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# Extended report: nail disease in psoriatic arthritis—clinically important, potentially treatable and often overlooked

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***Objectives*. To examine the relationship between the severity of nail disease and characteristics of psoriatic arthritis (PsA). We also wished to assess the clinical management of nail disease in patients with PsA.**
***Methods*. We studied 69 patients with PsA at two visits. On the first visit, a rheumatology assessment of joint, skin and nail disease was made. On the second visit, a detailed dermatology assessment of skin and nails was made. Nail disease was analysed using a 20-nail psoriasis nail severity score (PNSS).**
***Results*. There were 57 (83%) patients with clinical evidence of psoriatic nail disease. Although 66 (96%) patients had been treated for skin disease, only one (1%) had received any treatment for nail disease. Severe nail disease measured by the PNSS correlated with severe skin psoriasis as indicated by the percentage of body surface area affected by psoriasis ($r = 0.34$, $P = 0.004$) and physician global assessment of psoriasis ($r = 0.45$, $P < 0.001$). Patients with distal interphalangeal (DIP) joint disease had higher PNSS scores ($P = 0.03$). The PNSS was also associated with unremitting and progressive arthritis ($P < 0.001$), and correlated with Stanford health assessment questionnaire (HAQ) ($r = 0.34$, $P = 0.004$), depression ($r = 0.39$, $P < 0.001$) and anxiety ($r = 0.34$, $P = 0.004$) scores. Compared with dermatology assessment, the rheumatology examination of nail disease had a positive predictive value of 84% and negative predictive value of 83%.**
***Conclusions*. In patients with PsA, the severity of nail disease correlates with indicators of severity of both skin and joint disease. Although rheumatologists can adequately screen for nail disease, the management of this aspect of PsA is often overlooked.**

KEY WORDS: Psoriatic arthritis, Nail disease.

Nail disease is known to occur frequently in patients with psoriatic arthritis (PsA) [1]. PsA is associated with higher rates of nail disease than psoriasis alone [2]. Although many nail abnormalities have been described in psoriasis, the typical changes are pitting, subungual hyperkeratosis, discoloration, dystrophy and onycholysis [3, 4]. The relationship between distal interphalangeal (DIP) joint and nail disease is well recognized [5– 7]. However, the association between other aspects of PsA and nail disease is not fully understood. In particular, there has been little emphasis placed on the severity of nail disease in relation to arthritis.

Nail disease has been shown to be associated with functional impairment in patients with psoriasis [8]. In addition, the psychological distress caused by hand problems in patients with arthritis has been recognized [9]. Although there have been a number of advances in the treatment of psoriatic nail disease [10–15], it is uncertain whether these therapies have been widely adopted in clinical practice.

Our aim was to make a comprehensive study of nail disease in a group of PsA patients, and to assess the relationship between nail, skin and joint disease. We also wished to assess the practical management of nail disease, including detection and current treatments of this problem.

## Methods

Patients with PsA attending rheumatology out-patient clinics in Oxford were invited to participate in this study. Ethical approval was obtained from the Central Oxford Research Ethics Committee, and patients provided written consent. Patients were studied from January 1999 to September 2000.

Patients were considered to have PsA if they had inflammatory arthritis and psoriasis; those with a rheumatoid factor titre of $>1{:}160$ or reactive arthritis with a clear infective trigger were excluded. Of 149 patients invited, 103 were eventually recruited to the study (41 declined to take part, 2 had rheumatoid arthritis, 1 had reactive arthritis and 2 had never had psoriasis). The clinical characteristics of this group have been reported previously [16].

