

Tailored approach to early psoriatic arthritis patients: clinical and ultrasonographic predictors for structural joint damage

Yasser El Miedany · Maha El Gaafary · Sally Youssef · Ihab Ahmed · Annie Nasr

Received: 13 November 2013 / Revised: 6 March 2014 / Accepted: 10 April 2014 / Published online: 3 May 2014
© Clinical Rheumatology 2014

Abstract This study aims to identify the clinical predictors of arthritis in patients with psoriasis and to evaluate the use of musculoskeletal ultrasonography (US) as a predictor for inflammatory structural progression in psoriatic patients. Measures of association (odds ratio (OR)) were tested, in a prospective, cohort 1-year follow-up study, between structural deterioration and the presence of baseline inflammation, or its persistence. One hundred twenty-six psoriatic patients were prospectively evaluated both clinically and by US at 0, 6, and 12 months for synovitis/ joint damage, enthesitis, and onychopathy. X-ray was performed at 0 and 12 months. One hundred twelve sex and age-matched psoriatic patients without histories of musculoskeletal symptoms were included as control group. Structural deterioration was observed in 47 % of the 5,292 evaluated joints. Clinical variables associated with arthritis risk: BMI>25 (OR=1.7), body surface area (OR=1.13), family history (OR=5.72) and nail involvement (OR=2.25). BMI>30 was significantly correlated ($P<0.01$) with shorter time for the onset of arthritis. Baseline synovial score/PD score ≥ 2 was associated with increased risk of

structural progression: OR=1.98 versus 2.61 versus 2.66 ($P<0.001$) for the clinical versus US-gray scale (GS) versus US-power Doppler (PD) evaluation, respectively. An increased probability for structural progression in the presence of enthesitis was observed (OR=2.79 and 3.50) for both US-GS and US-PD, whereas OR was 2.46 for clinical examination. Onychopathy was associated with structural joint damage (OR=2.30). In multivariate logistic regression analysis, persistent of synovitis/enthesitis at 6 months of therapy was predictive of subsequent structural progression. Family history of psoriatic arthritis, large BMI (>25), high percentage of psoriatic body surface area, and nail involvement were significantly associated with early onset psoriatic arthritis. Baseline GS score of ≥ 2 , PD score of ≥ 2 , presence of enthesitis, enhanced vascularity at enthesitis, higher GUESS score, and onychopathy, all at base line as well as persistent synovitis and enthesitis at 6 months are predictors of progressive early psoriatic arthritis. Regular ultrasonographic monitoring of these patients is mandatory to assess the progression of their arthritis status.

Y. El Miedany (✉)
Darent Valley Hospital, Dartford, Kent, UK
e-mail: drelmiedany@rheumatology4u.com

Y. El Miedany · S. Youssef
Rheumatology & Rehabilitation Department, Ain Shams University,
Cairo, Egypt

M. El Gaafary
Department of Community, Environmental and Occupational
Medicine, Ain Shams University, Cairo, Egypt

I. Ahmed
Internal Medicine Department, Cairo University, Cairo, Egypt

A. Nasr
Radiology, Ain Shams University, Cairo, Egypt

Keywords Early psoriatic arthritis · PROMs · US

Introduction

The recognition that psoriatic arthritis (PsA) can lead to marked musculoskeletal damage with consequent impairment to the patients' functional ability and quality of life (QoL) has modified the disease management approach and treatment paradigm. Over the past two decades, evidence has accumulated that the majority of patients with psoriasis experience progressive joint destruction over a relatively short period of time. Research studies estimated that PsA is erosive and deforming in 40 to 60 % of patients with joint damage that appears in the first years of disease onset [1–4]. Furthermore,

PsA patients who suffer reduced quality of life and impairment of functional status are at greater risk of death compared to the general population [5–7]. Until some years ago, management approach for PsA has not reached satisfactory levels. Traditional disease-modifying drugs (DMARD) have been used in PsA mainly to control the symptomatic manifestations, but they did not show enough evidence that they prevent or significantly decrease the rate of progression of structural joint damage [8]. The use of biologic therapy agents for psoriasis and/or PsA represented a new horizon in the treatment paradigm. Studies revealed that Anti-TNF- α inhibitors and anti-cytokine agents (e.g., ustekinumab) were able to reduce the signs and symptoms of inflammation and skin affection, inhibit the progression of structural damage in both the spine and peripheral joints, as well as improve QoL and functional status [9–12]; hence, guidelines recommended commencing biologic therapy agents for psoriasis/PsA early in the disease course after failure of traditional measures including DMARD [8–13].

