Swollen joint count in psoriatic arthritis is associated with progressive radiological damage in hands and feet

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Abstract

Objectives

Psoriatic arthritis (PsA) may progress to joint damage. Determining clinical predictors of joint damage assessed by radiography is important. The aim of this study was to determine clinical factors as possible predictors for radiological damage in hands and feet of PsA patients with a 12-month follow-up.

Methods

We conducted a retrospective study on 53 PsA patients who were taking disease-modifying anti-rheumatic drugs (DMARDs) and/or tumour necrosis factor (TNF)-alpha-blockers at a fixed dosage. The patients were observed in 118 follow-up visits (intervals of 12 months ± 3 months), according to a clinical and radiological protocol which included the documentation of the number of swollen and tender joints in hands and feet, the applied therapy, psoriasis, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and global health assessment. Outcome was defined as radiographic damage of hands and feet (Ratingen score). For the statistical analysis the Chi-Square test for 2x2 crosstables (with Fisher's correction, as required) was used.

Results

Progressive radiological damage was more frequent among patients with an increasing swollen joint count (8 of 26 visits; 30.8%) than among those with a stable or decreased number of swollen joints (5 of 89 visits; 5.6%; p=0.001). The analysis of the patients stratified into the different treatment modalities resulted in a significant higher rate of radiological progress (20.8%) in patients on DMARD therapy compared with TNF-alpha blocking agents (0%) (p=0.009).

Conclusion

During a 12-month follow-up of PsA patients, an increasing number of swollen joints heralds progression of radiological damage. TNF-alpha-blocker therapy appears to be superior to DMARDs in the protection from radiological progress.

Key words

psoriatic arthritis, radiography, risk factors, tumour necrosis factor alpha inhibitors

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Introduction

Psoriatic arthritis (PsA) is a heterogenous inflammatory rheumatologic disorder with inflammation of the spine, enthesitis, and peripheral joints, affecting 6–39% of the patients suffering from psoriasis (1, 2). In previous studies, 20% of the patients were found to have >5 deformed joints at the first visit to the clinic. In addition, 11% showed a significant decline in the physical function (3). Other investigators have found that 47% of the patients developed erosive disease within 2 years of onset of symptoms (4).

Patients often suffer from joint destruction and a reduced quality of life (5). Moreover, PsA is prone to progressive disability and is associated with an increased risk of health-related retirement and an increased mortality rate compared to the general population (6).

If patients could be detected at an early stage, physicians could adapt their treatment to the course of PsA. The treatment includes DMARDs like methotrexate, ciclosporine A, and leflunomide (26); in addition, the effectiveness of the TNF-alpha antagonist agents in the treatment of inflammatory arthritis in PsA patients have been proved in several studies (7-9). Other studies have examined the role of clinical assessment tools in the course of disease (10, 11). Genetic variations in candidate genes encoding for TNF-alpha, PTPN22 or MHC (*e.g.* Human leukocyte antigen Cw6), are supposed to be associated with the occurrence and severity of PsA in the population (12-15). Further work has investigated the possible role of clinical variables as prognostic factors for progressive damage: the number of actively inflamed joints, particularly swollen joints, the current level of damage, the disease duration at presentation and the initial ESR level (11, 25). Furthermore, the recently published study of Cresswell *et al.* (25) has demonstrated that tenderness and swelling of the joints of the foot and/or hand seem to predict radiological joint damage in PsA.

In PsA conventional x-ray is basically inferior to other imaging modalities like CT or MRI; however, most of the studies with a follow-up design of imaging prefer conventional radiography because of the practical character and established radiological scoring systems. The aim of the current study was therefore the identification in PsA patients of clinical variables as possible predictors for radiographic damage in a 12-month follow-up.

Patients and methods

Patient selection

The medical records of 69 PsA patients with documented follow-up over more than 12 months were available, of whom 53 patients were included in the analysis. Sixteen patients were excluded because the follow-up was incomplete: either the clinical data including drug administration and/or the radiographic data were insufficient. We conducted a retrospective study on 118 follow-up visits of 53 patients treated between 2004 and 2009 at the rheumatology departments of Saarland University Medical School and the city hospital of Ludwigshafen, Germany. All patients satisfied the CASPAR criteria for PsA (16). Inclusion criteria were: PsA patients under therapy with DMARDs and/or TNF-alpha-blockers; documented clinical and radiological course of disease during the follow-up of the PsA patients (including baseline x-ray imaging and at least one follow-up imaging of the hands and feet). Table I shows the demographic and baseline clinical characteristics of the study participants. Relating to the different treatment regimes, the study population was stratified into patients treated with DMARDs and those receiving TNF-alpha blocking agents.

