Psoriatic Nail Dystrophy Is Associated with Erosive Disease in the Distal Interphalangeal Joints in Psoriatic Arthritis: A Retrospective Cohort Study

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ABSTRACT. ***Objective.*** To assess whether the association between psoriatic nail dystrophy and radiographic damage in the hands of patients with psoriatic arthritis (PsA) is specific to the distal interphalangeal (DIP) joints.

Methods. A convenience sample of patients was collated from the Bath longitudinal PsA cohort. All patients had PsA according to the ClASsification for Psoriatic ARthritis criteria (CASPAR) criteria, scored radiographs of their hands, and documented nail scores as measured by the Psoriatic Nail Severity Score. Chi-square tests were performed to examine for association between features of nail dystrophy and radiographic damage in the DIP joints, and proximal interphalangeal or metacarpophalangeal (non-DIP) joints of the corresponding digits.

Results. There were 134 patients included, with a median age of 53 years (interquartile range; IQR 44–61) and disease duration of 7 years (IQR 3–17). The presence of any form of psoriatic nail dystrophy was associated with erosion at the DIP joints of the corresponding digit (OR 1.9, 95% CI 1.23–2.83; $p < 0.004$) and this association was primarily driven by the presence of nail onycholysis (OR 1.72; 95% CI 1.12–2.62; $p = 0.02$). Nail subungual hyperkeratosis was more strongly associated with joint space narrowing, erosions, and osteoproliferation at the corresponding DIP joint compared to non-DIP joints ($p < 0.001$). Nail pitting was not associated with erosions or osteoproliferation.

Conclusion. The presence of psoriatic nail dystrophy, particularly onycholysis, is associated with erosive disease at the DIP joints. Subungual hyperkeratosis is more strongly associated with erosive damage at the DIP than non-DIP joints. These findings support the anatomical and pathological link between nail and DIP joint disease. (First Release June 1 2019; J Rheumatol 2019;46:1097–1102; doi:10.3899/jrheum.180796)

Key Indexing Terms:
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Nail psoriasis affects 80% to 90% of patients with psoriasis at some point in their disease course[1]. There are a number of different manifestations of nail disease. Some manifestations arise from the nail bed, such as onycholysis (separation of the nail bed from the plate), subungual hyperkeratosis (thickening or lifting of the nail plate), and oil drop discoloration (red spots on the lunula). Others arise from the nail matrix, including pitting (shallow depressions), leukonychia (pale/white discoloration), and Beau's lines (horizontal grooves in the nail)[2].

The relationship between nail disease and small joint involvement in psoriatic arthritis (PsA) has been examined in a number of studies[3,4,5], as the anatomical relationship between the distal interphalangeal (DIP) joint, extensor tendon insertion, and the nail matrix is of significant importance in PsA. Seminal work by McGonagle and colleagues has demonstrated that extensor tendon fibers link closely with the periosteum of the distal phalanx, the nail bed and the nail matrix[6,7], and the entheseal complex is now proposed as the initiating site of inflammation in PsA[6].

While clinical and radiographic studies appear to support

the anatomical and pathological link between nail disease and DIP joint involvement[8,9,10], none have concurrently assessed the presence of radiographic damage at non-DIP joints to ascertain whether this relationship is specific to the DIP joints.

The aim of our study was to assess whether previously demonstrated associations between psoriatic nail dystrophy (pitting, onycholysis, subungual hyperkeratosis, and severe nail deformity) and radiographic damage [erosion, osteoproliferation, and joint space narrowing (JSN); Figure 1] in patients with PsA are unique to the DIP joints.

MATERIALS AND METHODS

Study subjects. Patients were selected from the Bath PsA cohort, in which patients have clinical and patient-reported outcomes collected during routine clinical appointments. A convenience sample of patients was selected for inclusion if there were completed nail assessments and scored radiographs of hands. All patients were ≥ 18 years old and met the ClASsification criteria for Psoriatic ARthritis (CASPAR)[11]. Demographic data collected included age, sex, and duration of disease at the time of radiographic assessment. Medical records were retrospectively reviewed to determine the presence of coexisting diagnoses of osteoarthritis (OA) and gout.

