings in the two groups. In patients with PsO, the structure of nail was mainly preserved, but an increased blood flow, identified by PD, was found as elongated, dilated, and tortuous blood vessels because of an active inflammatory process. Assessing the nails in patients with PsA, HFUS evaluation showed some structural changes. Thickened matrix, inhomogeneous echogenicity nail bed, enlarged nail enthesis, increased blood flow, and loss of ventral and dorsal plate definition were observed in this group of patients. The nail US abnormalities were also scored by BUNES. Median BUNES morphometry was 1.5 (range 0.9), while median BUNES PD was 2.2 (range 4.03). Clinical and ultrasonographic findings of evaluated patients are reported in Table 1.

Clinical/Ultrasonographic Characteristics of Patients With Onychopathy and PsA and Results of Correlation Analysis

Considering the population of patients with onychopathy, 21/43 (48.8%) were males, 30/43 (69.7%) were affected with PsA, the median age was 54 years (range 14), median BMI was 26.70 (range 5.45), median disease duration was 12 years (range 18), median PASI was 4.7 (range 11.8), median DLQI was 5 (range 19), median NAPSI was 24 (range 20.5), median BUNES morphometry was 1.60 (range 2), and median BUNES PD was 2.5 (range 6). A significant difference between patients with and without onychopathy was found in terms of sex (P=0.002), BUNES morphometry (P=0.008), and PSA (P= 0.04).

Considering the population of patients with PsA, 10/37 (27%) were males and 27/37 (73%) were females; the median age was 54 years (range 7.5), median BMI was 26.20 (range 5.6), median disease duration was 10 years (range 50), median PASI was 3 (range 22.8), median DLQI was 6 (range 19), median NAPSI was 20 (range 68), median BUNES morphometry was 1.6 (range 0.9), and median BUNES PD was 1.35 (range 6).

A significant difference between patients with and without PsA was found in terms of sex (P=0.05), age (P=0.04), and PASI (P=0.02) (Table 2).

A further analysis was conducted to explore correlations between NAPSI and clinical/ultrasonographical scores. The correlation analyses estimated significant positive associations between NAPSI and BMI (coefficient/p-values 0.335/0.009), BSA (coefficient/p-values 0.102/0.013), PASI (coefficient/p-values 0.366/0.005), Physician Global Assessment score (PGA) (coefficient/p-values 0.360/0.005), PEST (coefficient/p-values 0.275/0.035), and BUNES morphometry (coefficient/p-values 0.528/<0.001). Table 3 shows correlations between NAPSI and clinical/ultrasonographic scores. Furthermore, no correlation was found between onychopathy and smoking habits, hypertension, DM II, dyslipidemia, heritability, or different variants of psoriasis. In addition, the values of BUNES morphometry correlated with PEST (coefficent 0.295/P=0.029), whereas the values of BUNES PD did not. A clinical and ultrasonographic description of two patients included in the study is provided in Figure 1 and Figure 2.

Discussion

Our cross-sectional study was dedicated to the analysis of clinical and HFUS nail characteristics of a PsO population comparing patients with/without onychopathy and those with/without PsA. Regarding sex-based differences, we observed a higher frequency of female patients among patients with onychopathy and PsA; the disproportion between male (36.7%) and female (63.3%) patients could explain this result. The correlation between the severity of nail lesions, assessed by NAPSI score, and BUNES, BSA, PASI, PGA, PEST scores and body mass index (BMI) was evaluated. The results revealed significant association between NAPSI with BUNES and also with clinical indexes of disease severity, including BSA, PASI, PGA, PEST, and BMI. Unlike other authors, no correlations with smoking habits, hypertension, DM II, dyslipidemia, heritability, or different variants of psoriasis were observed for either onychopathy or PsA.

First, our study proved a correlation between NAPSI and the ultrasonographic features of nails (BUNES). NAPSI is a useful and practical tool to assess nail psoriasis that strongly correlates with HFUS findings. The close correlation we found between NAPSI and BUNES score indicates that HFUS changes of the nail structures are strongly associated with clinically assessed nail damage. Similar results were obtained by Tanaka et al. [20], who recently described

Table 2. Clinical Characteristics by Presence of Onychopathy and Psoriatic Arthritis.

