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ORIGINAL RESEARCH

Determinants of radiographic progression in early psoriatic arthritis: insights from a real-world cohort

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ABSTRACT

Objective Persistent articular inflammation in psoriatic arthritis (PsA) is associated with radiographic damage. Despite advances in diagnosis and therapy, radiographic structural damage remains prevalent in PsA. To elucidate this topic, we studied which baseline clinical characteristics determine radiographic progression.

Methods For this analysis, data were used from DEPAR (Dutch South West Psoriatic Arthritis) Study, a real-world cohort of patients with newly diagnosed PsA. Radiographic changes were assessed using the modified Total Sharp/van der Heijde Score (mTSS) for PsA. Univariable–multivariable mixed-effects negative binomial regression analysis was applied to define baseline predictors for radiographic progression over time.

Results The study included 476 patients with early PsA with 1660 hand and feet radiographs from four different time points (baseline, first, second and third year). The progressive group (n=71) had a higher mTSS compared with the non-progressive group (n=405) at diagnosis (17 (3–36) vs 0 (0–1)). A comparison of the two groups revealed that the progressive group had significantly older (59 (12) vs 49 (13)) and a higher rate of the presence of swollen joints (93% vs 78%) at diagnosis. Multivariable analysis identified age (incidence rate ratio (IRR)=1.10, p=0.000), sex (female) (IRR=0.48, p=0.043) and baseline mTSS (IRR=1.11, p=0.000) as significant determinants of radiographic change over time. For the progressive subset, additionally, the multivariable analysis highlighted baseline Disease Activity in PSoriatic Arthritis (IRR=1.05, p=0.006) and swollen joint count (IRR=1.07, p=0.034) as predictors.

Conclusions According to this real-world cohort, patients with early PsA exhibit minimal radiographic progression under current treatment protocols. This study indicates that while old age and initial radiographic damage predict progression, female sex confers a protective effect on it. Furthermore, disease activity score and swollen joints emerged as predictors for radiographic changes during the follow-up in progressive patients.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Despite advances in psoriatic arthritis (PsA) management, radiographic damage remains prevalent.
⇒ Existing studies emphasise rapid progression, but comprehensive real-world cohort data on predictors are scarce.

WHAT THIS STUDY ADDS

⇒ Our study reveals a low radiographic progression in early PsA under current treatment protocols.
⇒ Age and baseline damage predict progression, while the female sex acts as a protective factor.
⇒ These findings emphasise the critical role of initial assessments in shaping patient care.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ In daily clinical practice, prioritising initial radiographic assessments is crucial, serving not just for diagnosis but also as predictors of future radiographic changes.
⇒ In individuals with these predictors, close monitoring is recommended during the disease course.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory and clinically heterogeneous disease, characterised by arthritis enthesitis, dactylitis, spondylitis and psoriasis affecting the skin and nails.[1] Persistent articular inflammation in PsA can lead to structural damage in cartilage and bone, including bone erosions, joint space narrowing (JSN), complete joint destruction and sometimes abnormal new bone growth.[2 3] This structural damage is closely tied to reduced physical function and diminished quality of life.[4]

Conventional radiography (CR) remains the primary modality for assessing structural damage in PsA.[2 5] It plays a pivotal role in disease management by providing prognostic utility,[6] monitoring of disease activity[7] and assessing the effectiveness of treatment.[8]

Among the various scoring systems available for grading radiographic changes using CR, the modified Total Sharp/van der Heijde Score (mTSS) has been found as one of the most sensitive to show changes in radiographs of hands and feet.[9]

Our current understanding of radiographic damage in PsA largely stems from non-contemporary cohorts or randomised controlled trials (RCTs). These studies have underscored the presence of radiological damage in PsA, even in its early stages, and its progressive nature. For instance, Kane *et al* observed that, at baseline, 27% of patients presented with erosions and 21% displayed JSN. Within 2 years, the prevalence of erosive disease reached 47%.[10] In another study by Siannis *et al*, a baseline erosion prevalence of 33.6% was identified among 655 patients with PsA.[11] A recent study by Coates *et al*, in 2015, revealed that 25% of the study population exhibited signs of erosive disease at the beginning, with this percentage rising to 31% by the 48-week follow-up.[12] Another recent early PsA cohort study from Sweden revealed that, initially, 49% of patients with PsA displayed no radiographic changes. However, this proportion decreased to 29% after 5 years.[7]

Addressing the predictive clinical factors linked to radiographic progression is a still crucial unmet need.[13] Previous research has identified several baseline predictors, including delayed diagnosis of PsA (greater than 6 months), prolonged symptom duration (more than 1 year prior to diagnosis), advanced age (over 50 years), female sex, smoking, presence of dactylitis at the initial assessment, higher disease activity levels, polyarticular disease involvement, presence of erosive disease and nail changes in PsA.[14–19] However, these predictors have not consistently been validated for clinical applications.

A significant portion of current radiographic data on PsA is sourced from RCTs, often focusing on patients with severe disease manifestations. This has led to a paucity of real-world cohort study data. Moreover, limited insights are available on prognostic factors influencing radiographic changes in PsA, especially from studies conducted before the widespread adoption of modern treatment regimens. Our primary objective is to establish comprehensive radiographic data based on a real-world early PsA cohort using CR. Additionally, we aim to investigate whether any baseline clinical determinants can be identified for radiographic progression in an early PsA cohort. Through our study, we aim to provide comprehensive radiographic insights and identify baseline clinical predictors for radiographic progression, thereby enhancing our understanding of PsA and its monitoring.