So far, the concept of “early PsA” remains relatively new and still lags well behind the wealth of literature on early rheumatoid arthritis (RA) window of opportunity. Though the potential advantages of early diagnosis and management of PsA have been highlighted, identifying this group of patients early in the disease course remains a challenge. One of the main hurdles is the clinical spectrum of PsA which is wide and includes several targets such as the axial skeleton, joints, entheses, dactylitis, and nails, which can be involved in isolation, concomitantly or consequently [14]. In contrast with other autoimmune diseases, such as RA and SLE, a reliable and predictive/diagnostic biomarker in psoriasis has not been defined. Furthermore, at the population level, working out the early events in psoriatic disease is complicated by the erratic temporal associations between skin and joint disease. Skin disease predates arthritis in about 60 % of cases, arthritis predates skin involvement in 20 % and onset is concurrent in the remainder [15–17]. Therefore, the identification of subclinical musculoskeletal disease in patients with psoriasis early in the disease course plays a vital role in the patients’ management. Imaging studies have been of great benefit in early diagnosis of inflammatory arthritis, especially MRI and ultrasonography (US), which provide images of soft tissues and musculoskeletal structure [18, 19]. In addition, several questionnaires have been developed to help rheumatologists screen patients with psoriasis for the presence of musculoskeletal disease and its impact on their lives [20–22].

The aim of this work was to identify the clinical predictors of arthritis in patients with psoriasis and to evaluate the use of musculoskeletal US as a predictor for inflammatory structural progression consistent with early PsA in psoriatic patients, using rheumatological evaluation as the gold standard for diagnosis.

Methods

This was a prospective 1-year follow-up cohort study of psoriatic patients referred to the early inflammatory arthritis clinic for musculoskeletal symptoms. Local ethical and methodological approval of the study protocol was obtained. All patients who shared in the study signed an informed consent according to the Declaration of Helsinki.

Patients

One hundred forty-one patients were included in this work, 14 have been lost to follow-up and did not have a 1-year assessment and one was unaccounted for; therefore, the study was limited to 126 patients. All patients fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR) [23]. Inclusion criteria are as follows: age > 18, all patients had chronic plaque psoriasis and were not diagnosed previously to have PsA, had persistent pain involving any joint/finger/toe or inflammatory back pain symptoms for more than 6 weeks, or remittent pain involving any joint/finger/toe or inflammatory back pain symptoms for 3 months. Exclusion criteria are as follows: current or recent (3 months) systemic treatment for psoriasis, a recent history of hand or foot trauma, current/recent engagement in heavy manual work, positive rheumatoid factor. Patients with history of urogenital, intestinal or other forms of infection with clinical picture suggestive of other forms of spondyloarthritis were also excluded.

Clinical assessment

Full demographic details and history of skin and joint disease, family history, and previous as well as current medications were recorded for each patient at the time of initial assessment. Age of psoriasis symptoms onset was recorded. The severity of psoriasis was evaluated with the psoriasis area and severity index (PASI) as well as body surface area affected. Clinical examination of all joints was carefully performed recording the pattern of peripheral and axial joint disease in addition to the presence of skin and nail affection. Soft tissue tenderness suggestive of enthesitis/dactylitis/tenosynovitis examination was also recorded. Assessment of the axial spine affection was assessed using ankylosing spondylitis disease activity score (ASDAS) [24], whereas enthesitis was assessed using Maastricht score (0–13) [25]. The patients were reassessed at 3-month intervals. Prior to each visit, every patient completed a patient-reported outcome questionnaire [22].

Laboratory assessment

ESR was measured by the standard Westergren method (mm/h). C-reactive protein (CRP) was measured by standard nephelometry (mg/l). Rheumatoid factor was measured by enzyme-linked

immunosorbent assay (ELISA) and results were expressed in titers of 1/20 and higher. Anti-nuclear antibody (ANA) was measured using Hep-2 substrate and results were expressed in titers of 1/40 and higher. Rheumatoid factor and ANA were both measured using commercial kits in the hospital diagnostic laboratory.

Radiological assessment

Plain radiographs of the hands and feet were performed at the initial visit and after 12 months of follow-up. In addition, x-rays of other affected joints, including knees, and sacroiliac joints were obtained at baseline and at 12-month follow-up visits or whenever indicated. The radiographs were evaluated by two trained/expert observers using the Sharp score method [26, 27] modified to include the distal interphalangeal joints (DIP). X-rays were analysed in a chronological order and observers were blind to the patient disease activity or medication. The maximum score for erosions in the hands was 210 and the maximum score for erosions in the feet was 50; the maximum scores for joint space narrowing in the hands and feet are 168 and 40, respectively. X-ray of the sacroiliac joints was scored according to the New York radiological criteria for sacroiliitis [28, 29].