		Onychopathy				PsA		
		Total n=60	No n=17	Yes n=43	p	No n=23	Yes n=37	p
Characteristics of Patients								
Sex	Males, %	22 (36.7)	1 (5.9)	21 (48.8)	0.002	12 (52.2)	10 (27)	0.05
	Females, %	38 (63.3)	16 (94.1)	22(51.1)		11 (47.8)	27 (73)	
Age	Median age (IQR)	53.0 (61)	49.0 (57)	54.0 (14)	0.68	52.0 (57)	54.0 (7.5)	**0.04**
BMI	Median BMI (IQR)	26.05 (15)	23.70 (15)	26.70 (5.45)	0.09	25.50 (15)	26.20 (5.6)	0.88
Disease duration	Median (IQR)	10.0 (50.0)	6.0 (36.0)	12.0 (18)	0.32	10.0 (29)	10.0 (50)	
PASI	Median PASI (IQR)	4.4 (38.8)	4.2 (12.0)	4.7 (11.8)	0.74	7.6 (38.8)	3.0 (22.8)	**0.02**
DLQI	Median DLQI (IQR)	5.0 (24.0)	8.0 (24.0)	5.0 (19.0)	0.37	5.0 (24)	6.0 (19)	0.97
NAPSI total	Median NAPSI total (IQR)	16.0 (68.0)	.000 (18)	24.0 (20.5)	**<0.001**	13.0 (53)	20.0 (68)	0.27
BUNES morphometry	Median BUNES morphometry (IQR)	1.5 (2.4)	1.0 (2.199)	1.60 (2)	**0.008**	1.5 (0.8)	1.6 (0.9)	0.867
BUNES PD	Median BUNES PD (IQR)	2.2 (6.0)	1.1 (5.9)	2.5 (6.0)	0.60	3.0 (6)	1.35 (6)	0.13
Distribution of PSO/PsA	Patients with PSO (%)	23 (38.3)	10 (58.8)	13 (30.2)	**0.04**	-	-	-
	Patient with PsA (%)	37 (61.7)	7 (41.2)	30 (69.7)		-	-	-

Abbreviations: BMI: body mass index; BSA: body surface area; BUNES PD: Brown University Nail Enthesis Scale power Doppler; DLQI: Dermatology Life Quality Index; IQR: interquartile range; NAPSI: Nail Psoriasis Severity Index; NRS: numeric rating scale; PASI: Psoriasis Area and Severity Index; PEST: Psoriasis Epidemiology Screening Tool; PGA: Physician Global Assessment score; PsA: psoriatic arthritis; PSO: plaque type psoriasis.

ultrasonographic and clinical characteristics of the nails of patients with PsO and PsA, with and without nail involvement, and found a positive relationship between the US nail findings and the NAPSI index. The significant positive correlation between NAPSI scores and BUNES values underlines the validity of both methods for the diagnosis and the disease severity assessment of nail psoriasis. In both clinical practice and research studies, experts agree that, despite its limitations, NAPSI is the most reliable scoring system for nail psoriasis [15]. In a previous study, we demonstrated that HFUS is a practical and reliable tool in the clinical setting, capable of detecting nail and enthesis abnormalities in patients with PsO, PsA with PsO, and PsA sine PsO; it was useful in highlighting subclinical nail involvement in patients with PsA sine PsO as well as subclinical enthesis involvement in patients with PsO [11]. In this study, both clinical assessment and HFUS nail changes were demonstrated to be useful tools for a personalized and optimal management of psoriatic disease.

Moreover, we found a positive correlation between NAPSI and the scores of other psoriasis severity scales, including BSA, PASI, and PGA. Indeed, we correlated the severity of fingernail involvement with cutaneous severity tools.

Long et al. [21] found that BSA and PASI scores of patients with nail psoriatic involvement were higher than those without nail disease, suggesting that the disease and the underlying systemic inflammation might be more serious when nail psoriatic symptoms are present. Since NAPSI correlated with BSA, PASI, and PGA, our results confirm that the greater the severity of the disease and the systemic inflammation, the greater the nail damage, in agreement with what has also been reported by others [21, 22, 23].

Notwithstanding the fact that PASI does not include any type of assessment of the severity of nail disease, the positive correlation found also in our patients between the NAPSI and the severity indexes of psoriatic disease documents that nail involvement can predict a greater severity of the disease and a worse quality of life.