METHODS

Patients

Data were used from the Dutch South West Psoriatic Arthritis (DEPAR) cohort which is a cohort that consists of patients with PsA who were newly diagnosed in real-world data from the modern era. The study design of the DEPAR cohort has been previously reported.[20] In brief, the DEPAR includes patients with a new diagnosis of PsA made by the rheumatologist receiving usual care. Data from patients enrolled in the cohort between July 2013 and March 2022 and who had at least a 3-year follow-up (study initiation: 2013–2018) by this time were used in this study.

Clinical data

During the first year of our cohort, data were gathered at 3-month intervals, followed by 6-month intervals in the second year and then annually thereafter.[21] Our study visits were conducted by proficient research nurses who documented clinical information, including assessments of swollen and tender joints (swollen joint count (SJC) 66 and tender joint count 68 joints, respectively), enthesitis evaluations using the Leeds Enthesitis Index, and the assessment of psoriasis severity using the Psoriasis Area and Severity Index (PASI).[22 23]

Additionally, patients completed multiple questionnaires. For this study, we used data derived from the Health Assessment Questionnaire (HAQ) and patients' self-reported scores on the Visual Analogue Scale (VAS). The HAQ Disability Index was employed to assess functional ability. Pain and global disease activity were measured on a 0–100 mm VAS, where higher scores indicate a poorer health status.[24]

According to our study, disease activity was monitored with the Disease Activity in PSoriatic Arthritis (DAPSA). C reactive protein (CRP) levels were analysed by the laboratory of the respective inclusion sites.

In our study, 'biological use ever' was defined as a biological agent use at any point within a specified 3-year time frame and pre-PsA treatment. This criterion also encompasses patients who initiated and subsequently ceased biological therapy during follow-up.

Radiographic data and reading procedure

Baseline (T0) radiographs of both hands and feet were obtained, followed by subsequent radiographs at the first (T12), second (T24) and third (T36) year. The mTSS for PsA containing two components (JSN and erosion score) was employed to evaluate the radiographic changes.[2]

Two trained independent readers, who were blinded to patient identity and treatment, independently and chronologically (sequenced reading) assessed the X-rays of the first 30 patients. Agreement scores and kappa values were separately computed for each of the four time points (T0, T12, T24, T36) based on their assessments. The level of agreement between readers was determined by weighted kappa for the total mTSS and was found to be 0.78 with 97% agreement, indicating a high level of consistency.[25] Subsequently, given the observed high consistency in the first 30 patients according to calculated kappa values, the remaining dataset was divided into two equal parts for individual assessment. All radiographs of one patient were examined in sequential order during

single sessions, with a focus on JSN and erosion scores to ensure the stability of the mTSS.[26]

Radiographic progression, change and lesion (damage)

Radiographic progression over a 3-year follow-up period was determined according to the radiological outcome guidelines established in clinical trials.[27] It was defined as a change in mTSS greater than 0.7, precisely calculated as the smallest detectable change for our study. Patients were categorised into progressive and non-progressive groups based on this definition.[26]

Radiographic changes over time were derived from the mixed-effects negative binomial regression (MENBR) analysis. In this analysis, mTSS was used as a continuous outcome variable. Given the inability to establish a clinical cut-off for significance in terms of radiographic progression, the results obtained from the MENBR were designated as radiographic changes.

In our study, radiographic lesions (damages) were evaluated if the current mTSSs were observed to be higher than 0.

Furthermore, mTSS, our chosen scoring system for radiographic assessment, primarily focuses on evaluating distal peripheral joints (hands/feet). Therefore, when we refer to 'radiographic progression, change and lesion' in our study, we are specifically addressing changes in these distal peripheral joints.

Statistical analysis

The description of data and the comparison of groups

In this study, mean values were presented for normally distributed data, while medians were used for non-normally distributed data. Baseline patient characteristics and comparison of groups (non-progressive vs progressive) were analysed with simple descriptive statistics.

Descriptive statistics were employed to report baseline predictors and radiographic findings for each group (progressive vs non-progressive). Student's t-test, X^2 or Wilcoxon rank-sum tests were used to compare the groups as appropriate.

To handle missing values, multiple imputations using chained equations (MICE) were used for CRP, DAPSA and PASI which were missing more than 10%. For our analysis, we generated 20 imputed datasets to ensure sufficient variability among the imputed values, which is recommended to achieve reliable estimates. MICE was applied only for exposures. Linear interpolation was used to estimate missing values for mTSS which was our outcome, while data for T12 and T24 were interpolated from T0 and T36 data where necessary.[28] In MENBR analysis, we ran the dataset without linear interpolation. mTSS changes per patient over 3 years were presented using cumulative probability plots.[29]

Longitudinal analysis to define baseline predictors for radiographic changes

Due to the skewed distributions of radiographic scores generated by the mTSS method, linear regression was not considered appropriate. Instead, a generalised linear regression model with a negative binomial distribution, known as negative binomial regression (NBR), was used, as it provided the best fit to the data. NBR was chosen as it accounts for missing values, zero inflation and the positively skewed distribution of the radiographic data.[30] MENBR models were employed to appropriately model the longitudinal structure of the data, including the estimation of random intercept and time slope parameters. All four mTSSs at different measurement time points (T0, T12, T24 and T36) were used as dependent variables. Variables that were marginally associated with progression in univariate analyses ($p<0.20$) were simultaneously entered into the multivariable MENBR analysis model. A first-order autoregressive covariance structure for repeated measurements was used in the models, as this structure provided the best fit to the data based on Akaike and Bayesian information criteria and likelihood ratio tests. Results were reported as incidence rate ratios (IRRs) with 95% CIs. In both univariable and multivariable regression analyses, only baseline mTSS was included due to multicollinearity among different damage components at baseline, such as JSN and erosion scores. Similarly, to address the same issue with DAPSA and its components, multivariable NBR analysis was conducted twice in the progressive group: first with only DAPSA and then without DAPSA, focusing solely on its components.