Nail assessment. Nail disease was measured using the Psoriatic Nail Severity Score (PNSS; range 0–40 in hands), which documents the presence or absence of pitting, onycholysis, subungual hyperkeratosis, and severe nail destruction, with a maximum score of 1 per feature in each nail[5,8]. Severe nail destruction is defined as the presence of psoriatic nail dystrophy on both sides of the nail[5]. Cross-sectional PNSS data were selected at the timepoint when psoriatic nail dystrophy was most severe in each patient.

Radiographic scoring. Anteroposterior radiographs of the hands, wrists, and feet are taken every 2 years for clinical monitoring in the Bath PsA cohort. Radiographs are not formally scored routinely; instead, subpopulations of the cohort are identified and scored to answer study-specific questions. Scored hand radiographs that were most contemporaneous to an available assessment timepoint were included in our study. Radiographs were scored by WT, DJ, ASA, and AA. Training in radiographic scoring has been supported by a consultant musculoskeletal radiologist (GR). The presence and severity of erosive disease was graded using either the modified Sharp/van der Heijde score or the PsA Ratingen Score[9]. Proliferation was scored using the PsA Ratingen Score and the severity of JSN was graded using the modified Sharp/van der Heidje score[9]. Osteoproliferation data were missing for 29 patients. The time between clinical assessment and date of radiograph were calculated for all patients. The equipment and methods of viewing and interrater reliability have been reported elsewhere[9,10], with the

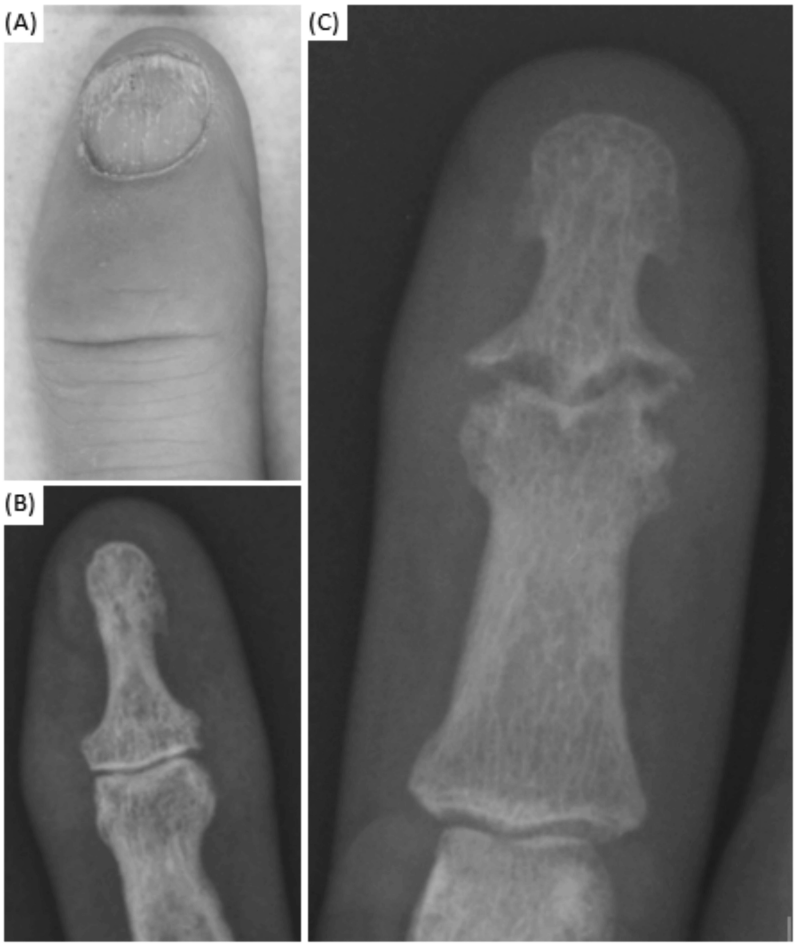

Figure 1. A. Representative clinical image of a patient with psoriatic nail dystrophy, with onycholysis, pitting, and hyperkeratosis. B. Contemporaneous radiographs from the same patient of the left 5th distal interphalangeal joint demonstrating early erosive and osteoproliferative change. C. Illustrative radiograph of the distal interphalangeal joint demonstrating more advanced changes of psoriatic arthritis, with erosions, osteoproliferation, and joint space narrowing, and with early pencil-in-cup deformities.

intraclass correlation for intra- and interrater reliability exceeding 0.9 for all individual features of radiographic damage.