US and PD examination

US examination was performed after the rheumatological assessment. The gray scale US and PD examination was performed by two musculoskeletal sonographers, who were blind to the history and clinical examination findings. All joints and tendons of all fingers and toes were examined using a multi-frequency linear array 14–21 MHz transducer. Power Doppler settings remained fixed throughout the study.

Assessment of enthesitis Examinations of the first and seventh costo-sternal joints, anterior superior iliac spine, and iliac crest were performed with the patients in supine position. The insertion of the Achilles tendons, the posterior superior iliac spine, and the fifth lumbar spinous process were examined with the patients in prone position, whereas rotator cuff insertion was examined while the patient was sitting. In B-mode, local hypoechoic swelling of the entheses (indicated by a convex surface of the enthesis adjacent to bone) were defined as sonographic signs of enthesitis. Detection of enhanced vascularity was defined as a sign of acute enthesitis.

Nail beds and nails were also assessed for onychopathy in the form of: (1) changes in the trilaminar appearance in the nails, (2) extensor tendon enthesopathy, and (3) enhanced vascularity at the nail bed.

US scoring is as follows: (1) The presence of synovial hypertrophy and vascularization were semi-quantitatively scored (0–3 scale) as well as the number and dimension of

bone erosions [30]; (2) Enthesitis: enthesitis scores were calculated using Glasgow ultrasound enthesitis scoring system (GUESS) index [31].

In order to assess reliability, every seventh participant was asked to return within 24 h to repeat the US examination. A total of 18 PsA patients and 16 controls were assessed for this purpose.

Control group

Clinical, laboratory, and US evaluation of fingers and toes was also performed in 112 sex and age-matched patients with chronic plaque psoriasis who did not have any history of finger and/or toe joint pain. Abnormal US findings warranted further clinical, laboratory as well as x-ray examination.

Assessment of disease progression

The outcome measure was an increase in the number of damaged joints. This is assessed (1) Clinically, based on the presence of joint deformities defined as a limitation of movement of more than 20 % of the range, the presence of flexion contractures, fused, or flail joints. (2) Radiologically based on development of erosions or persistent synovial hypertrophy or enhanced vascularity in either joints or enthesis attachment.

Statistical analysis

Values were presented as mean±standard deviation (SD) in continuous normally distributed variables while categorical data was described as numbers and percentages. Non-parametric variables means differences were tested using Mann-Whitney *U* test. Simple regression and the Spearman correlation coefficient were used to test correlation between variables. Clinical and sonographic predictors of joint damage progression were assessed using binary logistic regression analysis. Factors showing statistical border line significance were introduced to the regression model. Model showing the highest likelihood ratio was selected as the appropriate model identified the independent effect of these factors. Goodness of fit of the model was tested as well. Significant *P* value was always set at 0.05. All data manipulation and analysis of the data was performed using SPSS version 15 (SPSS, Inc., Chicago, IL)

Results

Demographic and disease characteristics at first visit (Table 1) revealed no significant difference between the psoriatic patients cohort who developed inflammatory arthritis changes and those who did not sustain any inflammatory musculoskeletal pathology, in terms of age, sex, PASI scoring, and mean

Table 1 Clinical characteristics of the patients included in this work

Character	PsA patients	Non PsA control
Number of patients	126	112
Age	35.9±8.7	34.5±9.6
Sex: F/M (%)	43.4/56.6	44.8/55.2
PASI	12.4±10.4	11.7±11.8
Mean duration of psoriasis (year)	4.8±3.1	4.6±3.6
Mean duration of musculoskeletal symptoms (months)	4.3±1.6	0
Positive family history of psoriasis	68/126 (54 %)*	12/112 (10.7 %)
Positive family history of psoriatic arthritis	31/112 (24.6 %)*	2/112 (1.8 %)
Number of patients off work for their musculoskeletal symptoms	32/126 (25.4 %)*	0
BMI	35.1±1.6*	27.8±1.7
Tender joints (total score 78)	5.6±3.4*	1.3±0.4
Swollen joints (total score 76)	0.9±2.2*	0
Dactylitis	4.1±2.6*	0.7±0.30
Enthesitis score (total score 13)	8.4±3.6*	0.6±0.20
ASDAS score	3.3±0.4*	1.1±0.2

F female, M male, PsA psoriatic arthritis, ASDAS ankylosing spondylitis disease activity score, PASI psoriasis area and severity index, BMI body mass index

* $P < 0.01$

duration of the psoriatic skin disease (Table 1). On the other hand, in contrast with the control group, the early PsA group of patients had significantly ($P < 0.01$) larger BMI (> 25) and higher prevalence of positive family history of psoriasis as well as psoriatic arthritis. By definition, the early PsA group had a significantly higher number of tender joints, enthesitis score, as well as axial spine ASDAS score. Structural deterioration was observed in 47 % of the 5,040 evaluated joints in 126 patients. Clinical variables associated with the risk of arthritis in psoriatic patients (Table 2) included higher BMI (OR=1.7, 95 % CI=1:02 to 1:10), percentage of body surface area affected (OR=1.13, 95 % CI=1:01 to 1:09), family