Sensitivity analysis

Joint involvement in hand and foot

The mTSS represents a comprehensive approach aimed at capturing the overall burden of joint damage. To validate and evaluate the robustness of this approach, sensitivity analyses were conducted in two different subgroups. The first subgroup consisted of patients with hand/foot involvement, identified by assessing the presence of swollen and/or tender joints in either the hands or feet at the study's onset. Subsequently, the MENBR was rerun specifically for these patients (n=409). In the second subgroup analysis, we targeted patients with diagnoses as 'mono-', 'oligo-' or 'poly-' arthritis, excluding those with axial involvement, enthesitis or dactylitis (n=375). This refined analysis aimed to differentiate patients without baseline peripheral arthritis, thereby ensuring that the study's conclusions remain consistent when focusing solely on hand and foot joint involvement.

Four-group categorisation of radiographic changes

To gain insights into how different exposures influenced mTSS changes over time, the study population was categorised into four distinct groups based on observed change trends over 3 years:

- Group 1: patients with no radiographic changes at baseline (BLmTSS=0) who remained stable without any mTSS changes (ΔmTSS <0.7) throughout the study.

Table 1 Baseline demographic and disease characteristics

	Included patients (n=476)
Clinical parameters	
Age (years)*	50 (14)
Female sex†	52 (245)
Symptom duration at diagnosis (months)‡	9 (3–29)
Body mass index (kg/m^2)*	28 (5)
Swollen joint count (0–66)‡	2 (1–5)
Tender joint count (0–68)‡	4 (2–8)
CRP (mg/dL)†	8.8 (12.4)
DAPSA*	18.6 (9.3)
PASI‡	2.8 (0.8–3.9)
HAQ‡	0.7 (0.4–1.1)
VAS*	48 (25)
Current dactylitis†	19 (90)
Current enthesitis†	37 (176)
Radiographic assessment	
mTSS‡	0 (0–2)
Current radiographic lesion§†	30 (143)

*Mean (SD).
†% (n).
‡Median (IQR).
§Baseline mTSS >0.
CRP, C reactive protein; DAPSA, Disease Activity in PSoriatic Arthritis; HAQ, Health Assessment Questionnaire; mTSS, modified Total Sharp/van der Heijde Score; n, number of case; PASI, Psoriasis Area and Severity Index; VAS, Visual Analogue Scale.

- Group 2: patients with initial radiographic changes (BLmTSS >0) but without progression (ΔmTSS <0.7) during the study.
- Group 3: patients who showed both initial radiographic changes (BLmTSS >0) and progression (ΔmTSS >0.7) over the study period.
- Group 4: patients with no baseline changes (BLmTSS=0) who displayed progression (ΔmTSS >0.7) over the 3 years.

To identify baseline predictors, particularly the impact of sex on radiographic progression, multinomial logistic regression analyses were executed based on the four-group categorisation. These logistic regression models were adjusted for factors such as age, sex and biological use during the study's follow-up.

RESULTS

Patients and clinical outcomes

Data from 476 patients, for whom baseline radiographs of the hands and feet were accessible, were included in the analysis. At baseline, patients had an average age of 50 years (SD: 14). An equal distribution between sexes was noted, with the symptom duration averaging 7 months (IQR: 3–28) (see table 1). Patients without available T0 mTSS or at least two time points of mTSS data were considered lost to follow-up (see online supplemental figure 1).

Radiographic outcomes

For this study, 1660 radiographs were included from four different time points. At baseline, radiographic lesions were observed in 30% of the entire study population. Further analysis revealed that 25% of patients exhibited erosive lesions and 28% demonstrated JSN (see table 2). At the upper extreme, only one patient had an mTSS of 167, composed of an erosion score of 85 and a JSN score of 82. Notably, only a small subset, precisely five patients, had mTSSs exceeding 100. 80% of these patients were female; the mean age was 69 years, the mean duration of symptoms was 59 months and the mean number of swollen joints at baseline was 6.

At baseline, both JSN and erosion scores had median values of 0, falling within an IQR of 0–1. Meanwhile, the median mTSS was recorded at 0, with an IQR of 0–2. To facilitate the understanding of mTSS changes over time, given the presence of numerous zero values in the

Table 2 Radiographic changes in time

	At baseline	1st year	2nd year	3rd year
mTSS, n	476	476	394	314
mTSS, median (IQR)	0 (0–2)	0 (0–3)	0 (0–5)	0 (0–6)
JSN, median (IQR)	0 (0–1)	0 (0–2)	0 (0–2)	0 (0–3)
Erosion score, median (IQR)	0 (0–1)	0 (0–2)	0 (0–2)	0 (0–2)
Estimated mTSS*, mean (95% CI)	6.9 (1.2–11.6)	7.4 (1.7–12.1)	7.9 (2.2–12.6)	8.4 (2.7–13.0)
Current radiographic lesion†, % (n)	30 (143)	32 (150)	35 (138)	38 (119)
Current erosive lesion†, % (n)	25 (122)	28 (124)	30 (117)	32 (101)
Current JSN†, % (n)	28 (135)	31 (137)	33 (130)	36 (112)

*Estimated marginal mean mTSS values by reaching to run a linear mixed model (adjusted for age).
†mTSS >0, erosion score >0, JSN>0.
JSN, joint space narrowing; mTSS, modified Total Sharp/van der Heijde Score; n, number of case.

observed data, a linear mixed model was employed. This approach aimed to help perceive the trend of change in mTSSs, allowing for the calculation of the estimated average mTSS for each time point. At baseline, the average estimated mTSS was observed to be 6.9, ranging from (95% CI) 1.2 to 11.6 (see table 2).