Statistical analysis. Demographic data reported include age, sex, disease duration, biologic use, and time between clinical assessment and radiograph. The overall frequencies of radiographic and nail variables were determined. Associations between the psoriatic nail dystrophy and radiographic damage in the joints of each individual corresponding digit were assessed using chi-square testing, and OR with 95% CI were calculated. Radiographic damage was assessed separately at 1340 DIP joints (i.e., joints with a close anatomical relationship to the nail), and 2680 proximal interphalangeal or metacarpophalangeal (non-DIP) joints (i.e., joints with a distant anatomical relationship to the nail). All statistical analyses were performed using SPSS version 23 (IBM Corp.).

Ethical consent. The data collection was approved by the South West 3 Research Ethics Committee (Reference no. BA74/00-01) and this study has been conducted in accordance with the Declaration of Helsinki. All participants signed informed consent.

RESULTS

There were 134 patients identified from the database for analysis (Table 1). The median (interquartile range; IQR) age was 53 years (44.0–61.0) and the median disease duration of psoriatic arthritis was 7 years (IQR 3.0–17.0). Of the participants, 52.4% were female, and 26.5% were taking biologics. The median time between nail score and radiograph was 0 days (IQR –578 to 686). Retrospective review of medical records determined that 39 patients had a documented coexisting diagnosis of small and/or large joint OA, and 4 patients had a coexisting diagnosis of gout.

Nail disease was present in 70.1% of patients, affecting 25.8% of nails. Onycholysis was the most frequent manifestation (24.2% of all nails), followed by pitting (22.8%), subungual hyperkeratosis (5.5%), and severe nail deformity (2.8%). Pitting was the only subtype of nail disease that was not associated with the presence of any other subtype of nail disease.

Table 1. Baseline demographics.

Demographics, n = 134	Digits, n = 1340
Age, yrs	53 (44.0–61.0)
Sex, female	52.4
PsA disease duration, yrs	7 (3.0–15.0)
Biologic use	26.5
Time between clinical assessment and radiograph, days	0 (–543.5 to 659.5)
Radiographic damage	
DIP joint space narrowing	34.3
DIP erosion	7.8
DIP osteoproliferation	11.8
Non-DIP joint space narrowing	30.2
Non-DIP erosion	12.6
Non-DIP osteoproliferation	13.9
Psoriatic nail dystrophy	
Pitting	22.8
Onycholysis	24.2
Subungual hyperkeratosis	5.5
Severe nail deformity	2.8

Values are median (IQR) or percent. IQR: interquartile range; DIP: distal interphalangeal joint.

The median PNSS was 2.5 (IQR 0–9) and the median number of nails affected per patient was 2 (IQR 1–7). The median PNSS in patients with radiographic damage at the DIP joints was 3 (IQR 0.0–9.8), while the median PNSS in patients without radiographic damage at the DIP joint was 1 (IQR 1–8), but this difference was not statistically significant (Mann-Whitney U test, p = 0.148).

JSN was the most frequent radiographic damage variable at the DIP joints (34.3% of 1340 joints scored) and non-DIP joints (30.2% of 2680 joints scored), followed by osteoproliferation (11.8% and 13.9%, respectively) and erosions (7.8% and 12.6%, respectively).

The presence of nail disease was associated with radiographic damage at the DIP joints (OR 1.4, 95% CI 1.11–1.82; p = 0.005) but not at the non-DIP joints (Table 2). This association was driven by the association between nail disease and erosion at the DIP joints (OR 1.9, 95% CI 1.23–2.83; p = 0.004).

Onycholysis was associated with erosion at the DIP joints (OR 1.7, 95% CI 1.12–2.62; p = 0.02), but not at non-DIP joints. Digits affected by onycholysis had corresponding erosions in 11.1% of DIP joints compared to 6.8% in digits without onycholysis (Figure 2).

Subungual hyperkeratosis was associated with the presence of overall damage, proliferation and JSN at the DIP joints (Table 2). Subungual hyperkeratosis was also associated with overall damage, erosion, and proliferation at non-DIP joints. However, the magnitude of the association was stronger between the presence of subungual hyperkeratosis and erosion at the DIP joints (OR 4.4, 95% CI 2.45–7.73; p < 0.001) than at the non-DIP joints (OR 2.6, 95% CI 1.49–4.45; p = 0.002).