On the first study visit a rheumatologist (LW or JD) assessed all patients. A careful history was taken about the pattern of their skin psoriasis and nail disease. Patients were questioned directly about a history of enthesitis, dactylitis and inflammatory back pain. Skin, nails and joints and spine were examined. A diagnosis of enthesitis was accepted if there was a history of inflammatory pain at an entheseal site or clinical evidence of enthesitis on examination. Dactylitis was diagnosed by a typical history or on clinical examination. Axial disease was defined by the presence of a history

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of inflammatory back or neck pain and/or reduced cervical, thoracic or lumbar movements [16]. The progression of arthritis was documented as episodic with complete resolution, episodic with incomplete resolution or unremitting and progressive. The history of arthritis progression was corroborated by reference to hospital records. Patients completed the Stanford health assessment questionnaire (HAQ) and hospital anxiety and depression scale (HADS) [17]. The severity of skin psoriasis was measured as a percentage of body surface area (BSA). In addition a global assessment of skin involvement was made using a scale of nil, mild, moderate, severe and very severe. All 103 patients were invited for a second visit, which included assessment of their skin and nail disease by a dermatologist (BG). We report results from the 69 patients who attended both visits. The mean and standard error of the mean (SEM) time interval between the first and second study visit was 7.0 (0.6) months. On the second visit, in addition to a full dermatological history and examination, the pattern of disease in all 20 nails was documented. A total of 1377 nails were examined in detail (three nails were not assessable due to previous trauma).

We analysed the severity of nail disease using an extension of the fingernail score described by Jones *et al*. [6] to also include toenails. All 20 nails were assessed for pitting, onycholysis, hyperkeratosis and severe nail deformity with involvement of both sides of the nail (dystrophy). Each of the listed features scored 1 with a possible maximum score of 80. This score is referred to as the psoriasis nail severity score (PNSS).

To determine the ability of the rheumatologists to detect psoriatic nail disease, the rheumatology and dermatology assessments were compared. The rheumatologists (LW or JD) assessed whether there was any evidence of psoriatic nail disease at the first visit. On the second visit the dermatologist (BG) assessed the severity of nail disease measured by the PNSS. The dermatologist was blinded to the rheumatology assessment.

The presence of HLA-B27 was tested by polymerase chain reaction using sequence-specific primers [18]. HLA-B27 results were available for 67/69 patients who underwent full nail assessment.

The association between PNSS and other clinical variables was explored initially using Student's *t*-tests and $\chi^2$ tests. Because some of the clinical variables may interact, we used regression methods to adjust the relationship between two variables for the possible influence of a third variable. Linear regression was used to retest relationships between PNSS and the other clinical variables (%BSA skin affected by psoriasis, HAQ, presence of progressive and unremitting arthritis and depression scores), adjusting for the presence or absence of DIP joint disease by adding this dichotomous variable to each regression model. A further analysis of the joint relationship of PNSS with HAQ and %BSA affected by psoriasis was carried out, also using regression methods. The analysis was carried out using Excel and Stata [19]. Unless otherwise stated, values are represented as mean (SEM).

## Results

### *Characteristics of nail disease*

Of the 69 patients undergoing both assessments, 57 (83%) were considered by the rheumatologists to have clinically evident nail disease. The median age of onset of nail disease was 32 years (range 15–60), compared with 28 years (5–65) for skin disease and 34 years (12–65) for arthritis. Results of the detailed dermatology nail assessment, including the PNSS, are summarized in Table 1. The most frequent findings were discoloration, onycholysis and subungual hyperkeratosis. The mean (SEM) PNSS was 15.5 (1.2). For fingernails, the mean PNSS was 7.4 (0.7) and for toenails 8.1 (0.6). The fingernail and toenail subscores were strongly correlated ($r = 0.6$, $P = 2.5 \times 10^{-8}$). Both fingernail and toenail subscores also strongly correlated with the PNSS ($r = 0.91$ and 0.89 respectively).

Table 1 (a). Results of the detailed dermatological nail assessment: characteristics of psoriatic nail disease

| Nail variable | Number of patients ($n = 69$) |
|---|---|
| Pits, total $>20$ | 18 (26%) |
| Onycholysis | 57 (83%) |
| Subungual hyperkeratosis | 56 (81%) |
| Dystrophy | 35 (51%) |
| Discoloration | 58 (84%) |
| Splinter haemorrhages | 26 (27%) |
| Midline depression | 12 (17%) |
| Trachyonychia | 18 (26%) |

Table 1 (b). Results of the detailed dermatological nail assessment: psoriasis nail severity score (PNSS)

| PNSS | Number of patients ($n = 69$) |
|---|---|
| $<10$ | 19 (28%) |
| 10–19 | 26 (38%) |
| 20–29 | 19 (28%) |
| $\geq 30$ | 5 (7%) |

### *Treatment for skin and nail disease*

A detailed history regarding all treatments for joint, skin and nail disease was taken. Disease-modifying anti-rheumatic drugs (DMARDs) were used by 27 (39%) patients on the first study visit and 25 (36%) on the second visit.