By the end of the third year, an upward trend emerged in radiographic lesions. The percentage of patients exhibiting a radiographic lesion had risen to 39%, and the average estimated mTSS increased to 8.4, with a range from (95% CI) 2.7 to 13.0 (see table 2).

However, a significant majority of study participants (405 out of 476) did not exhibit substantial radiographic progression. This group was classified as non-progressive, with 21% of them presenting radiographic lesions at the beginning of the study. In contrast, 71 patients (14% of the total participants) were categorised as progressive, with the majority (80%) showing radiographic lesions from their initial assessment (see table 3).

Figure 1 displays a cumulative probability plot illustrating changes in individual mTSS, JSN and erosion scores during the follow-up period. While the erosion

Table 3 Two-group comparison table of baseline characteristics

	Non-progressive group (n=405)	Progressive group (n=71)	P value
Clinical parameters			
Age (years)*	49 (13)	59 (12)	**0.000**
Female sex†	50 (202)	57 (40)	0.312
Symptom duration (months)‡	9 (4–28)	12 (4–35)	0.190
Body mass index (kg/m^2)*	28 (5)	28 (5)	0.247
SJC (0–66)‡	2 (1–5)	5 (2–6)	0.076
The presence of SJC§†	78 (335)	93 (58)	**0.011**
SJC >2†	46 (195)	61 (39)	**0.029**
TJC (0–68)‡	4 (1–8)	5 (3–9)	0.148
The presence of TJC§†	88 (353)	89 (63)	0.826
CRP (mg/dL)*	8.47 (12.04)	11.64 (14.74)	0.126
CRP >7†	50 (217)	59 (37)	0.197
DAPSA*	18.40 (9.45)	20.61 (8.48)	0.333
DAPSA >14†	73 (294)	82 (58)	0.107
PASI‡	2.87 (0.8–3.7)	2.68 (1.8–4.5)	0.258
HAQ‡	0.75 (0.38–1.13)	0.68 (0.5–1.0)	0.956
VAS*	48 (26)	44 (20)	0.272
Dactylitis‡	0 (0–0)	0 (0–0)	0.290
The presence of dactylitis§†	18 (73)	23 (16)	0.339
Enthesitis‡	0 (0–1)	0 (0–1)	0.749
The presence of enthesitis§†	37 (148)	39 (28)	0.641
Radiographic assessment			
mTSS‡	0 (0–1)	17 (3–36)	**0.000**
JSN‡	0 (0–1)	10 (1–19)	**0.000**
Erosion score‡	0 (0–0)	5 (0–20)	**0.000**
Baseline radiographic changes§†	26 (110)	81 (51)	**0.000**
Treatment			
Baseline biological use (yes/no)†	18 (70)	10 (7)	0.087

Bold values denote statistical significance at the p <0.05 level.
*Mean (SD).
†% (n).
‡Median (IQR).
§SJC >0, TJC >0, LEI >0, number of dactylitis >0, mTSS >0.
CRP, C reactive protein; DAPSA, Disease Activity in PSoriatic Arthritis; HAQ, Health Assessment Questionnaire; JSN, joint space narrowing; LEI, Leeds Enthesitis Index; mTSS, modified Total Sharp/van der Heijde Score; n, number of case; PASI, Psoriasis Area and Severity Index; SJC, swollen joint count; TJC, tender joint count; VAS, Visual Analogue Scale.

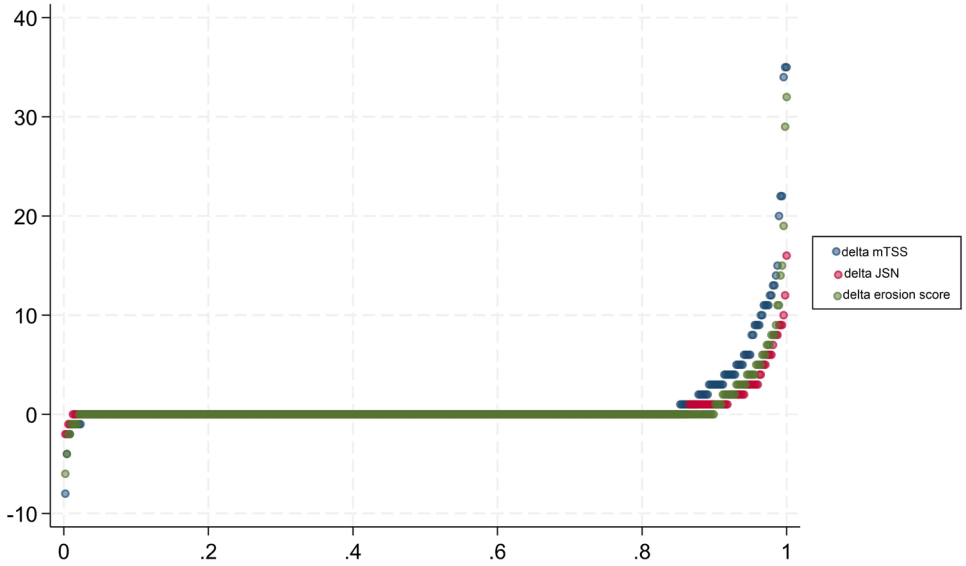

Figure 1 Cumulative probability plot per patient showing changes from baseline to 3 years in mTSS, JSN and erosion scores. delta JSN, changes in joint space narrowing; delta mTSS, changes in modified Total Sharp/van der Heijde Score.

score appeared slightly dominant, it generally followed a similar trend to JSN.