Treatment regime

The different anti-rheumatic drugs and their dosages administered to the study participants are outlined in Table I and II. Only patients abiding by the medication and the dosage regime were included in the study. Seven patients were excluded from the study: three patients stopped the DMARD therapy after more than three-fold elevation of liver enzyme levels. Three patients discontinued treatment with DMARDs, two because of a lack of efficacy and one patient had increasing serum creatinine concentrations. TNF-alpha block-

Table I. Characteristics of patients at first observational intervall.

Number of patients	53
Female/male	20/33
Mean age at clinic entry (years) (min–max)	54.8 (23–73)
Mean duration of disease before therapy (months) (min–max)	39.7 (0–240)
Family history of psoriasis (arthritis) (number of patients)	56.8% (25/44)
Mean number of tender joints (all joints) (min-max)	6.6 (0–29)
Mean number of swollen joints (all joints) (min–max)	4.7 (0–30)
Physician global assessment (number of patients)	
- good	13.2% (7/53)
- medium	52.8% (28/53)
- poor	34% (18/53)
Medication	
- NSAIDs	49% (26/53)
- corticosteroids	35.8% (19/53)
- DMARDs	74% (39/53)
- TNF-α blocker	26% (14/39)

NSAID: non-steroidal anti-inflammatory drug; DMARD: disease-modifying anti-rheumatic drug; TNF-α: tumour necrosis factor-α.

Table II. Anti-rheumatic drugs with their therapeutic ranges and the number of application intervals.

Drugs used	Dosage (mean)	Ranges	Number of observation intervals n=118 (%)
NSAIDs			
ibuprofen	828.6±458.9 mg/day	600–2400 mg	12 (10.2%)
diclofenac	86±48 mg/day	25–150 mg	10 (8.5%)
rofecoxibe	25 mg/day	25 mg	6 (5.1%)
Corticosteroids (prednisone-equivalent)	4.8±4.9 mg/day	2.5–10 mg	41 (34.8%)
DMARDs			
sulfasalazine	1947.4±437.6 mg/day	1000–3000 mg	23 (19.5%)
methotrexate	15.8±3.8 mg/week	10–20 mg	80 (67.8%)
leflunomide	19.4±2.5 mg/day	10–20 mg	19 (16.1%)
cyclosporine A	225±86.6 mg/day	150–300 mg	4 (3.4%)
TNF-α blocker			
etanercept	45.8±9.58 mg/week	25–50 mg	19 (16.1%)
adalimumab	40 mg/every 2 weeks	40 mg	16 (13.6%)

PsA: psoriatic arthritis; NSAID: non-steroidal anti-inflammatory drug; DMARD: disease-modifying anti-rheumatic drug; TNF-α-blocker: tumour necrosis factor-α blocker.

ers were given in the following mean doses: etanercept 50 mg/week and adalimumab 40 mg every two weeks. One patient stopped the treatment with adalimumab due to inefficiency. No severe allergies or infectious complications were observed among the study population.

In addition to the specific antirheumatic therapy with DMARDs or TNF-alpha blockers, 26 patients (49%) were on concomitant treatment with fixed doses of NSAIDs and 19 patients (35.8%) on corticoisteroids (10 mg per day prednisolone or less) for the time of observation.

Study protocol

The follow-up of PsA patients was documented in medical records containing the medical history and a physical examination including rheumatologic assessment of tender and swollen joints. Furthermore, physicians recorded demographic characteristics of the patients such as sex, age, family history, arthritis duration, time of onset of psoriasis, and the medication actually taken by the patients; a routine laboratory assessment including C-reactive protein (CRP) and elevated sedimentation rate (ESR) was carried out. For all patients x-ray radiographs of both hands and feet were available. Patients were followed up at 12-month (±3-month) intervals. The radiologist was responsible for reading the x-rays and evaluating them according to the scoring system (see below) at the end of the study.

Assessment of clinical activity of PsA

Patients were seen at baseline and then at intervals of approximately 12 months by the same rheumatologist. The physical function and clinical disease activity of the joints were recorded at all visits. Physicians examined the clinical disease activity using the American College of Rheumatology (ACR) 66/68 counts for swollen and tender joints. The following 68 joints were assessed for tenderness: all these joints, except the hips, were also examined for swelling.