Patients had received a median of four (0–8) treatments for their skin disease. Only three (4%) patients had received no treatment for their skin disease. Most commonly prescribed were topical steroids, tar-based topical therapies and calcipotriol.

Although over 80% of patients had clinically evident nail disease, only one patient (1%) had received any treatment for nail disease. This patient had been treated with topical corticosteroids.

### *Severity of nail disease and skin disease*

Severe nail disease as measured by the PNSS was strongly associated with severe skin disease (Fig. 1). The PNSS correlated with percentage body surface area (%BSA) affected by psoriasis ($r = 0.34$, $P = 0.004$) and physician global assessment of psoriasis ($r = 0.45$, $P < 0.001$). In addition, other indicators of skin severity such as the number of psoriasis treatments ($P = 0.002$) and hospital admissions for psoriasis ($P = 0.005$) were associated with severe nail disease. However, there was no association with particular patterns of skin disease and the severity of nail disease.

### *Severity of nail disease and characteristics of arthritis*

As expected, those patients with DIP joint disease had more severe nail disease; for patients with DIP joint arthritis the mean (SEM) PNSS was 18.4 (1.6) compared with 13.2 (1.6) for those without DIP joint disease ($P = 0.03$). However, the severity of nail disease was also associated with other characteristics of arthritis. In particular, the PNSS was associated with the presence of clinically evident enthesitis; those with enthesitis had a mean PNSS of 19.8 (1.96) compared with 13.0 (1.3) in those without enthesitis ($P = 0.005$). The presence of dactylitis and axial disease was not associated with the PNSS. HLA-B27 was more frequent in those patients with very low PNSS values; 4/9 patients with PNSS $< 5$ compared with 7/58 of those with PNSS $\geq 5$ ($P = 0.01$). However, overall there was no significant