Comparison of baseline determinants of groups according to radiographic progression

In comparing between groups (progressive vs non-progressive), the average age of patients in the progressive group stood at 59 (±12) years, notably higher than the non-progressive group, which averaged 49 (±13) years (p=0.000). There were not any observed differences between the sexes. The median SJCs were higher in the progressive group, though this difference was not statistically significant. However, a larger proportion of progressive patients reported swollen joints (93%) compared with those in the non-progressive group (78%) (p=0.011). While disease activity indicators like baseline CRP and baseline DAPSA did not differ significantly between groups, those in the progressive group did present with higher mean values (see table 3).

Baseline predictors for radiographic changes over time

For the entire study cohort (n=476), univariable regression analysis of 1660 radiographs identified several factors significantly linked to radiographic outcomes (mTSS). These factors included age, sex, SJC, PASI, VAS, HAQ, dactylitis, enthesitis, baseline mTSS and biological agent use during follow-up. However, after running the multivariable analysis, only age, female sex and BLmTSS were found to be significant predictors of radiographic changes over time. Notably, old age (IRR=1.10, p=0.000) and high baseline mTSS (IRR=1.11, p=0.000) were associated with radiographic changes over 3 years; the female sex had a protective effect on radiographic changes (IRR=0.48, p=0.043) (see table 4).

Focusing on the progressive subgroup, the univariable regression analysis identified age, symptom duration, SJC, baseline CRP, DAPSA, BLmTSS and the use of biological agents during follow-up as significant factors. Subsequent multivariable analysis revealed age (IRR=1.03, p=0.014), SJC (IRR=1.07, p=0.034), DAPSA (IRR=1.05, p=0.006) and mTSS (IRR=1.04, p=0.000) as substantial baseline predictors (see table 5).

Sensitivity analysis

We conducted a sensitivity analysis to assess whether there were disparities in baseline variables between the patients included in the study and those excluded due to an inability to complete the 3-year follow-up or missing baseline data. Although there were generally no significant differences, we observed that the included patients were older and had higher PASI values (please refer to online supplemental table 5).

Additionally, figure 1 illustrates that mTSS and its components exhibit a similar trend of change over time. In online supplemental tables 3 and 4, we substituted erosion score and JSN for mTSS as the baseline radiographic measures, respectively. The results of the multivariable analysis remained consistent with our primary findings.

Joint involvement in hand and foot

In the entire cohort, 67 patients did not exhibit hand and foot involvement at baseline. After excluding these patients and focusing only on those with hand and foot joint involvement (n=409), the univariable MENBR revealed findings consistent with the main analysis of the entire population. Specifically, age, sex, VAS, HAQ, dactylitis, enthesitis, BLmTSS and biological use during follow-up were identified as significant factors. Upon multivariable adjustment, age (IRR=1.09, p=0.000), female sex (IRR=0.53, p=0.040) and BLmTSS (IRR=1.11, p=0.000) remained as the principal predictors for radiographic changes, consistent with findings from the

Table 4 Univariable–multivariable negative binomial regression analysis in the entire study population (n=476)

	Univariable			Multivariable		
	IRR	95% CI	P value	IRR	95% CI	P value
Age	1.17	1.13 to 1.20	**0.000**	1.10	1.07 to 1.14	**0.000**
Female sex	0.27	0.15 to 0.48	**0.000**	0.48	0.29 to 0.96	**0.043**
Symptom duration	1.00	0.99 to 1.00	0.652			
Body mass index	1.01	0.95 to 1.07	0.611			
Swollen joint count	1.12	1.05 to 1.18	**0.000**	1.02	0.95 to 1.09	0.623
Tender joint count	1.00	0.96 to 1.06	0.831			
CRP	0.99	0.98 to 1.02	0.976			
DAPSA	1.00	0.97 to 1.03	0.880			
PASI	0.95	0.87 to 1.04	0.293			
HAQ	0.58	0.34 to 1.10	**0.050**	0.91	0.43 to 1.94	0.820
VAS	0.98	0.96 to 0.99	**0.001**	1.00	0.99 to 1.01	0.692
Dactylitis	0.72	0.48 to 1.07	**0.104**	0.82	0.51 to 1.34	0.532
Enthesitis	0.64	0.51 to 0.81	**0.000**	0.89	0.68 to 1.16	0.374
Baseline mTSS	1.12	1.10 to 1.13	**0.000**	1.11	1.09 to 1.14	**0.000**
Biological use ever*	0.26	0.15 to 0.45	**0.000**	0.76	0.39 to 1.50	0.439

Bold values denote statistical significance at p <0.20 level in univariable models and the p <0.05 level in multivariable models.
*Biological use (yes/no) during follow-up and pre-PsA treatment.
CRP, C reactive protein; DAPSA, Disease Activity in PSoriatic Arthritis; HAQ, Health Assessment Questionnaire; IRR, incidence rate ratio; mTSS, modified Total Sharp/van der Heijde Score; n, number of case; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; VAS, Visual Analogue Scale.

