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ORIGINAL PAPER

Ultrasonography reveals nail thickening in patients with chronic plaque psoriasis

P. Gisondi · L. Idolazzi · G. Girolomoni

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Abstract Nail psoriasis is usually investigated and diagnosed by clinical examination. Ultrasonography is a non-invasive imaging technique for studying soft tissue involvement. The objective of this study was to estimate nail involvement in patients with chronic plaque psoriasis by ultrasonography. Prevalence, clinical type and severity of nail involvement according to nail psoriasis and severity index (NAPSI) were investigated in 138 patients with psoriasis. The thickness of the plate and bed of the fingernails was measured in 54 patients with psoriasis, 46 healthy controls and 37 patients with chronic eczema, using an ultrasonographic system equipped with a frequency transducer of 18 MHz. The prevalence of nail psoriasis was 73 % (102 out of 138). Onycholysis and thickening of the nail plate were the most common clinical type affecting 56 and 50 % of patients, respectively; splinter haemorrhages was the less common involving 10 % of patients. The mean NAPSI score was 18.4 ± 17.5 (SD; range 0–107). The thickness of fingernail plate and bed was significantly higher in patients with psoriasis with nail disease compared to healthy controls and patients with chronic eczema ($p < 0.001$). There was a linear correlation between NAPSI and plate and bed nail thickness ($r = 0.52$ and $r = 0.38$, $p = 0.001$). Increased nail plate and bed thickness was observed also in patients with psoriasis without clinically apparent nail involvement. In conclusion, thickening of the nail is a common feature of nail psoriasis also in patients without clinically apparent nail involvement.

Keywords Chronic plaque psoriasis · Nails psoriasis · Ultrasonography · Psoriatic arthritis

Abbreviations

PASI	Psoriasis area and severity index
NAPSI	Nail psoriasis and severity index
BMI	Body mass index
PsA	Psoriatic arthritis

Introduction

Nail involvement is common in patients with psoriasis. In particular, nails can be affected in 15–50 % of patients with psoriasis and the lifetime incidence of nail involvement approaches 80–90 % of patients [5, 11]. There is a relatively broad spectrum of dystrophies related to nail psoriasis, including pitting, nail bed discoloration, onycholysis, subungual hyperkeratosis, thickness of the nail plate and splinter haemorrhages. Recent studies have revealed the importance of the nail in understanding the link between the skin and joint in psoriatic arthritis (PsA) [13]. Indeed, nail is intimately linked to enthesis which in turn is associated to the synovium forming a distinct organ referred as synovio-entheseal complex [3]. Nail psoriasis could be a clinical predictor of PsA [19]. Traditionally, nail psoriasis is investigated and diagnosed clinically. Ultrasonography has been proposed to be a non-invasive imaging technique for studying nail and skin involvement in patients with psoriasis [10]. Ultrasonography was used for measuring the thickness of the psoriatic plaque following

P. Gisondi (✉) · G. Girolomoni
Section of Dermatology and Venereology,
Department of Medicine, University of Verona,
Piazzale A. Stefani 1, 37126 Verona, Italy
e-mail: paolo.gisondi@univr.it

L. Idolazzi
Section of Rheumatology, Department of Medicine,
University of Verona, Verona, Italy

the treatment with etanercept [7]. In another study, nail plate and matrix parameters were calculated in patients with several skin diseases including psoriasis [9, 20].

In our study, ultrasonography was used to measure the thickness of the fingernail plate and bed in patients with chronic plaque psoriasis. The main finding was that the thickness of the plate and bed of the fingernails was significantly higher in patients with psoriasis compared to healthy controls and patients with chronic eczema. Moreover, increased nail thickness was observed also in patients with psoriasis without clinically apparent nail involvement.

Patients and methods

This was an observational study including 138 adult patients with chronic plaque psoriasis, 46 healthy controls and 37 patients with chronic eczema. All the subjects were aged >18 years and Caucasian, there were no dark-skinned people or those belonging to other racial groups. Patients with psoriasis and chronic eczema were recruited from those consecutively attending the outpatients clinic of the Dermatology Section of the University Hospital of Verona (Verona, Italy) from June to December 2011. Healthy controls were the partners or relatives of the patients not affected by psoriasis. The inclusion criteria for cases were a clinical diagnosis of chronic plaque psoriasis (i.e., lasting at least 6 months) independently of the actual PASI score; the absence of systemic or topical anti-psoriatic treatments for at least 3 months before study inclusion. Patients with chronic eczema were affected by atopic eczema (20 patients), nummular eczema (13 patients) and asteatotic eczema (4 patients) lasting at least 6 months. Patients with eczema localized around the nail folds were not included. Patients with other types of psoriasis (guttate, erythrodermic and pustular psoriasis), those with concomitant diabetes mellitus, inflammatory bowel diseases (i.e., Crohn's disease and ulcerative colitis) and those receiving therapeutic interventions that might have influenced nail status, including amino-acidic supplements were excluded.