The global health assessment was evaluated by patients using a scoring system ranging from 0 (no activity) to 4 (very high disease activity), according to the functional class model previously published (11). The severity of psoriasis was determined by the presence of nail lesions and the percentage of the body surface area (BSA) involved. The psoriasis was rated as mild (<5% of the BSA), moderate (5–20% of the BSA, or lower if the hands and feet were involved), moderate-severe (20–30% of the BSA, or lower if the hands and feet were involved) and severe (>30% of the BSA). Finally, the documentation of the medication regime by each patient was complete. It included the circumstances in case the treatment regime had been changed during the follow-up interval.

Assessment of radiological damage in PsA

An x-ray radiography was performed by posterior-anterior and optional semisupine projections of the hands and feet. The radiographic damage grade was measured with the Osirix medical imaging software. Radiographic joint damage was defined as progressive if new lesions like erosions or proliferations had been detected or if pre-existent lesions had increased.

In order to classify radiological damage accurately, the evaluation of any radio-

logical damage was based on the Ratingen scoring system that was developed specifically for PsA (17). It includes 40 joints of the hands and feet: eight distal interphalangeal joints, two interphalangeal joints of the thumbs, eight proximal interphalangeal joints, ten metacarpophalangeal joints, both wrists, both IPs of the great toes, and second to fifth metatarsophalangeal joint.

All joints were scored separately for destruction (on a 0–5 scale) and proliferation (on a 0–4 scale), which could be summed up to give the total score (0–360).

Joint surface destruction was categorised on a 0–5 scale as: 0. normal, 1. destruction <10% of the total joint surface, 2. destruction of 11–25%, 3. destruction of 26–50%, 4. destruction of 51–75%, 5. destruction >75%.

The proliferation grade was determined on a 0–4 scale: 0. normal, 1. bone growth less than 25% of the original diameter of the bone, 2. bone growth between 25–50%, 3. bone growth between 51–75%, and 4. ankylosis.

Statistical analysis and principal outcome variables

The aim of this retrospective study was to investigate if any of the mentioned clinical variables had a predictive value for progressive radiological damage. As x-rays were taken at a mean time of 12-month intervals, only visits at which both clinical and radiological damage were assessed were evaluated.

The main outcome was the progression of radiographic damage between two clinic visits; it was estimated by substracting the initial score of damage from the score measured after one year. To analyse the relations between the clinical variables and their possible association with the development of radiological progression, the data were stratified into two groups in order to describe the changes in the scores of joint destruction and clinical damage after one year: the first group showed a stable or regressive damage score and the second group had a worse damage score compared to the last examination. For statistical analyses the Chi-square test for 2x2 crosstables (with Fisher's correction, as required) was used, and *p*-values below 0.05 were considered significant. The Statistical Package for the Social Sciences (SPSS version 17.1) was used.

The ethics committee of the medical association of the Saarland, Germany, approved the study, and all study participants gave written informed consent for the retrospective analysis of their medical data.

Table III. Clinical variables in association with progressive radiological joint damage in PsA.

Clinical variables	Radiological joint damage		Odds ratio	*p*-value
	progressive	stable or regressive		
Clinical health assessment				
progressive	10% (3/30)	90% (27/30)	0.822	0.999
stable or regressive	11.9% (10/84)	88.1% (74/84)	[0.210–3.214]	
Number of tender joints				
progressive	17.1% (6/35)	82.9% (29/35)	2.141	0.211
stable or regressive	8.8% (7/80)	91.3% (73/80)	[0.668–6.967]	
Number of swollen joints				
progressive	30.8% (8/26)	69.2% (18/26)	7.503	0.001
stable or regressive	5.6% (5/89)	94.4% (84/89)	[2.187–25.490]	
ESR level				
progressive	10.5% (4/38)	89.5% (34/38)	0.891	0.999
stable or regressive	11.7% (7/60)	88.3% (53/60)	[0.242–3.274]	
CRP level				
progressive	11.8% (4/34)	88.2% (30/34)	1.257	0.740
stable or regressive	9.6% (7/73)	90.4% (66/73)	[0.342–4.622]	
Psoriatic skin damage				
progressive	9.1% (1/11)	90.9% (10/11)	0.850	0.999
stable or regressive	10.5% (10/95)	89.5% (85/95)	[0.098–7.352]	
Drugs				
DMARDs	20.8% (14/67)	79.2% (53/67)	53.772	0.009
TNF-α blocker	0% (0/28)	100% (28/28)	[0.491–33.647]	

(…): number of observation intervals; […]: confidence interval; PsA: psoriatic arthritis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; DMARD: disease modifying antirheumatic drug; TNF-α-blocker: tumour necrosis factor-α blocker.

Results

We evaluated a total of 118 follow-up intervals from 53 patients. Depending on the number of radiological examinations per patient, more than one follow-up visit was included for some patients. The time interval between radiological examinations was 12±3 months.