Table 5 Univariable–multivariable negative binomial regression analysis in the progressive group (n=71)

	Univariable			(A) Multivariable*			(B) Multivariable*		
	IRR	95% CI	P value	IRR	95% CI	P value	IRR	95% CI	P value
Age	1.13	1.09 to 1.17	**0.000**	1.04	1.00 to 1.06	**0.006**	1.03	1.00 to 1.05	**0.014**
Female sex	0.79	0.33 to 1.86	0.598						
Symptom duration	1.01	1.00 to 1.01	**0.037**	1.00	0.99 to 1.01	0.368	1.00	0.99 to 1.00	0.963
Body mass index	1.04	0.96 to 1.13	0.349						
Swollen joint count	1.19	1.07 to 1.32	**0.001**	1.07	1.00 to 1.14	**0.034**			
Tender joint count	1.02	0.96 to 1.10	0.438						
CRP	1.04	0.99 to 1.08	**0.114**	1.02	0.99 to 1.04	0.055			
DAPSA							1.05	1.02 to 1.09	**0.002**
PASI	1.00	0.83 to 1.21	0.964						
HAQ	1.27	0.54 to 2.98	0.574						
VAS	0.99	0.97 to 1.01	0.550						
Dactylitis	0.82	0.51 to 1.28	0.374						
Enthesitis	0.88	0.63 to 1.23	0.468						
Baseline mTSS	1.06	1.05 to 1.07	**0.000**	1.04	1.03 to 1.05	**0.000**	1.04	1.03 to 1.05	**0.000**
Biological use ever†	0.55	0.23 to 1.31	**0.178**	0.91	0.53 to 1.58	0.742	0.81	0.47 to 1.39	0.448

Bold values denote statistical significance at p <0.20 level in univariable models and the p <0.05 level in multivariable models.
*A. MENBR analysis was performed with only DAPSA components (CRP, SJC); B. MENBR analysis was performed only with DAPSA without its components.
†Biological use (yes/no) during follow-up and pre-PsA treatment.
CRP, C reactive protein; DAPSA, Disease Activity in PSoriatic Arthritis; HAQ, Health Assessment Questionnaire; IRR, incidence rate ratio; MENBR, mixed-effects negative binomial regression; mTSS, modified Total Sharp/van der Heijde Score; n, number of case; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; SJC, swollen joint count; VAS, Visual Analogue Scale.

primary cohort analysis (see online supplemental table 1).

Similar to the previous sensitivity analysis results, in only patients with monoarthritis, oligoarthritis and polyarthritis phenotypes at diagnosis (n=375), after multivariable analysis, age (IRR=1.06, p=0.000), female sex (IRR=0.48, p=0.022) and BLmTSS (IRR=1.10, p=0.000) were observed as predictors (see online supplemental table 6).

Four-group categorisation of radiographic changes

The study population was categorised based on the observed trends of mTSS changes over the 3-year duration. Online supplemental figure 2 illustrates the distribution of mTSS changes across these groups. Notably, within the progressive group (n=71), 80% had radiographic lesions at baseline. However, only 20% showed progression without initial radiographic damages, translating to merely 3% of the entire study cohort.

Multinomial logistic regression analysis based on four-group categorisation: the multinomial logistic regression analyses, adjusted for age, sex and biological use, indicated that female sex offered protection against baseline radiographic lesions (group 2, β=−0.58 (95% CI −1.1 to −0.7), p=0.025). Yet, no significant sex effect was observed on radiographic progression over time. Contrarily, the presence of SJC at baseline was strongly associated with both baseline radiographic damages and radiographic progression at follow-up for patients with early PsA (group 2, β=1.00 (95% CI 0.24, 1.18), p=0.010; group 3, β=1.1 (95% CI 0.16, 2.1), p=0.022) (online supplemental table 2).

DISCUSSION

The present study delves into radiographic progression in a cohort of patients with early PsA within a real-world setting. Our objectives were to describe the radiographic outcomes in our early PsA cohort and identify baseline clinical predictors associated with radiographic progression over a span of 3 years. The elucidated data offer critical insights into the disease, aiding clinical decision-making and patient monitoring.

In our cohort of 476 patients with early PsA, totalling 1660 hand and feet radiographs, baseline radiographic lesions were noted in 30%. This prevalence increased to 38% over 3 years. In the study population, only 3% showed progression without initial radiographic damage, while 80% of those who exhibited radiographic progression had baseline damage. These findings echo those of prior studies that emphasise the presence of radiological damage in PsA, even in its early phases, and underscore its progressive nature. Notable comparisons include Kane *et al*, who reported a progression from 27% to 47% over 2 years,[10] and a previous PsA cohort study in Canada, involving 655 patients, which revealed a baseline rate of 33.6% for radiographic damage.[11] A recent comprehensive study on early PsA by Coates *et al* found that 25% had at least one erosion at baseline, with this figure rising to 31% at 48 weeks.[12]

One key finding from this study is the identification of baseline clinical factors associated with radiographic progression in early PsA. Our refined multivariable analysis observed older age and elevated mTSS at the initial as potential risk factors. Interestingly, the female sex appeared to confer a degree of resistance against radiographic changes. These findings are consistent with previous research, one of which is an age over 50 years at diagnosis correlating with deteriorated physical functionality.[15] In another study investigating the impact of tenderness on PsA, baseline radiographic damage was the only variable significantly associated with radiographic progression, despite many factors not having a marked influence, including joint tenderness.[31]

Complementing our data, the role of baseline SJC and disease activity level (DAPSA) in radiographic progression has been consistently underscored in earlier studies as a predictor for radiographic progression.[18 32 33] Especially in the subgroup of patients who exhibited radiographic progression, multivariable analysis revealed high SJC and disease activity (DAPSA) as statistically significant predictors for radiographic changes. Our results resonate with studies showing that high disease activity correlates with functional impairment and structural progression on radiographs.[34] Bond *et al* found that the number of actively inflamed joints, particularly the number of swollen joints, was associated with the progression of radiological damage.[18] Furthermore, Gladman *et al* reported that the progression of clinical and radiographic damage in PsA has been related to disease activity and severity, both at presentation and follow-up, emphasising the significance of disease activity in radiographic progression.[32] These findings underscore that baseline swollen joints and disease activity may play a pivotal role in the radiographic progression of PsA.