Clinical evaluation

All subjects were interviewed and examined to collect age, gender, body mass index, alcohol consumption and smoking habit. Alcohol consumers were defined as those who used to consume alcohol on a daily basis. Current smokers were defined as participants who smoked cigarettes daily or who had stopped smoking <5 years before the enrolment in the study. Non-smokers were participants who had smoked <5–10 packs of cigarettes during their lifetime or who had stopped smoking >5 years before the enrolment. BMI was calculated as weight in kilograms divided by height squared in meters. Psoriasis-related variables included disease duration and severity according to the psoriasis area and severity index (PASI), nail involvement according to the nail psoriasis and severity index (NAPSI) and the presence of PsA according to the CASPAR criteria [22]. The number of finger and toe nails affected by psoriasis and the presence of pitting, onycholysis, salmon patches, sub-ungual hyperkeratosis, thickening of the nail plate and splinter haemorrhages was clinically assessed. Patients with psoriasis were defined as having diabetes mellitus when they were taking hypoglycaemic medications or if a physician had ever told them that they had diabetes. Cases and controls were interviewed about the use of drugs or supplements affecting nails status.

Ultrasonography

Real-time ultrasonography was performed by an experienced rheumatologist, using an Voluson I portable ultrasound machine (General Electrics, United States) with linear 10–18 MHz probe equipped with a variable-frequency transducer of 18 MHz. Within the focal area, the transducer had an axial resolution of 30 μm and a lateral resolution of 60 μm. The fields of view in the depth and lateral directions were 50 and 60 mm, respectively. Rheumatologist received a certified University training in muscle–skeletal ultrasonography and he was very familiar in the routine use of ultrasounds for the detection of signs of joint involvement mainly in patients with rheumatoid arthritis or PsA. The rheumatologist was blinded, i.e., he was not aware if patients were affected by psoriasis or not, and the ultrasonographic examination was performed in a darkened room. Right finger nails were assessed by ultrasonography in 54 patients with psoriasis, 46 healthy controls and 37 patients with chronic eczema. The ultrasound transducer was gently placed over the nail with the transducer directed perpendicular to the surface with gel applied to the examined area to provide a correct acoustic interface. The nails were scanned with the patient seated with the hands in a neutral position over the table. Each nail was scanned in the grey scale mode. The thickness of right fingernails plate and bed was measured in longitudinal ultrasonographic view. In particular, nail plate thickness was the distance between the dorsal and ventral plates which appear as two hyperechoic lines with a virtual hypoechoic space in between (Fig. 1). The nail bed appears as a hypoechoic area under the plates. The nail bed thickness was the distance between the ventral nail plate and the distal phalanx. The measurement was repeated for three times in continue points and the definite value resulted from the mathematic mean of three measurements. Informed consent was obtained from all participants before the ultrasonographic examinations.