Pitting was not associated with an increased risk of radiographic damage in either DIP or non-DIP joints. Conversely, pitting was associated with a lower risk of JSN at the DIP joints (OR 0.7, 95% CI 0.51–0.90; p = 0.007) and non-DIP joints (OR 0.7, 95% CI 0.49–0.88; p = 0.005).

Further analyses on digits affected by severe nail disease are not included because of the very low frequency of occurrence.

DISCUSSION

We report an association between the presence of nail disease and radiographic damage at the DIP joints, driven by the association between nail dystrophy arising from the nail bed (onycholysis and subungual hyperkeratosis), and erosions at the DIP joints. The DIP joint damage is a reflection of disease activity in the DIP joint, and emphasizes the close anatomical relationship between inflammation in the nail bed matrix complex and the DIP joint. These associations were not reproduced at non-DIP joints, which are anatomically distant from the nail entheseal complex.

Table 2. Univariate analysis of associations between psoriatic nail dystrophy and features of radiographic joint damage.

Radiographic Damage	Any Nail Dystrophy OR (95% CI)	p	Onycholysis OR (95% CI)	p	Subungual Hyperkeratosis OR (95% CI)	p	Pitting OR (95% CI)	p
Any								
DIP	1.4 (1.11–1.82)	0.005*	0.9 (0.72–1.23)	0.6870	2.7 (1.68–4.34)	< 0.001*	0.8 (0.62–1.07)	0.150
Non-DIP	1.0 (0.89–1.32)	0.4930	0.8 (0.57–1.00)	0.0580	3.1 (1.90–4.90)	< 0.001*	1.0 (0.75–1.32)	1.000
Joint space narrowing								
DIP	1.3 (1.00–1.67)	0.0590	0.9 (0.92–1.54)	0.6870	1.9 (1.18–3.01)	0.008*	0.7 (0.51–0.90)	0.007*
Non-DIP	1.0 (0.76–1.30)	1.0000	0.8 (0.69–1.20)	0.5320	1.4 (0.89–2.34)	0.1520	0.7 (0.49–0.88)	0.005*
Erosion								
DIP	1.9 (1.23–2.83)	0.004*	1.7 (1.12–2.62)	0.017*	4.4 (2.45–7.73)	< 0.001*	1.2 (0.75–1.88)	0.452
Non-DIP	1.2 (0.87–1.77)	0.2320	1.1 (0.76–1.62)	0.5640	2.6 (1.49–4.45)	< 0.002*	0.8 (0.56–1.25)	0.433
Osteoproliferation								
DIP	1.4 (0.91–2.03)	0.1330	1.3 (0.88–1.99)	0.1880	3.2 (1.82–5.75)	< 0.001*	1.0 (0.67–1.61)	0.910
Non-DIP	1.2 (0.81–1.73)	0.4230	1.1 (0.72–1.59)	0.7590	3.1 (1.78–5.39)	< 0.001*	1.5 (1.01–2.17)	0.057

* $P < 0.05$. DIP: distal interphalangeal joint.

The relationship between nail disease and DIP joint involvement was described in 1994 by Jones, *et al*[8], who noted that nail disease was more common in patients with DIP joint disease and more likely to be associated with adjacent DIP joint disease, which was later confirmed in a prospective study of patients with early PsA[12]. Further studies have demonstrated that patients with clinical or radiographic DIP involvement tend to have higher nail scores as measured by the PNSS and modified Nail Psoriasis Severity Index (NAPSI)[4,5]. We have confirmed the association between nail disease and erosive change in the corresponding DIP joint, but while patients with DIP joint damage did have higher nail scores than patients without DIP joint damage, this did not reach statistical significance in our cohort.

The association between onycholysis and radiographic DIP involvement has previously been investigated by Lai, *et al* in 45 patients. While an association between nail crumbling, onycholysis, and radiographic damage was found, multivariate analysis did not confirm an association with subtypes of nail disease, and non-DIP joints were not assessed[4]. Our study reinforces these findings with larger numbers, validated radiographic scoring methods, and examination of non-DIP joints. Because onycholysis has also been shown to be associated with overall clinical small joint disease in the hands and the feet in patients with PsA[3] and with more severe osteolysis in patients with PsA mutilans[13], separate radiographic assessment of non-DIP joints is particularly important to illustrate the specificity of the relationship between onycholysis and DIP joint damage.