The sex-specific patterns we unearthed, suggesting that females had a protective effect against radiographic progression given existing damage, align with findings from the early PsA Sweden cohort.[7] Nevertheless, contrasting observations have been documented, where female sex correlates with structural damage and physical disability in PsA.[15 17] These sex-dichotomous trends necessitate further investigative depth.

Our investigation, conducted in a real-world cohort, offers a nuanced perspective distinct from the conventional RCTs. Indeed, real-world cohorts provide detailed insight into the natural progression of diseases, capturing the complexities commonly encountered in clinical settings. Such insights, unaffected by the constraints of clinical trial settings, make our conclusions especially relevant to daily patient care. Considering the inherent variability arising from the diverse demographic spectrum in real-world studies is crucial. Nevertheless, our data demonstrated a remarkable consistency in outcomes despite this diversity.

The limitations of this study include the temporal constraint of a 3-year follow-up, which necessitates acknowledgement despite the robustness of our findings. Extending the observational window would offer richer insights into the disease's long-term trajectory. Most studies, ours included, have consistency in reporting erosive changes; however, there is variability in results, especially concerning JSN and specific factors.[10–12] These variations may arise from differences in the X-ray reading procedure, which can influence outcomes. In our study, we used a sequenced reading method to evaluate radiographic data. This involved pairing and assessing radiographs of the same patient at different time points in known chronological order. It is known from previous rheumatoid arthritis, osteoarthritis and PsA studies that this approach increases sensitivity by accounting for changes in positioning and film quality, thus reducing commonly encountered evaluation errors.[9 35–37] However, the limited radiographic changes over 3 years suggest that longer intervals or alternative imaging methods like MRI are needed to adequately detect radiographic progression in PsA under contemporary treatment approaches. Moreover, the reliance on mTSS to evaluate radiographic damage introduces inherent limitations, notably its restriction to assessing only small peripheral joints (hands and feet). Nonetheless, it is noteworthy that our primary findings were validated by sensitivity analyses conducted across diverse subgroups, taking into account these acknowledged limitations.

In conclusion, based on this longitudinal real-world cohort, patients with early PsA demonstrated low rates of radiographic progression with current treatment protocols. This study provided comprehensive radiographic data from the DEPAR cohort study and identified baseline clinical predictors associated with radiographic progression. The present study shows that radiographic change in PsA is associated with old age and baseline radiographic damage, with an observed protective effect noted in females. Additionally, the presence of a swollen joint at baseline is related to the exhibition of radiographic progression. Baseline disease activity score and SJC were also a significant predictor for radiographic changes during follow-up in the progressive group.

The implications for daily clinical practice are clear: initial radiographic assessments are paramount, not only as diagnostic tools but also as predictors of radiographic changes over time. In patients exhibiting these markers, rigorous monitoring is advocated to pre-empt and manage potential radiographic progression during the disease course.

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REFERENCES

1 Coates LC, Helliwell PS. Psoriatic arthritis: state of the art review. *Clin Med (Lond)* 2017;17:65–70.
2 Wassenberg S. Radiographic scoring methods in Psoriatic arthritis. *Clin Exp Rheumatol* 2015;33:S55–9.
3 van der Heijde D, Sharp J, Wassenberg S, *et al*. Psoriatic arthritis imaging: a review of scoring methods. *Ann Rheum Dis* 2005;64 Suppl 2:ii61–4.
4 Kerschbaumer A, Baker D, Smolen JS, *et al*. The effects of structural damage on functional disability in Psoriatic arthritis. *Ann Rheum Dis* 2017;76:2038–45.
5 Mathew AJ, Østergaard M, Eder L. Imaging in Psoriatic arthritis: status and recent advances. *Best Pract Res Clin Rheumatol* 2021;35:S1521-6942(21)00032-2.