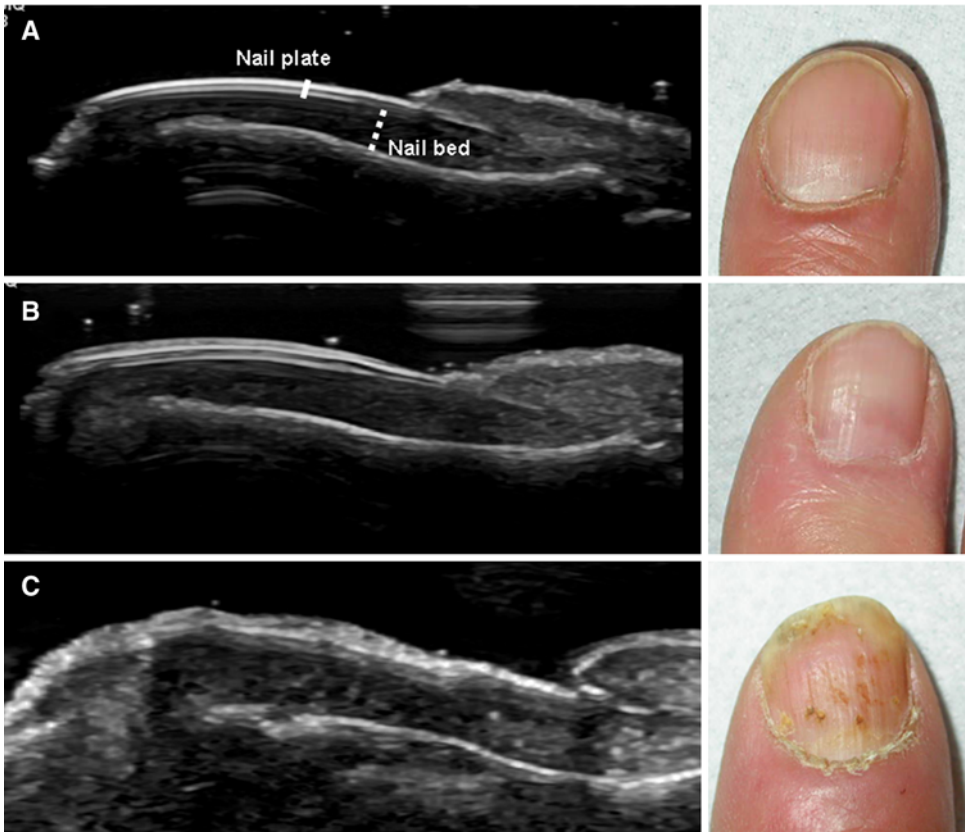

Fig. 1 Gray scale ultrasonograms of the fingernail in a healthy control (**a**), in a patient with psoriasis without clinically apparent nail involvement (**b**) and in a patient with nail psoriasis (**c**). In the longitudinal view the dorsal and ventral nail plates appear as bilaminar structures, characterized by two hyperechoic parallel lines with a hypoechoic space in between. Nail plate thickness was the distance between the dorsal and ventral plates (*continue line*). The nail bed appears as a hypoechoic area under the plates. The nail bed thickness was the distance between the ventral nail plate and the distal phalanx (*dashed line*)

Table 1 Characteristics of the patients with psoriasis

Number	138
Male, *N* (%)	85 (61)
Alcohol consumers, *N* (%)	62 (44)
Smokers, *N* (%)	50 (36)
Body mass index, mean ± SD	27.1 ± 3.5
Psoriasis duration, mean ± SD	20 ± 12
PASI, mean ± SD (range)	18 ± 8.4 (1–44)
PsA, *N* (%)	44 (32)
Nail psoriasis, *N* (%)	102 (73)
NAPSI, mean ± SD (range)	18.4 ± 17.5 (0–107)
Hand nails involved, mean ± SD	2.3 ± 3.3
Foot nails involved, mean ± SD	3.2 ± 3.5
Onycholysis, *N* (%)	78 (56)
Thickening of the nail plate, *N* (%)	70 (50)
Sub-ungueal hyperkeratosis, *N* (%)	56 (40)
Pitting, *N* (%)	53 (38)
Salmon patches, *N* (%)	42 (30)
Splinter haemorrhages, *N* (%)	14 (10)

N absolute number

Statistical analysis

All analyses were performed using STATA 10.0 (STATA Corp. LP, College Station, Texas) and GraphPad 4.0 (San Diego, California). Data are expressed as mean ± standard deviation (SD) or percentages. Skewed variables were logarithmically transformed to improve normality for statistical purposes and then back-transformed to their natural units for presentation in tables and figures. Statistical analyses included ANOVA (for continuous variables) and Chi-square test with Yates correction for continuity (for categorical variables). Pearson test was used to explore the linear correlation between variables, including between NAPSI and nail thickness. Independence of the association of the nail thickness with presence of psoriasis was assessed by multivariate regression analysis. In the fully adjusted regression model age, gender, BMI, psoriasis, PASI score and PsA were included as independent covariates. A p value <0.05 was considered statistically significant.