NAPSI as well as PASI and PGA demonstrated correlations with both disease severity and risk of PsA development. In daily clinical practice, it is still a challenge for dermatologists to identify those patients with PsO who are at increased risk of developing PsA. In addition to cutaneous extent and

Table 3. Correlations between NAPSI/ Clinical and Ultrasonographic Scores.

	NAPSI	
	Spearman coefficient	p
BMI	0.335	0.009
BSA	0.102	0.013
PASI	0.366	0.005
PGA	0.360	0.005
PEST	0.275	0.035
BUNES morphometry	0.528	<0.001

Abbreviations: BMI: body mass index; BSA: body surface area; BUNES: Brown University Nail Enthesis Scale; NAPSI: Nail Psoriasis Severity Index; NRS: numeric rating scale; PASI: Psoriasis Area and Severity Index; PEST: Psoriasis Epidemiology Screening Tool; PGA: Physician Global Assessment score.

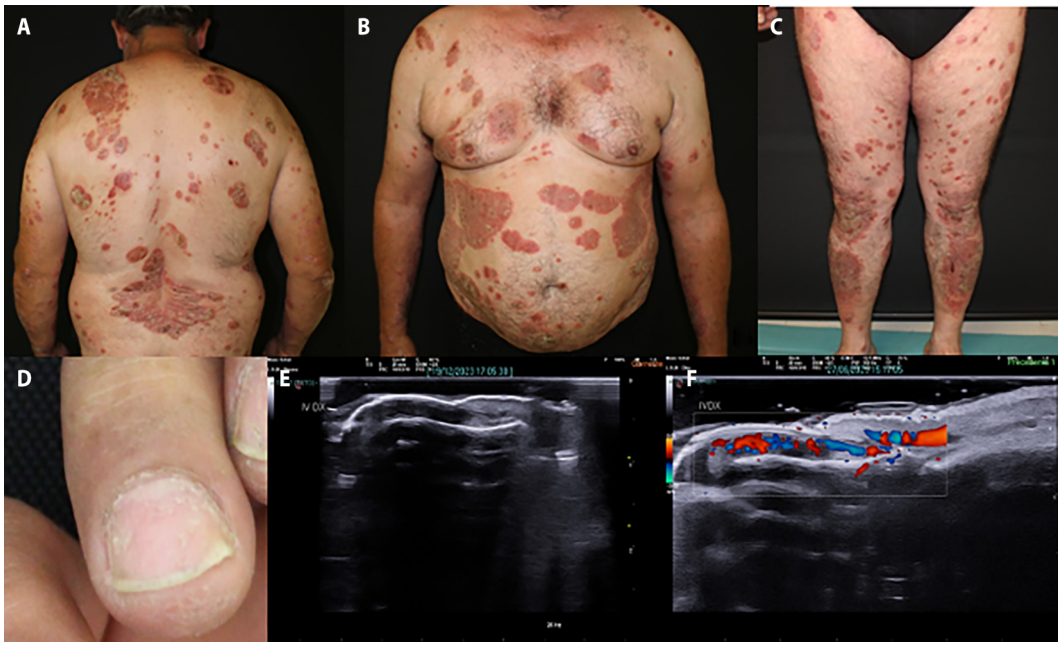

Figure 1. (A-C) A clinical case of a male patient, 54 years old, PASI 38.8, BSA 65, BMI 28 (D) with a coexistent mild nail involvement characterized by pitting and onycholysis (fourth right finger NAPSI 5), (E) BUNES morphometry score 3, and (F) BUNES power Doppler 6.