We also demonstrated an association between subungual hyperkeratosis and all types of radiographic damage at the DIP; this was a less specific finding, because similar associations were also demonstrated between subungual hyperkeratosis and erosion, proliferation, and overall damage at non-DIP joints. The approach of analyzing metacarpophalangeal and proximal interphalangeal joints in the corresponding digit is also relevant. The appreciation of PsA being a disease that affects digit "rays" rather than across "rows" of joints as seen in rheumatoid arthritis, mediated perhaps by dactylitis or tenosynovitis of the digits[7], does make it more challenging to demonstrate a significance between associations at the DIP versus non-DIP joints when the number of patients affected is small, which is the case with subungual hyperkeratosis. Another possible hypothesis is that subungual hyperkeratosis may be a more persistent feature of nail disease, and therefore more likely to be recorded during routine clinical assessments.

The lack of association between pitting and radiographic damage in our study may reflect the lack of specificity of pitting in PsA[14]. In one study where the presence of pitting was defined as > 20 pits, the prevalence of pitting in patients with PsA was found to be much lower at 26% compared to 56.7% in our study, where the presence of pitting was defined as ≥ 1 pit[5]. Similarly, the lack of positive association between nail variables and JSN may reflect the poor specificity of JSN for inflammatory disease. The mean age of our cohort was 51.9 years, and radiographic scoring methods do not discriminate between JSN related to PsA or OA.

The inverse association between pitting and JSN is an interesting finding. The possible rationales for this include the presence of a confounder, such as the effect of treatment on subtypes of nail disease, and the lack of specificity of both pitting and JSN to PsA.

The strengths of our study include the cohort size, the formal scoring of nails and joints, and data analysis by individual joint (as opposed to group level analysis of total nail and joint score). To our knowledge, this is the largest study examining the association between individual features of nail disease and radiographic damage, and the only study in which formal radiographic scoring methods were used in all small joints of the digits.

The main limitations of our study are the lack of complete longitudinal clinical data such as the Psoriasis Area and