Table 2 Results of measures of association analysis on clinical predictors for progression of joint damage in patients with early psoriatic arthritis adjusted for sex

Variable	OR	95 % CI	P value
Sex (men vs women)	1.02	0.81–1.29	0.84
Positive family history of PsA	5.72	2.79–91.62	0.001
BMI	1.7	1.02–1.10	0.01
Percentage of body surface area	1.13	1.01–1.09	0.01
Nail involvement	2.25	1.36–3.41	0.001

PsA psoriatic arthritis, BMI body mass index, OR odds ratio, CI confidence interval

history of PsA ($P < 0.001$ /OR=5.72, 95 % CI=2.79 to 91.62), and nail involvement (OR=2.25, 95 % CI=1:36 to 3:41). High BMI (> 30) was significantly correlated ($P < 0.01$) with shorter interval of time for the onset of arthritis in psoriatic patients.

US assessment at baseline revealed abnormal B-mode US findings suggestive of PsA in at least one finger and/or toe (joints and/or tendons) seen in 87/126 (69 %) patients. In particular, enthesitis, dactylitis, and tenosynovitis were detected in 37/87 (42.5 %) of the early PsA patients. Of these 37 patients with soft tissue affection, 10/37 was identified as subclinical enthesitis. On assessment of enhanced vascularity, 70/86 patients (81.4 %) showed increased vascularization on PD assessment in synovial and/or at enthesitis sites; 6/86 (7 %) had one or more x-ray abnormalities mainly in the form of joint space narrowing, whereas erosions were seen in only two patients at baseline assessment.

Nails A relatively good agreement between clinical and sonographic nail findings was noted (kappa value=0.79, $P < 0.001$). US showed loss of trilaminar appearance in 91/126 (72.2 %) of the examined nails which could be visualized as a single hyperechoic layer within homogeneous thickness. Enteseal thickening of the extensor tendon on US was more frequent in patients with clinical nail disease compared to patients without clinical nail disease in both non-arthritic and arthritic psoriasis patients (38 vs. 16 %, $P = 0.03$, and 47 vs. 19 %, $P = 0.008$, respectively).

Over the 12-month follow-up period, structural deterioration was observed in 47 % of the 5,040 evaluated joints in 126 patients (Table 3). The mean Sharp erosion score of the hands and feet increased to 3.1 ± 3.1 in contrast to 0.17 ± 0.9 at baseline ($P = 0.002$). The mean narrowing of hands and feet joint

Table 3 Radiological features of psoriatic arthritis patients at baseline and 1-year follow-up

	Baseline	12 months follow-up
Total number of joints with erosions		
Hands	3/3,780 (0.07 %)	45/3,780 (1.2 %)
Feet	4/1,260 (0.1)	24/1,260 (1.9 %)
Mean number of joints with erosions per patient±SD		
Hands	0.02±0.5	1.0±1.4
Feet	0.07±0.6	1.1±1.6
Total number of joints with joint space narrowing		
Hands	11/3,780 (0.3 %)	24/3,780 (0.6 %)
Feet	21/1,260 (1.6 %)	33/1,260 (2.6 %)
Mean number of joint space narrowing per patient±SD		
Hands	0.1±0.5	0.7±1.1
Feet	0.2±0.7	0.5±0.9

SD standard deviation,

spaces increased to 3.2 ± 4.6 in comparison to 1.9 ± 0.8 at baseline ($P < 0.001$). At 12-months follow-up, sacroiliitis was present in 15/126 (11.9 %) patients, being unilateral in nine patients and bilateral in six patients.

Analysis of sonographic variables associated with the risk of progression in psoriatic patients at 12-months (Table 4) revealed that baseline synovial score of ≥ 2 /PD score ≥ 2 were significantly associated with increased risk of structural damage progression where gray scale ultrasound OR was 2.61 (1.26–2.94) $P < 0.001$ and power Doppler OR was 2.66 (1.08–2.76) ($P < 0.001$) versus 1.98 (1.05–2.65) for the clinical evaluation. In the joints with normal baseline examination (clinical or US), an increased probability for structural progression in the presence of enthesitis was also observed (gray scale ultrasound OR=2.46 (1.15–4.12) ($P < 0.01$) and power Doppler OR=3.50 (1.77–6.95) $P < 0.001$. This was supported by the finding that the baseline GUESS scores in psoriatic patients who developed progressive PsA later were significantly higher than those of patients who did not develop joint disease (9.86 ± 2.4 vs. 5.62 ± 2.31 , respectively, $P < 0.01$). Onychopathy was also associated with structural joint damage (OR 2.30, 95 % CI=1.17–3.69). In multiple conditional logistic regression analysis, persistent (vs. disappearance) of synovitis/enthesitis at 6 months of therapy was also predictive of subsequent structural progression.