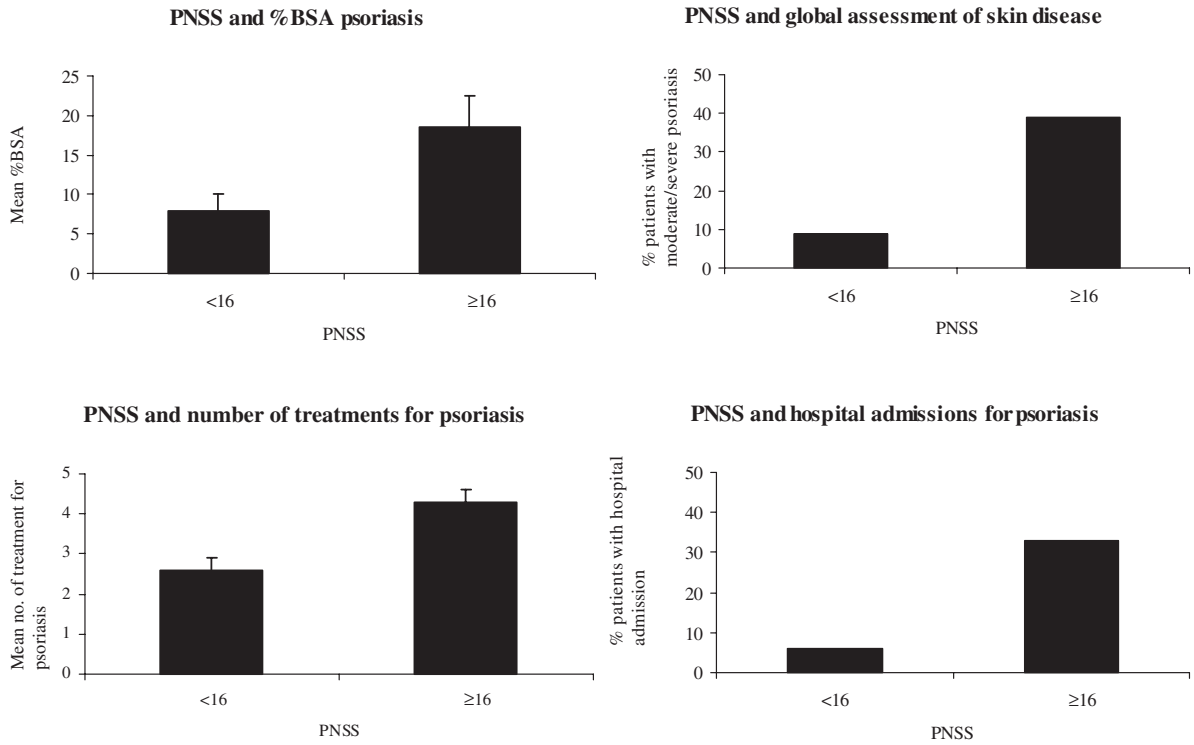


FIG. 1. Severe nail disease measured by the PNSS is associated with severe psoriasis as indicated by %BSA affected by psoriasis, physician global assessment of psoriasis, number of treatments for psoriasis and hospital admissions for psoriasis. Error bars indicate SEM.

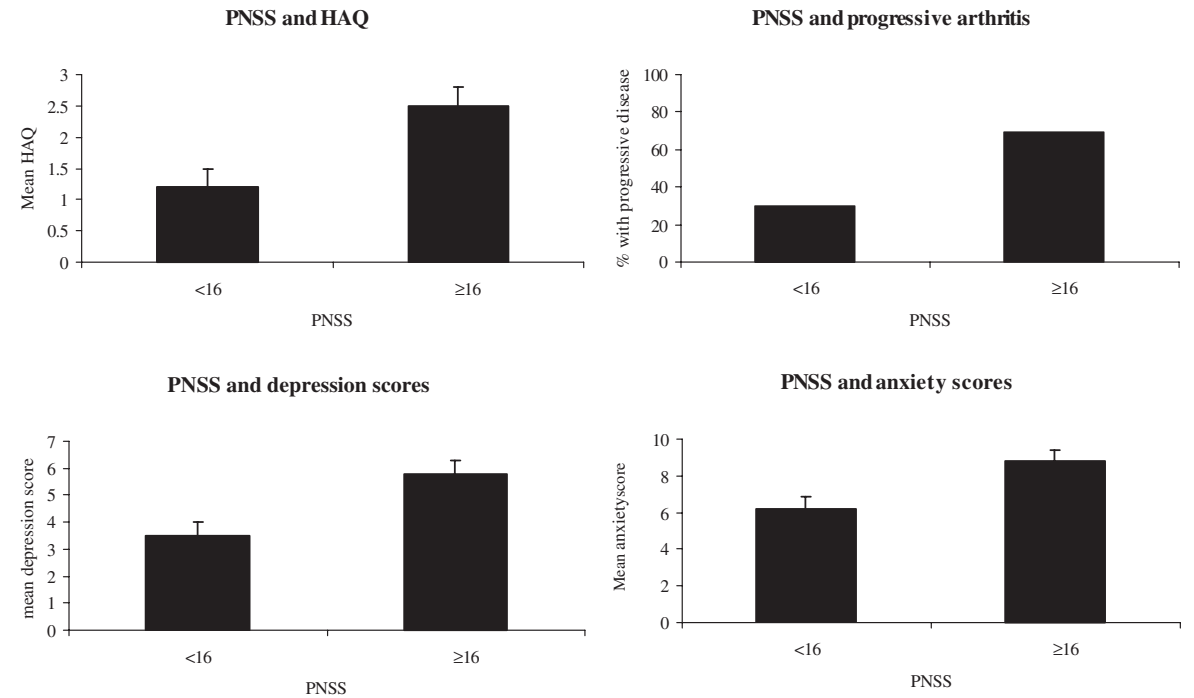


FIG. 2. Severe nail disease as measured by the PNSS is associated with higher HAQ scores, unremitting and progressive arthritis, and greater depression and anxiety scores. Error bars indicate SEM.

difference in the PNSS in those patients with and without HLA-B27 ($P = 0.2$).