A radiological progression was found in 14 follow-up intervals (from 11 patients). Thus, three patients showed a deterioration of damage twice in the subsequent observation interval. The mean change from baseline in the Ratingen score was +2.21±3.21.

Radiological damage and level of treatment

Altogether, 67 follow-up intervals were evaluated, during which 39 patients were treated with DMARDs (Table I and II). In 14 of 67 (20.8%) intervals (12 patients), a progression of radiological damage was found (Table III). The mean change in the Ratingen Score was +2.27±3.58. Six patients discontinued the treatment with DMARDs and changed to the biological arm. In the further follow-up all patients showed an inhibition of radiographic progression (Ratingen score -0.71±1.11).

Biologicals were administered in a total of 28 follow-up intervals of 14 patients (Table I). None of these patients showed a radiological progression (Ratingen score -0.22±0.66) (p=0.009) (Table III, Fig. 1).

Radiological damage and swollen joint count

The number of actively inflamed joints also correlated with radiographic dam-

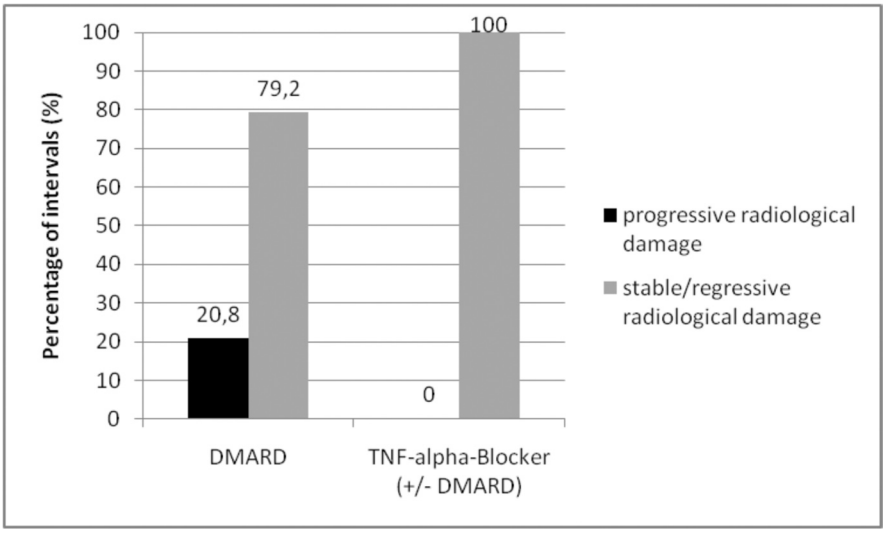

Fig. 1. Antirheumatic therapy stratified for radiological damage in PsA patients.
Progressive radiological damage was much more frequent among patients treated with DMARDs than among those receiving a TNF-α-blocker therapy (p=0.009). DMARD: disease modifying anti-rheumatic drug, TNF-α-blocker: tumour necrosis factor-α-blocker.

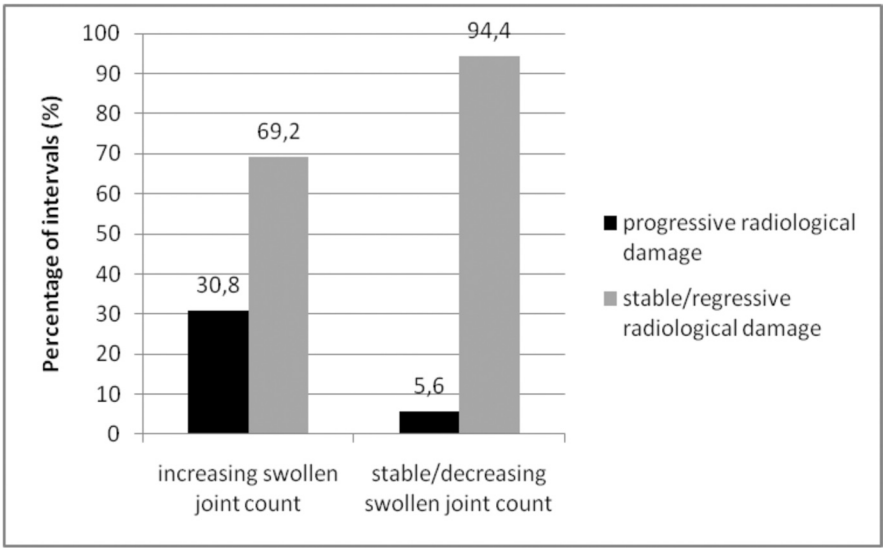

Fig. 2. Changing swollen joint count stratified for radiological damage in PsA patients. Patients with an increasing number of swollen joints had a significant (p=0.001) higher rate of radiological progress than patients with a stable or decreased swollen joint count.