Based on the radiographic and clinical outcomes, the CASPAR criteria had a sensitivity and specificity of 79.4 and 77.6 %, respectively, in diagnosing arthritis in psoriatic patients with PsA when compared with psoriatic patients. Adding US assessment parameters revealed further improvement of the CASPAR criteria sensitivity and specificity which increased to 93.4 and 98.6 %, respectively.

Reliability tests for US scoring of joints were performed with median (range) intra-observer intra-class correlation coefficients (95 % CI) of 0.89 (0.90 to 0.96) for gray scale US scores and 0.90 (0.91 to 0.96) for PD scores.

Table 4 Results of measures of association analysis on US predictors for progression of joint damage in patients with early psoriatic arthritis

Variable	OR	95 % CI	P value
Baseline US-gray scale joint synovial score ≥ 2	2.61	1.26–2.94	0.001
Baseline joint PD score ≥ 2	2.66	1.08–2.76	0.001
Presence of enthesitis at baseline on gray scale US	2.79	1.15–4.12	0.01
Baseline enhanced vascularity on PD at enthesitis sites	3.50	1.77–6.95	0.001
Baseline GUESS scores	2.46	1.17–2.24	0.001
Baseline onychopathy	2.30	1.26–2.58	0.01
Persistent synovitis/enthesitis at 6 months	6.62	1.11–1.83	0.0001

US ultrasound, PD power Doppler, GUESS Glasgow ultrasound enthesitis scoring system index

Discussion

The term “early PsA” remains imprecisely defined, and the duration of “early” disease can range from several months to anything less than 5 years. The delay in the emergence of arthritis after the initial presentation of psoriasis provides a unique opportunity to screen PsA patients for early evidence of joint disease. Results of this demonstrated that while some clinical parameters can serve as a screening tool for the psoriatic patients in standard clinical practice, US is able to depict reliably the early inflammatory changes in both joints and soft tissue. US showed also acceptable specificity for overall joint/soft tissue pathology in both affected and clinically unaffected patients with PsA. These findings are in agreement with earlier data reporting that US proved valuable in detecting joint and/or tendon abnormalities in the fingers and toes of patients with suspicious changes [32, 33]. Therefore, it can be suggested that US can be used as a tool for accurate assessment of early findings in psoriatic patients, especially in the presence of clinical risk factors.

Most studies to date in PsA have been performed on patients with longstanding disease. In most trials, the mean disease duration was greater than 7 years. The results of this work revealed inflammatory changes in psoriatic patients as early as 4 months of musculoskeletal symptoms and that these manifestations are less severe early in the disease course. Such findings are crucial if we are to catch the window of opportunity in this cohort. Early intervention would not only help to prevent further joint damage, but also will have a positive impact on the patients’ lives as well as ability to work. Earlier studies [34, 35] documented that joint damage is predictive of both functional limitation and mortality in PsA patients; therefore, it is important to prevent the progression of joint damage. In addition, these findings are of importance when considering appropriate treatment options for patients with early disease. This is in concordance with earlier data suggesting that PsA patients should be treated earlier in the course of their disease [36, 37].

Persistent activity seen on gray scale US or power Doppler ultrasound in the psoriatic patients was found to be a risk factor for disease progression. Yet, with all the recent advances and published research, the clinical relevance of what should be considered a positive ultrasound finding needs to be precisely clarified. This is especially important in the case of borderline results found on gray scale US, where it is difficult to distinguish between a pathologic and a physiologic state. Results of this work revealed that the presence of synovial hypertrophy or enhanced vascularity of score ≥ 2 were predictors of poor outcome. This is in agreement with the results of a recent study done to assess the clinical relevance of gray scale US grading of the joints in RA patients revealing that grade 1 findings on gray scale US have limited clinical relevance [38]. This is also in concordance with earlier findings assessing clinical joint examination, where grading of results has been abandoned in favor of a bilinear evaluation of the presence or

absence of pain and swelling [39, 40]. This is in part because of a lack of reproducibility and wide interrater variability [41] and because assignment of a grade of 1 to borderline abnormal findings poses the danger of over interpreting clinically irrelevant findings [42].