Using the PNSS, severity of nail disease was associated with polyarticular disease ($P = 0.02$) and unremitting and progressive arthritis ($P < 0.001$) (Fig. 2).

### *Severity of nail disease and functional status*

Severe nail disease was also associated with functional impairment related to arthritis (Fig. 2). The PNSS correlated with HAQ ($r = 0.34$, $P = 0.004$) and ACR functional class ($r = 0.30$, $P = 0.01$).

Higher PNSS scores also correlated with higher depression ($r = 0.39$, $P < 0.001$) and anxiety ($r = 0.34$, $P = 0.004$) scores.

### *Regression analysis*

Univariate analysis showed that there was an association between HAQ and extent of psoriasis as measured by %BSA affected ($P = 0.04$). When both were included in the same analysis, they were each still significantly associated with PNSS (Table 2a). We also analysed the data adjusting for the presence of DIP joint disease, and found that the associations between PNSS and indicators of skin disease, joint disease and functional status persisted (Table 2b).

### *Rheumatological assessment of nail disease*

Of the 57 patients assessed by the rheumatologists to have clinically evident nail disease, 48 (84%) had a PNSS (as assessed by the dermatologist) of $\geq 10$. Of those 12 patients considered not to have nail disease by the rheumatologists, 2 (17%) had a PNSS of $\geq 10$ (rheumatology *vs* dermatology assessments, $P = 2 \times 10^{-6}$). Overall, the sensitivity of the rheumatology assessment to detect a PNSS of $\geq 10$ was 96% and the specificity 53%.

Of the 9 patients considered by the rheumatologists to have psoriatic nail disease, but with a PNSS of $< 10$, the dermatology diagnoses were: nail trauma (2 patients), onychomycosis (2), onychoschizia (1), very mild psoriatic nail changes (3) and no significant nail disease (1).

## Discussion

Nail disease occurs commonly in patients with PsA. In our study, over 80% had clinically detectable nail disease. This is similar to previous studies [5, 6, 20] of PsA patients. However, we have also assessed the severity of nail disease and show that patients with more severe nail disease have worse skin disease and higher rates of unremitting and progressive arthritis with associated functional impairment. Although mild skin disease is often found in PsA [5], this condition is associated with high rates of nail disease. Our study lends support to the hypothesis that nail pathology may provide a mechanistic link between skin disease and joint disease in PsA.

This study has also confirmed that despite previous reports showing nail disease to be an important determinant of functional impairment in psoriasis [8], management of nail disease is often overlooked. Although most of our patients had received treatment for skin disease and had regular specialist rheumatology outpatient assessments, only one had received any treatment for nail disease. One possible explanation for this under-treatment is that therapies for psoriatic nail disease are perceived to be ineffective. However, nail disease has also been overlooked in published clinical trials in PsA. There have been case reports suggesting that DMARDs such as sulphasalazine and cyclosporin [21, 22] used for psoriasis or PsA have a therapeutic benefit in nail disease. Yet, despite increasing numbers of clinical trials for PsA, very few of these studies report the severity of nail disease at baseline, or the effect of treatment on the severity of nail disease.

Another explanation for the lack of attention to nail disease is that rheumatologists are poor at detecting nail disease. To examine this possibility, we compared the rheumatology and dermatology assessments of nail disease. Our study shows that a rheumatology assessment of nail disease is actually highly sensitive at detecting disease. Rheumatology assessment had a positive predictive value of 84% and negative predictive value of 83%. Although the rheumatology assessment lacked specificity, this is arguably less important when considering screening for nail disease in the rheumatology clinic. The good correlation between rheumatology and dermatology nail assessments, despite the time interval between the two study visits, lends weight to our conclusion that rheumatologists are able to make competent assessments of nail disease in PsA.