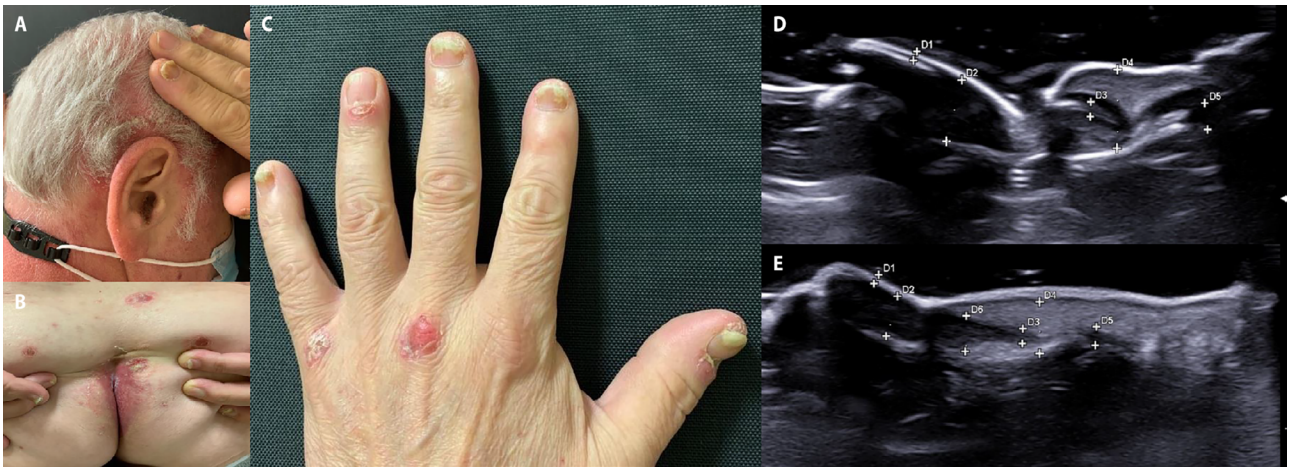

Figure 2. (A-B) A clinical case of male patient, 62 years old, PASI 19, BSA 17 (C) with a coexistent moderate nail involved characterized by pitting, leukonychia, onycholysis, and subungual hyperkeratosis (TOTAL NAPSI 30), (D) first left finger hand BUNES morphometry score 3, (E) second left finger BUNES morphometry score 3.

severity of PsO and the presence of nail involvement, sex and BMI, among others, have been identified to be associated with the development of PsA [24]. We demonstrated a significant association between NAPSI and PEST, a clinical score commonly used to screen PsO patients to assess their risk of developing arthritis, indeed confirming that the presence of nail involvement and its severity could represent a clinical predictor of joint involvement [24].

Several studies indicate that patients with nail damage are more likely to experience higher disease activity and to have PsA [25, 26]. In a cohort of diagnosed PsO and PsA cases, Liu et al. [27] showed nail involvement as a predictor for PsA. Therefore, identifying nail involvement in PsO based on clinical examination may enable dermatologists to recognize and manage patients at an early stage, allowing early interception of PsA [28]. In this regard, this study highlights the importance of an integrated approach between rheumatology and dermatology through nail evaluation [29].

NAPSI correlates with increased BMI, suggesting that nail involvement, as well as skin involvement, is linked to increased body weight and obesity. Overweight and obesity represent a negative prognostic factor in PsO. Michalak-Stoma et al. [30] addressed the relationship between clinical markers of activity (PASI, BSA, PGA, NAPSI) and overweight/obesity according to the BMI of PsO and healthy controls. They underlined an association between the clinical activity of the disease, assessed with PASI, BSA, and PGA, and BMI, confirming the contribution of the increased obesity inflammatory background in conditioning the severity of PsO and its progression.

Limitations

The main limitations of the study include the limited sample size, particularly for subgroup analyses, and the interrater/intra-rater variability. Moreover, the study's single-center design may introduce selection bias, potentially limiting the generalizability of the findings. Finally, the lack of a control group, such as healthy individuals, restricts direct comparisons.

Conclusions

Given that NP is a PsA predictor, integrated strategies can allow identification of PsO patients with a higher risk of developing PsA early, thus optimizing the management of these patients and the therapeutic choices in order to prevent or delay joint involvement and decrease progression. Although additional studies are needed, our findings highlight the importance of the close collaboration between dermatologists and rheumatologists in the evaluation of PsO patients, taking advantage of both clinical and ultrasonographic assessment of nail damage.

Strengthening multidisciplinary cooperation with rheumatologists is crucial to ensuring appropriate disease management and preventing PsA progression. Patients with significant nail involvement or other PsA risk factors should be promptly referred to rheumatologists for a comprehensive musculoskeletal evaluation.

Further longitudinal multicenter studies with larger cohorts and standardized imaging protocols are essential to validate and expand these results, evaluate the potential impact of treatments on nail and skin findings, and establish evidence-based guidelines for integrating nail assessment into routine PsO and PsA screening.

Ethics Approval: The local ethics committee approved the study (protocol number Internal Review Board University of L'Aquila 01/2022), which was performed according to Good Clinical Practice guidelines and Declaration of Helsinki.

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