The lack of a validated case definition for PsA has been a major impediment to scientific research in this disease. In 2006, the CASPAR criteria were developed based on the results of a large prospective study [43] to be used in the context of clinical research and had a sensitivity and specificity of 91.4 and 98.7 %, respectively, in patients with PsA when compared with patients with other forms of inflammatory arthritis (primarily RA). A major limitation of this study was, however, that the patients enrolled had longstanding disease (mean disease duration 12.5 years). Another challenge is that these criteria require patients to have inflammatory arthritis, a finding that is open to interpretation and, as discussed above, is not always evident, particularly in the early stages of PsA. The high sensitivity and specificity of the CASPAR classification criteria suggest that they might also be used as diagnostic criteria for PsA. Several studies have tested the sensitivity of the CASPAR criteria for detecting early PsA [34, 35] in a retrospective study of 107 patients with early PsA (disease duration of less than 2.5 years) seen at a specialist PsA clinic over a 14-year period, 106 of the patients satisfied the CASPAR criteria (99.1 % sensitivity) [44]. A subsequent prospective study of patients with mean disease duration 15.8 weeks, however, noted a sensitivity of only 77.3 % [45]. Results of this study revealed the value of US in the diagnosis of early PsA patients. Based on the clinical and radiological outcomes, the sensitivity of the CASPAR criteria were 79.4 % whereas its specificity was 77.6 % which is in agreement with D'Angelo et al.'s study [45] study. This might be attributed to the fact the both D'Angelo et al.'s study and this study included patients of similar short disease duration. Adding US findings to the equation results in significant increase in both the sensitivity as well as specificity of the CASPAR criteria (93.4 and 98.6 %, respectively); this would highlight the role of US in identifying this group of patients suffering from active inflammatory disease. However, in general, though classification criteria should not be used for diagnostic purposes; the role of CASPAR criteria in the identification of patients with early PsA remains to be established.

Nail disease, occurs in 10–55 % of patients with psoriasis and in 53–86 % of patients with PsA, is increasingly recognized to be of major clinical and research relevance [46]. Results of this work showed significant correlation between the US and clinical findings for the assessment of the nail in psoriatic disease and that nail changes were found in 72.2 % of the patients. This is in agreement with earlier studies noting that the presence of psoriatic nail disease is more likely to be associated with the development of PsA [47]. The demonstration of extensor tendon

enthesopathy in both psoriasis and psoriatic arthritis supports the importance of enthesopathy in nail disease pathogenesis whether or not clinical arthritis is present. This might also be attributed to the finding that the nail is functionally integrated with entheses associated with the distal phalanx that provides anchorage to the skin and joint [48]. These findings are supported by histological studies showing that the nail and the enthesis are linked via the DIP joint extensor tendon. Also, the extensor tendon at its enthesis was found to send superficial fibers that make a substantial contribution to the thick periosteum on the dorsal aspect of the distal phalanx. At this site, dense fibrous connective tissue links the nail plate to the periosteum (and hence, indirectly to the extensor tendon itself) [49].

In conclusion, identifying predictor risk factors for the development of inflammatory arthritis in psoriatic patients are essential to clinical practice. The presence of US determined synovial thickness, enthesitis, and/or onychopathy associated with positive PD signal at baseline and the persistent PD signal over time have relevant prognostic value for the development of articular damage in psoriatic patients. These results could be an appropriate reference to dermatologists and rheumatologists, and a step forward to tailor the medical management to the patient's condition.

Acknowledgments The authors would like to express thanks to all participants, colleagues, research assistants, and nurses for their cooperation and help to bring this research to its final conclusions. The authors have no relevant financial disclosures.

References

1. McHugh NJ, Balachrishnan C, Jones SM (2003) Progression of peripheral joint disease in psoriatic arthritis: a 5-year prospective study. *Rheumatology (Oxford)* 42:778–783
2. Gladman DD, Stafford-Brady F, Chang CH, Lewandowski K, Russell ML (1990) Longitudinal study of clinical and radiological progression in psoriatic arthritis. *J Rheumatol* 17:809–812
3. Torre Alonso JC, Rodriguez Perez A, Castrillo JM, Ballina Garcia J, Riestra Noriega JL, Lopez Larrea C (1991) Psoriatic arthritis (PA): a clinical and radiological study of 180 patients. *Br J Rheumatol* 30: 245–250
4. Kane D, Stafford L, Bresnihan B, FitzGerald O (2003) A prospective, clinical and radiological study of early psoriatic arthritis: an early synovitis clinic experience. *Rheumatology (Oxford)* 42:1460–1468
5. Gladman DD, Farewell VT, Wong K, Husted J (1998) Mortality studies in psoriatic arthritis: results from a single outpatient center. II. Prognostic indicators for death. *Arthritis Rheum* 41:1103–1110
6. Gladman DD (2005) Disability and quality of life considerations. Psoriatic arthritis. In: Gordon GB, Ruderman E (eds) *Psoriasis and psoriatic arthritis: an integrated approach*. Springer-Verlag, Heidelberg, pp 118–123
7. Bandinelli F, Prignano F, Bonciani D, Pallanti S, Lotti T, Giovannini L, Maddali Bongi S, Matucci Cerinic M (2013) Clinical and socio-demographic factors influence on anxiety and depression in early psoriatic arthritis (ePsA). *Clin Exp Rheumatol* 31:0318–0319
8. Kavanaugh AF, Ritchlin CT (2006) and the GRAPPA Treatment Guideline Committee. Systematic review of treatments for psoriatic