age. In 8 of 26 visits (30.8%) of the follow-up, patients with swollen joints also showed radiological progress (Ratingen score +2.55±3.94), whereas only 5 of 89 visits (5.6%) of the follow-up patients with a stable or even decreased swollen joint count showed new or progressive radiological damage (Ratingen score +1.75±1.5) (p=0.001) (Table III, Fig. 2). The numbers of tender joints, skin damage, nail involvement, ESR, CRP and global health assessment did not correlate with any radiographic outcome (Table III).

Discussion

This study on PsA patients documents that an increasing number of swollen joints is significantly associated with progression of radiological damage.

In PsA, joint damage as determined by previously published assessment tools and histology is an important outcome measure (18, 19). Some patients develop damage early and rapidly progress towards an "arthritis mutilans" with massive joint destruction. It is therefore important to detect these patients at an early stage of disease and to start an appropriate treatment. In this context, the meaningfulness of different clinical parameters as potential predictors for progressive radiological damage is of great importance. In agreement with our data, previous studies pointed to the role of clinical variables as prognostic factors for progressive radiological damage in the long-term observation: the number of actively inflamed joints, particularly the swollen joints, the number of clinically damaged joints and the initial ESR at presentation. These variables could be associated with progression of joint disease and early mortality in PsA (11, 20). Furthermore, a polyarticular joint inflammation at first clinic presentation was found as a possible predictor for progression as well (11, 21). In addition, the recently published data from Creswell *et al*. (25) presented a clear association of both joint tenderness and welling with radiological damage in hands and feet. In that study, all patients did not show any radiographic damage at the beginning of the follow-up period.

In the present study, the radiological examination also focussed on the joints of the hands and feet as these are the joints that are primarily involved in the inflammatory process. However, the evaluation of the radiological data is based on follow-up intervals and not on patients. This procedure means that one patient is evaluated in one observation interval as "stable or regressive" and possibly in the next interval as "progressive". Furthermore, in contrast with previous studies, PsA patients were also included into the analysis with already proved radiological damage. This strategy allowed a dynamic observation of different developments in the course of disease over the observation intervals. However, the limitation of this procedure model is the presence of inter- and intraindividual interferences influencing the meaningfulness of the presented data with regard to statistically significant differences. Furthermore, the study has recruited a relatively small number of participants (only fifty-three) for the retrospective analysis based on clinical and radiological data out of medical records; therefore, a sensible statistical analysis by a multivariate analysis model was not possible. Nevertheless,

the data also seem to verify the importance of the clinical parameter of swelling joint count as a predictive factor for radiological damage.

The radiological joint destruction was quantified with the Ratingen score (17). In this study, the Ratingen score was preferred over Larson score because it only scores bony changes of the joints: we did not consider soft tissue swelling as a criterium, because its evaluation might be influenced by the quality of the radiograph, especially the hardness of the x-ray source. In addition, it only reflects the activity of the inflammatory process in the soft tissues and is often quickly reversible.

In our study, 20.8% of the patients taking DMARDs had a progressive erosion score. In contrast, none of the patients treated with anti-TNF agents showed an increased radiological joint damage. Although the influence of the treatment modality was not the primary aim of the present study, the subgroup analysis of the data showed that PsA patients on medication with TNF-alpha-blockers, unlike the patients on DMARDS, developed neither new erosions nor a progression of existent erosions. This result supports earlier studies, which observed that anti-TNF agents actually have higher clinical and radiological response rates in PsA patients than DMARDs. In addition to a beneficial effect on the clinical symptoms of joint inflammation, the anti-TNF antagonist agents also showed potential to slow down, and to some extent even reverts, radiographic joint damage in PsA (7-9, 22-24, 27).

Conclusion

The presented data indicate that an increasing swollen joint count in patients with PsA is associated with progression of radiological damage.

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Authors' contributions

P. Simon collected and analysed the data and wrote the main paper. G. Assmann conceived and supervised the study, corrected the paper and gave conceptual advice and support. R. Bergner provided additional clinical data from the rheumatological centre of the city of Ludwigshafen. M. Schreiber scanned and converted conventional x-rays into high quality digital files (Osirix). C. Pföhler provided dermatological data to help us estimate their course of psoriasis. M. Pfreundschuh was involved in the interpretation of the clinical data. All the authors were included in the writing and correction of the manuscript, and they all read and approved the final manuscript.

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