Why is the nail assessment important? It has been reported that in patients with psoriasis, nail disease causes cosmetic problems in 93%, pain in 52% and difficulty with activities of daily living in 58% [8]. Our study extends this knowledge to show that in PsA patients with severe nail disease also have greater functional impairment. In addition, severe nail disease correlates with greater anxiety and depression scores in patients with established PsA. While we have not shown that nail disease is the reason for such functional and emotional difficulty, these findings raise the possibility that severity of nail disease may be a prognostic indicator in patients presenting with PsA. Prospective studies of patients presenting with early disease are required to confirm this hypothesis.

Detection of nail disease is also important because treatments, although not perfect, are improving. The most practicable management involves the use of topical steroid and vitamin D analogues. Daily application for at least 3 months will result in a significant improvement in both nail signs and symptoms [10]. Basic nail care is important, and patients need to trim onycholytic nails so that the treatment can be applied to the nail bed.

TABLE 2 (a). Regression analysis: univariate analysis showed an association between HAQ and %BSA skin affected by psoriasis (%BSA) ($P = 0.04$)

| Independent variable | Regression coefficients | | |
|---|---|---|---|
| | $b$ (S.E.($b$)) | $P$ | $R^2$ |
| %BSA skin affected by psoriasis | 0.136 (0.057) | 0.020 | 0.1863 |
| HAQ | 0.461 (0.194) | 0.020 | |

When both HAQ and %BSA are included in the same analysis, they are each still significantly associated with PNSS. [$b$ is the slope of the linear regression, with PNSS as the dependent variable. S.E.($b$) is the standard error of the slope, and $P$ the significance level of the test of the hypothesis that the slope is zero].

TABLE 2 (b). Regression analysis: adjusting for the presence of DIP joint disease. Comparison of unadjusted and adjusted $b$ values shows that after allowing for the DIP joint disease, the association between PNSS and indicators of skin disease, joint disease and functional status remains

| Independent variable | Univariate analysis | | | Adjusted for the presence of DIP joint disease | | |
|---|---|---|---|---|---|---|
| | $b$ (S.E.($b$)) | $P$ | $R^2$ | $b$ (S.E.($b$)) | $P$ | $R^2$ |
| DIP joint disease | 5.14 (2.28) | 0.027 | 0.07 | – | – | – |
| %BSA skin affected by psoriasis | 0.17 (0.06) | 0.004 | 0.12 | 0.15 (0.06) | 0.009 | 0.16 |
| Unremitting or progressive arthritis | 6.53 (1.68) | <0.001 | 0.19 | 5.97 (1.71) | 0.001 | 0.21 |
| HAQ | 0.58 (0.19) | 0.004 | 0.12 | 0.52 (0.19) | 0.001 | 0.16 |
| Depression | 1.16 (0.33) | <0.001 | 0.16 | 1.08 (0.33) | 0.002 | 0.21 |

Notation as for Table 2 (a).

Triamcinolone injections into the nail fold are effective [11] but often require ring blocks and are less popular. Acitretin, a systemic vitamin A analogue used in skin psoriasis, may be specifically beneficial for the treatment of subungual hyperkeratosis [12]. A recent placebo-controlled trial of topical oil-dissolved cyclosporin A solution showed this treatment to be effective, safe and cosmetically acceptable [13]. Although not formally assessed in clinical trials, DMARDs such as methotrexate and cyclosporin A may also be of therapeutic benefit.

In summary, the severity of nail disease correlates with indicators of both skin and joint disease severity in PsA. This aspect of PsA is often overlooked in the clinic and in published therapeutic trials. Our study raises questions about the potential importance of nail disease in both understanding the underlying pathogenesis of PsA and also predicting outcome of early disease.

The authors have declared no conflicts of interest.

| *Rheumatology* | Key messages |
|---|---|
| | • In PsA, the severity of nail disease correlates with indicators of severity of both skin and joint disease.<br>• Rheumatologists are able to adequately screen for psoriatic nail disease.<br>• Nail disease is often overlooked in the clinic and in published therapeutic trials. |

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