- arthritis: an evidence based approach and basis for treatment guidelines. *J Rheumatol* 33:1417–1421
9. Mease PJ, Kivitz AJ, Burch FX et al (2004) Etanercept treatment of psoriatic arthritis: safety, efficacy, and effect on disease progression. *Arthritis Rheum* 50:2264–2272
 10. Kavanaugh A, Antoni CE, Gladman D et al (2006) The Infliximab Multinational Psoriatic Arthritis Controlled Trial (IMPACT): results of radiographic analyses after 1 year. *Ann Rheum Dis* 65:1038–1043
 11. Mease PJ, Gladman DD, Ritchlin CT et al (2005) Adalimumab for the treatment of patients with moderately to severely active psoriatic arthritis: results of a double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 52:3279–3289
 12. McInnes I, Kavanaugh A, Gottlieb A et al (2013) Efficacy and safety of ustekinumab in patients with active psoriatic arthritis: 1 year results of the phase 3, multicenter, double-blind, placebo-controlled PSUMMIT 1 trial. *Lancet* 382(9894):780–789
 13. Salvarani C, Olivieri I, Pipitone N et al (2006) Recommendations of the Italian Society for Rheumatology for the use of biologic (TNF α blocking) agents in the treatment of psoriatic arthritis. *ClinExpRheumatol* 24:70–78
 14. Salvarani C, Cantini F, Olivieri I et al (1997) Isolated peripheral enthesitis and/or dactylitis: a subset of psoriatic arthritis. *J Rheumatol* 24:1106–1110
 15. Jones SM, Armas JB, Cohen MG et al (1994) Psoriatic arthritis: outcome of disease subsets and relationship of joint disease to nail and skin disease. *Br J Rheumatol* 33:834–839
 16. Gladman DD, Shuckett R, Russell ML et al (1987) Psoriatic arthritis (PSA)—an analysis of 220 patients. *Q J Med* 62:127–141
 17. McGonagle D, Ash Z, Dickie L, McDermott M, Aydin SZ (2011) The early phase of psoriatic arthritis. *Ann Rheum Dis* 70(Suppl 1):i71–i76
 18. Ory PA, Gladman D, Mease P (2005) Psoriatic arthritis and imaging. *Ann Rheum Dis* 64(2):ii55–ii57
 19. Wiell C et al (2007) Ultrasonography, magnetic resonance imaging, radiography, and clinical assessment of inflammatory and destructive changes in fingers and toes of patients with psoriatic arthritis. *Arthritis Res Ther* 9:R119
 20. Peloso PM, Behl M, Hull P, Reeder B (1997) The psoriasis and arthritis questionnaire (PAQ) in detection of arthritis among patients with psoriasis. *Arthritis Rheum* 40(Suppl):S64
 21. Gladman DD et al (2009) Development and initial validation of a screening questionnaire for psoriatic arthritis: The Toronto Psoriatic Arthritis Screen (ToPAS). *Ann Rheum Dis* 68:497–501
 22. El Miedany Y, El Gaafary M, Youssef S, Palmer D (2010) Towards a multidimensional patient reported outcome measures assessment: development and validation of a questionnaire for patients with ankylosing spondylitis/spondyloarthritis. *Joint Bone Spine* 77(6): 575–581
 23. Taylor W, Gladman D, Helliwell P et al (2006) Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum* 54:2665–2673
 24. Fernández-Espartaco C, de Miguel E, Loza E et al. Validity of the Ankylosing Spondylitis Disease Activity Score (ASDAS) in patients with early spondyloarthritis from the Esperanza programme. *Ann Rheum Dis* doi:10.1136/annrheumdis-2012-202976
 25. Heuft-Dorenbosch L, Spoorenberg A, van Tubergen A et al (2003) Assessment of enthesitis in ankylosing spondylitis. *Ann Rheum Dis* 62:127–132
 26. Sharp JT, Lidsky MD, Collins LC, Moreland J (1971) Method of scoring the progression of radiologic changes in rheumatoid arthritis. *Arthritis Rheum* 14:706–720
 27. Sharp JT, Young DY, Bluhm GP et al (1985) How many joints in the hands and wrists should be included in a score of radiologic abnormalities used to assess rheumatoid arthritis? *Arthritis Rheum* 28:1326–1335
 28. Bennet PH, Burch TA (1967) New York Symposium of population studies in rheumatic diseases: new diagnostic criteria. *Bull Rheum Dis* 17:453–458
 29. Moll J, Wright V (1973) New York clinical criteria for ankylosing Spondylitis. A statistical evaluation. *Ann Rheum Dis* 32:354–363