Results

The characteristics of the study population are reported in Table 1. The prevalence of nail psoriasis was 73 % (i.e., 103 out 138) and the prevalence of PsA was 32 (i.e., 44 out 138). The PASI and NAPSI scores were 18 ± 8.4 and 18.4 ± 17.5 (mean ± SD), respectively. There was no linear correlation between PASI and NAPSI score (Pearson $r = 0.16$; $p = 0.23$). Onycholysis and thickening of the

nail plate were the most common clinical type of nail psoriasis, affecting 56 and 50 % of patients, whereas splinter haemorrhages was the less common, involving 10 % of patients. The characteristics of patients with chronic plaque psoriasis stratified by nail involvement ($N = 102$) showed that there were no statistically significant differences between patients with or without nail involvement as far as age, gender, smoking habit, BMI, psoriasis severity, psoriasis duration and the presence of PsA. A subgroup of 54 patients with psoriasis, 46 healthy controls and 37 patients with chronic eczema underwent ultrasonographic nail plate and bed examination. There were no differences in gender distribution, age, alcohol consumption and smoking habit between patients and controls. However, the mean BMI was significantly higher in patients with psoriasis compared to healthy controls and patients with eczema, respectively (26.8 ± 4 vs. 23.7 ± 4.3 and 24.1 ± 3.8; $p = 0.003$). The thickness of fingernails plate and bed was significantly higher in patients with psoriasis compared to healthy controls and patients with chronic eczema (Fig. 2). Interestingly, the thickness of fingernails plate and bed of patients with psoriasis but without clinically apparent nail involvement was also significantly higher compared to healthy controls and patients with chronic eczema (Fig. 2). The independence of the association of the fingernails thickness with the presence of psoriasis was confirmed by multivariate regression analysis (Table 2). In particular, psoriasis was significantly ($t = 3.74$, $p = 0.0001$) associated to the fingernail thickness independently from age, gender, BMI, PASI score and PsA. Moreover, male gender was an independent predictor of nail plate thickness ($t = 2.75$, $p = 0.0007$). When considering only patients with nail involvement, there was a linear correlation between NAPSI score (50 ± 20) and plate and bed nail thickness, with Pearson $r = 0.52$ and $r = 0.38$, $p = 0.001$, respectively. In an additional linear regression model, fingernail thickness was not a predictor of PsA ($t = 0.99$, $p = 0.32$). A group of ten patients (4 females and 6 males) showing no apparent nail changes but thickened nail plate at baseline were revisited after a mean of 38 ± 7 days. None of them developed signs of nail psoriasis and nail thickness was unchanged.

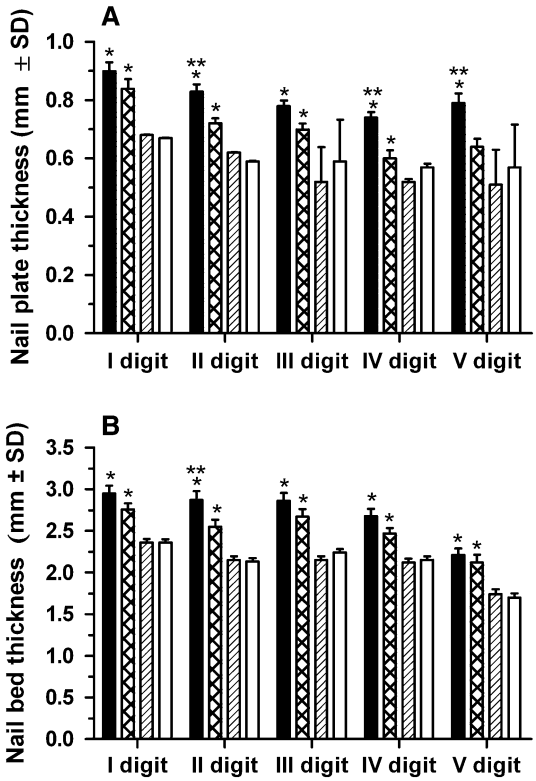

Fig. 2 Histograms showing nail plate (**a**) and bed (**b**) thickness (mean mm ± SD) in patients with nail psoriasis (*black bar*), patients with psoriasis without clinically apparent nail involvement (*cross hatched bar*), patients with chronic eczema (*dashed bar*) and healthy controls (*white bar*). *$p < 0.01$ versus healthy controls and patients with chronic eczema. **$p < 0.01$ versus patients with psoriasis without clinically apparent nail involvement

Table 2 Independent predictors of fingernail thickness in patients with psoriasis

Independent variables	*t*	*p*
Fingernail thickness		
Age (years)	1.63	0.107
Gender (male vs. female)	2.75	0.007
Body mass index (kg/m^2)	1.75	0.084
Psoriatic arthritis (yes vs. no)	1.82	0.072
PASI	1.74	0.086
Psoriasis (yes vs. no)	3.74	0.001

$N = 100$

PASI psoriasis area and severity index

Discussion

In this study, it was confirmed that nail involvement was very frequent in patients with chronic plaque psoriasis, involving 73 % of patients. Onycholysis and thickening of the nail plate were the most common clinical patterns, affecting approximately half of the patients, whereas splinter haemorrhages was the less frequent, involving 10 % of the patients. These findings are consistent to those already reported [5, 11, 13]. The presence of nail psoriasis is clinically relevant for several reasons including functional and cosmetic issues. Patients with nail psoriasis experience pain, functional impairment and social stigma, with significant restriction of daily activities and quality of life [8, 15]. Despite this, nail psoriasis often goes untreated.