6 Laasonen L, Lindqvist U, Iversen L, *et al*. Radiographic scoring systems for Psoriatic arthritis are insufficient for Psoriatic arthritis Mutilans: results from the Nordic PAM study. *Acta Radiol Open* 2020;9:2058460120920797.
7 Geijer M, Lindqvist U, Husmark T, *et al*. The Swedish early Psoriatic arthritis Registry 5-year followup: substantial radiographic progression mainly in men with high disease activity and development of Dactylitis. *J Rheumatol* 2015;42:2110–7.
8 Husni ME, Kavanaugh A, Murphy F, *et al*. Efficacy and safety of intravenous Golimumab through one year in patients with active Psoriatic arthritis. *Arthritis Care Res (Hoboken)* 2020;72:806–13.
9 Tillett W, Jadon D, Shaddick G, *et al*. Feasibility, reliability, and sensitivity to change of four radiographic scoring methods in patients with Psoriatic arthritis. *Arthritis Care Res* 2014;66:311–7.
10 Kane D, Stafford L, Bresnihan B, *et al*. A prospective, clinical and radiological study of early Psoriatic arthritis: an early Synovitis clinic experience. *Rheumatology (Oxford)* 2003;42:1460–8.
11 Siannis F, Farewell VT, Cook RJ, *et al*. Clinical and radiological damage in Psoriatic arthritis. *Ann Rheum Dis* 2006;65:478–81.
12 Coates LC, Moverley AR, McParland L, *et al*. Effect of tight control of inflammation in early Psoriatic arthritis (TICOPA): a UK Multicentre, open-label, randomised controlled trial. *Lancet* 2015;386:2489–98.
13 Jadon DR, Stober C, Pennington SR, *et al*. Applying precision medicine to unmet clinical needs in Psoriatic disease. *Nat Rev Rheumatol* 2020;16:609–27.
14 Haroon M, Gallagher P, FitzGerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in Psoriatic arthritis. *Ann Rheum Dis* 2015;74:1045–50.
15 Tillett W, Jadon D, Shaddick G, *et al*. Smoking and delay to diagnosis are associated with poorer functional outcome in Psoriatic arthritis. *Ann Rheum Dis* 2013;72:1358–61.
16 Brockbank JE, Stein M, Schentag CT, *et al*. Dactylitis in Psoriatic arthritis: a marker for disease severity *Ann Rheum Dis* 2005;64:188–90.
17 Husted JA, Tom BD, Farewell VT, *et al*. Description and prediction of physical functional disability in Psoriatic arthritis: a longitudinal analysis using a Markov model approach. *Arthritis Rheum* 2005;53:404–9.
18 Bond SJ, Farewell VT, Schentag CT, *et al*. Predictors for radiological damage in Psoriatic arthritis: results from a single centre. *Ann Rheum Dis* 2007;66:370–6.
19 Antony AS, Allard A, Rambojun A, *et al*. Psoriatic nail dystrophy is associated with erosive disease in the distal Interphalangeal joints in Psoriatic arthritis: A retrospective cohort study. *J Rheumatol* 2019;46:1097–102.
20 Wervers K, Vis M, Tchetveriko I, *et al*. Burden of Psoriatic arthritis according to different definitions of disease activity: comparing minimal disease activity and the disease activity index for Psoriatic arthritis. *Arthritis Care Res (Hoboken)* 2018;70:1764–70.
21 Kasiem FR, Luime JJ, Vis M, *et al*. Lessons learned from clinical phenotypes in early Psoriatic arthritis: the real-world Dutch South West early Psoriatic arthritis study. *Scand J Rheumatol* 2021;50:124–31.
22 Healy PJ, Helliwell PS. Measuring clinical Enthesitis in Psoriatic arthritis: assessment of existing measures and development of an instrument specific to Psoriatic arthritis. *Arthritis Rheum* 2008;59:686–91.
23 Henseler T, Schmitt-Rau K. A comparison between BSA, PASI, PLASI and SAPASI as measures of disease severity and improvement by therapy in patients with psoriasis. *Int J Dermatol* 2008;47:1019–23.
24 Cauli A, Gladman DD, Mathieu A, *et al*. Patient global assessment in Psoriatic arthritis: a multicenter GRAPPA and OMERACT study. *J Rheumatol* 2011;38:898–903.
25 van Tuyl LHD, van der Heijde D, Knol DL, *et al*. Chronological reading of Radiographs in rheumatoid arthritis increases efficiency and does not lead to bias. *Ann Rheum Dis* 2014;73:391–5.
26 Bruynesteyn K, Boers M, Kostense P, *et al*. Deciding on progression of joint damage in paired films of individual patients: smallest detectable difference or change. *Ann Rheum Dis* 2005;64:179–82.
27 van der Heijde D, Simon L, Smolen J, *et al*. How to report radiographic data in randomized clinical trials in rheumatoid arthritis: guidelines from a Roundtable discussion. *Arthritis Rheum* 2002;47:215–8.
28 Landewé R, van der Heijde D. Presentation and analysis of radiographic data in clinical trials and observational studies. *Ann Rheum Dis* 2005;64 Suppl 4:iv48–51.
29 Landewé R, van der Heijde D. Radiographic progression depicted by probability plots: presenting data with optimal use of individual values. *Arthritis Rheum* 2004;50:699–706.
30 Park GS, Wong WK, Khanna D, *et al*. Examining radiographic outcomes over time. *Rheumatol Int* 2014;34:271–9.
31 Gessl I, Hana CA, Deimel T, *et al*. Tenderness and radiographic progression in rheumatoid arthritis and Psoriatic arthritis. *Ann Rheum Dis* 2023;82:344–50.
32 Gladman DD, Mease PJ, Choy EHS, *et al*. Risk factors for radiographic progression in Psoriatic arthritis: Subanalysis of the randomized controlled trial ADEPT. *Arthritis Res Ther* 2010;12:R113.
33 Simon P, Pfoehler C, Bergner R, *et al*. Swollen joint count in Psoriatic arthritis is associated with progressive radiological damage in hands and feet. *Clin Exp Rheumatol* 2012;30:45–50.
34 Aletaha D, Alasti F, Smolen JS. Disease activity States of the DAPSA, a Psoriatic arthritis specific instrument, are valid against functional status and structural progression. *Ann Rheum Dis* 2017;76:418–21.
35 van Der Heijde D, Boonen A, Boers M, *et al*. Reading Radiographs in chronological order, in pairs or as single films has important implications for the Discriminative power of rheumatoid arthritis clinical trials. *Rheumatology (Oxford)* 1999;38:1213–20.
36 Bruynesteyn K, van der Heijde D, Boers M, *et al*. Minimal clinically important difference in radiological progression of joint damage over 1 year in rheumatoid arthritis: preliminary results of a validation study with clinical experts. *J Rheumatol* 2001;28:904–10.
37 Botha-Scheepers S, Watt I, Breedveld FC, *et al*. Reading Radiographs in pairs or in chronological order influences radiological progression in osteoarthritis. *Rheumatology (Oxford)* 2005;44:1452–5.