 30. Szkudlarek M, Court-Payen A, Strandberg C (2001) Power Doppler ultrasonography for assessment of synovitis in the metacarpophalangeal joints of patients with rheumatoid arthritis: a comparison with dynamic magnetic resonance imaging. *Arthritis Rheum* 44:2018–2023
 31. Balint PV, Kane D, Wilson H, McInnes IB, Sturrock RD (2002) Ultrasonography of enthesial insertions in the lower limb in spondyloarthritis. *Ann Rheum Dis* 61:905–910
 32. De Simone C, Caldarola G, D'Agostino M et al (2011) Usefulness of ultrasound imaging in detecting psoriatic arthritis of fingers and toes in patients with psoriasis. *Clin Dev Immunol*. doi:10.1155/2011/390726
 33. Bandinelli F, Prignano F, Bonciani D et al (2013) Ultrasound detects occult enthesial involvement in early psoriatic arthritis independently of clinical features and psoriasis severity. *Clin Exp Rheumatol* 31: 0219–0224
 34. Husted JA, Tom BD, Farewell VT (2007) et al. A longitudinal study of the effect of disease activity and clinical damage on physical function over the course of psoriatic arthritis: does the effect change over time? *Arthritis Rheum* 56:840–849
 35. Gladman DD, Farewell VT, Wong K (1998) et al. Mortality studies in psoriatic arthritis: results from a single outpatient center. II. Prognostic indicators for death. *Arthritis Rheum* 41:1103–1110
 36. Gladman D, Thavaneswaran A, Chandran V, Cook R (2011) Do patients with psoriatic arthritis who present early fare better than those presenting later in the disease? *Ann Rheum Dis*. doi:10.1136/ard.2011.150938
 37. Bandinelli F, Bonacci E, Maticci M (2013) Ultrasound-integrated tight control in early psoriatic arthritis (PsA) during Adalimumab treatment. *Clin Exp Rheumatol* 31:440–442
 38. Witt M, Mueller F, Nigg A et al (2013) Relevance of grade 1 gray-scale ultrasound findings in wrists and small joints to the assessment of subclinical synovitis in rheumatoid arthritis. *Arthritis Rheum* 65(7):1694–1701
 39. Scott DL, Antoni C, Choy EH, van Riel PC (2003) Joint counts in routine practice [editorial]. *Rheumatology (Oxford)* 42:919–923
 40. Van der Heijde DM, van 't Hof M, Van Riel PL, van de Putte LB (1993) Validity of single variables and indices to measure disease activity in rheumatoid arthritis. *J Rheumatol* 20:538–541
 41. Hart LE, Tugwell P, Buchanan WW, Norman GR, Grace EM, Southwell D (1985) Grading of tenderness as a source of interrater error in the Ritchie articular index. *J Rheumatol* 12:716–717
 42. Grunke M, Antoni CE, Kavanaugh A, Hildebrand V, Dechant C, Schett G (2010) et al. Standardization of joint examination technique leads to a significant decrease in variability among different examiners. *J Rheumatol* 37:860–864
 43. Taylor W et al (2006) Classification criteria for psoriatic arthritis: development of new criteria from a large international study. *Arthritis Rheum* 54:2665–2673
 44. Chandran V et al (2009) Sensitivity of the classification of psoriatic arthritis criteria in early psoriatic arthritis. *Arthritis Care Res* 57: 1560–1563
 45. D'Angelo S et al (2009) Sensitivity of the classification of psoriatic arthritis criteria in early psoriatic arthritis. *J Rheumatol* 36:368–370
 46. Williamson L, Dalbeth N, Dockerty J et al (2004) Nail disease in psoriatic arthritis—clinically important, potentially treatable and often overlooked. *Rheumatology* 43:790–794
 47. Wilson FC, Icen M, Crowson CS et al (2009) Incidence and clinical predictors of psoriatic arthritis in patients with psoriasis: a population-based study. *Arthritis Rheum* 61:233–239
 48. McGonagle D, Benjamin M, Lyn TA (2009) The pathogenesis of psoriatic arthritis and associated nail disease: not autoimmune after all? *Curr Opin Rheumatol* 21:340–347
 49. Tan AL, Benjamin M, Toumi H et al (2007) The relationship between the extensor tendon entheses and the nail in distal interphalangeal joint disease in psoriatic arthritis: a high-resolution MRI and histological study. *Rheumatology (Oxford)* 46:253–256