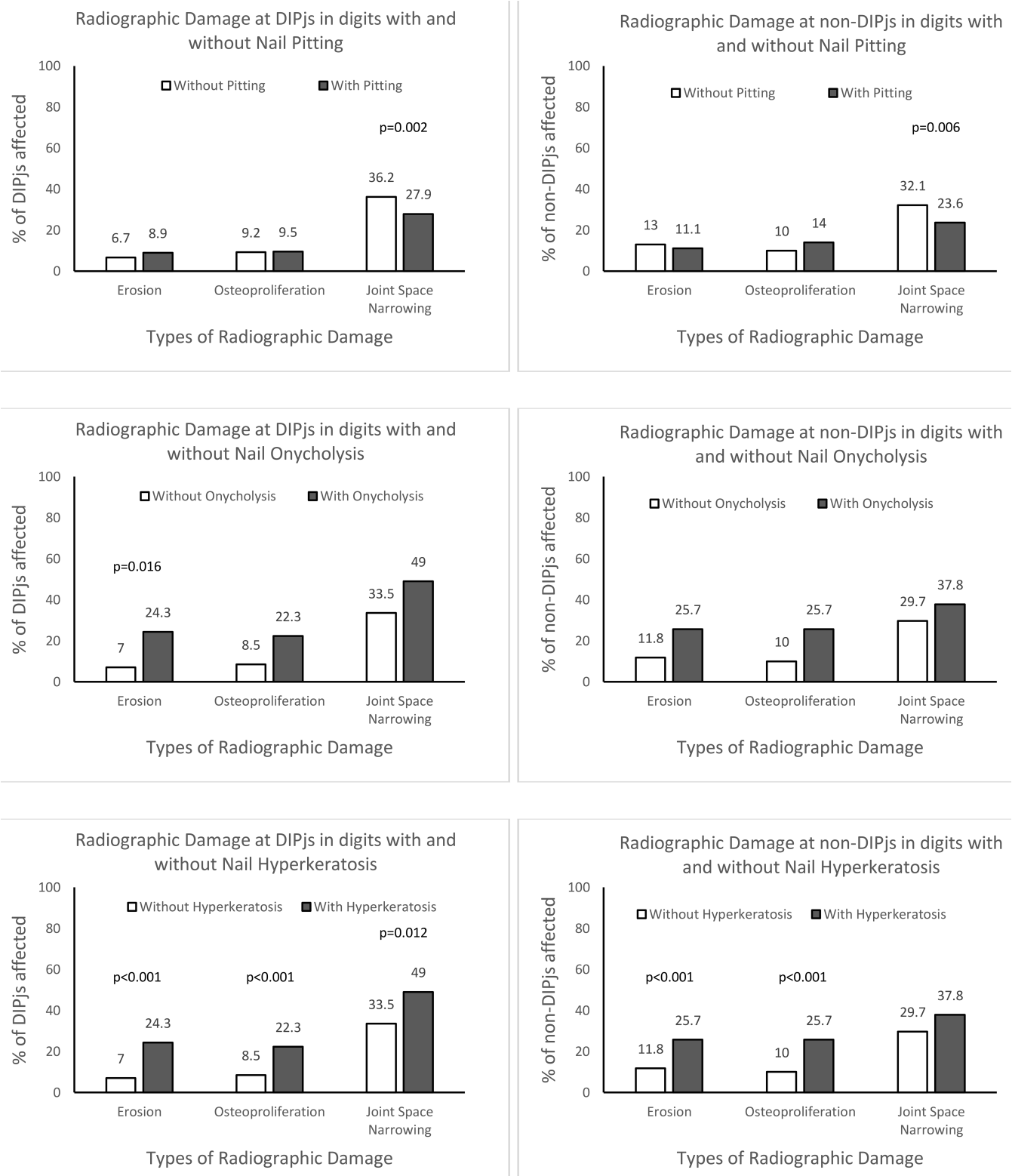

Figure 2. Chi-square tests demonstrating associations between subtypes of psoriatic nail disease and radiographic damage at the corresponding DIP and non-DIP joints. DIPj: distal interphalangeal joint.

Severity Index Score and body surface area, which may serve as confounders, and the absence of serial radiographic data, which precludes meaningful regression analysis to analyze the effect of subtypes of nail disease. However, existing

observational studies, which use multivariate analysis to demonstrate the independence of the association between psoriatic nail dystrophy and radiographic damage in DIP joints, are also limited by their lack of complete longitudinal data, the fluctuating features of nail dystrophy, and variable treatment exposure. We used a study design to offset this limitation by analyzing the differences in association between nail disease and radiographic damage in the joints of the corresponding DIP joints and comparing this to the association between nail disease and radiographic damage in the joints of the corresponding metacarpophalangeal or proximal interphalangeal (non-DIP) joints. The presence of an association with the former but not the latter adds confidence to the hypothesis that there is a relationship between the presence of nail disease and radiographic damage at the DIP joints.

This study did not assess all potentially relevant radiographic measures of damage related to PsA, such as periostitis, which may have affected the significance of the relationship between overall radiographic damage and individual features of psoriatic nail disease. Further, the NAPSI score, which scores individual nail quadrants, is not routinely used in our longitudinal cohort; therefore, the effect of the severity of a nail lesion is not accounted for in our analysis.

Another consideration in the interpretation of our findings is the concept of subclinical nail disease. In one study of 23 patients with PsA, 42% of patients with magnetic resonance imaging (MRI) nail disease had DIP involvement compared to 0% of patients without MRI nail disease; importantly, most patients without clinical nail disease had MRI nail disease[15]. This suggests that clinical examination is not as sensitive as MRI for detecting nail disease. While using MRI to assess nail disease is difficult to justify clinically and financially, the use of clinical nail assessment in assessing the association with radiographic damage is a limitation of our study.

Finally, PsA is a heterogeneous condition with various proposed subtypes such as polyarticular disease, oligoarticular disease, DIP-predominant disease, spondyloarthritis, and arthritis mutilans[16,17]. Our study does not stratify patients by disease subtype; it may be that the demonstrated associations are driven by particular disease subtypes and may not necessarily apply to all patients with PsA.

There is an association between the presence of psoriatic nail dystrophy, in particular onycholysis, and erosive damage at the DIP joints. The association between subungual hyperkeratosis and erosive disease is stronger at the DIP than in non-DIP joints. These findings support studies that demonstrate the anatomical, radiological, and clinical association between psoriatic nail dystrophy and DIP disease, and support the clinical utility of assessing the nail entheseal DIP complex in clinical practice.

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