Managing nail psoriasis presents a challenge due to the difficulty of delivering effective topical drugs to the nail unit and the limited efficacy of the conventional systemic therapies. However, the newer biological therapies have demonstrated that a significant reduction or clearance of nail psoriasis is possible [12]. Nail psoriasis is diagnosed usually only by clinical examination; scrapings for fungal detection is sometimes performed to exclude onychomycosis. Nail biopsy is not routinely performed because it is a painful procedure and may cause detrimental cosmetic changes. Non-invasive methods to supplement clinical examination of the nails are therefore warranted. Magnetic resonance scanning and optical coherence tomography have been proposed, but they are not broadly available and could be expensive [14, 16]. Moreover, the accuracy of optical coherence tomography, which is a low-penetration imaging device, in evaluating thickened nail may be poor [2]. Ultrasonography provides a more appropriate and more widely available alternative [21]. In our study, ultrasonography revealed that the thickness of the fingernails plate and bed was higher in patients with psoriasis with nail involvement compared to healthy controls and patients with chronic eczema. This was expected, because nail psoriasis affecting the lamina and/or the matrix easily induce an increased thickness of these structures. However, fingernails plate and bed of patients without clinically apparent nail psoriasis were also significantly thicker compared to healthy controls and patients with chronic eczema. No histopathological investigation of nail was performed, and therefore the anatomical reasons underlying this nail thickening could not be further investigated. Psoriasis is characterised by the Koebner phenomenon on the skin which occurs in response to tissue trauma. A sort of Koebner response has been postulated to occur in the entheses and tendons, which have been shown to have microscopic damage and inflammatory changes in patients with psoriasis but not PsA [7]. Similarly, there is also a clear epidemiological link between joint trauma and the development of PsA [14]. Consequently, it is possible that much of nail thickening is linked to an aberrant response to repeated micro-trauma of the nail matrix and/or the distal interphalangeal joints. Indeed, the nail is anatomically and functionally integrated with the musculoskeletal system, particularly the enthesis of the distal interphalangeal joints [4]. The extensor tendon of the phalanx continues from its bone insertion to envelop the nail root and the collateral ligaments form an integrated network on the side of the joints, helping to anchor the nail margins. This virtual continuum of connective tissue structures merges with a thick periosteum on the distal phalanx and with numerous cutaneous ligaments that anchor the fatty pads of the finger pulp to the skin [17]. The psoriatic onycho-pachidermo-periostitis which manifests as nail dystrophy, digital swelling and periosteal reaction is considered a clinical variant of PsA which confirms the functional and anatomical link between nail, entheses, joint and the periosteum [4]. Moreover, recent investigations showed that nail psoriasis could be a sign of underlying systemic subclinical enthesopathy and systemic inflammation [1]. In particular, ultrasonography was used for investigating 804 entheses of upper and lower limbs in patients with psoriasis and revealed that enthesopathy and inflammation scores of patients with nail disease were higher than in patients without nail disease [1]. Because it has been suggested that enthesitis is the primary lesion that underscores the diverse skeletal manifestations of PsA, nail disease is a harbinger for the future development of PsA [18]. Consequently, dermatologists who usually see patients with psoriasis before that arthritis develops and recognize nail involvement are well placed to diagnose PsA early [6].

Limitations of the study include that power Doppler for nail bed vasculature evaluation and nail histopathology were not performed. Moreover, the cross-sectional nature of the study could not discriminate the directionality of the association between nail thickening and skin manifestation of psoriasis.

In conclusion, nail psoriasis is very common and manifests more frequently as onycholysis and thickening of the nail plate. Ultrasonography reveals that the patients with psoriasis have a thickening of fingernails plate and bed also in nails with no clinically apparent disease. Whether this subclinical nail thickening is an early sign of clinically evident nail involvement and/or enthesopathy requires further investigations.

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Conflict of interest The authors declare that they have no conflict of interest.

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