Clinical and Demographic Characteristics of Erosion-free and Erosion-present Status in Psoriatic Arthritis in a Cohort Study

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ABSTRACT. ***Objective.*** Psoriatic arthritis (PsA) has been recognized as a severe erosive disease. However, some patients do not develop erosions. We aimed to determine the prevalence, characteristics, and predictors of erosion-free patients (EFP) as compared with erosion-present patients (EPP) among patients with PsA followed prospectively.

Methods. This is a retrospective analysis conducted on patients from the Toronto PsA cohort. Patients with at least 10 years of followup and radiographs were analyzed. Radiographs were scored with the modified Steinbrocker method. Baseline (first visit to clinic) characteristics were used to predict the development of erosions with logistic regression models. To examine the effect of time-varying covariates, Cox regression models were fit for the time to development of erosions from baseline.

Results. Among 290 patients, 12.4% were EFP and 87.6% were EPP over the study period. The mean time to development of erosion in the EPP over the course of followup was 6.8 ± 6.1 years. EFP were diagnosed with psoriasis at a younger age compared with EPP. In both models, actively inflamed joints and clinically damaged joints were predictive of the development of erosion, whereas a longer duration of psoriasis at baseline decreased the odds of developing erosion. EPP had a higher percentage of unemployment as compared with EFP at baseline and followup visits.

Conclusion. Among patients with PsA followed for at least 10 years, 12.4% never develop erosions. The clinical and radiographic findings can ultimately assist in the stratification of a patient's prognosis regarding the development of erosions. (First Release April 1 2016; J Rheumatol 2016;43:1057–62; doi:10.3899/jrheum.150466)

Key Indexing Terms:
PSORIATIC ARTHRITIS EROSION PSORIASIS PREDICTION PROGNOSIS

Psoriatic arthritis (PsA) is a chronic, progressive disease that is associated with a high rate of radiographic joint erosions at an early stage in the course of the disease. Erosions are considered a typical destructive feature of PsA that has been reported in 67% of patients at their first visit to the clinic after an average duration of 9 years, and in 27% of patients at 10 months after onset of arthritis[1,2,3,4]. Kane, *et al* showed that despite clinical improvement with disease-modifying antirheumatic drugs (DMARD), at a followup examination at 2 years from onset of arthritis, 47% of patients had erosions[2]. The presence of erosions has been recognized as a predictive factor for progression of joint damage as well as for mortality[5,6,7,8]. Although erosions are very common in PsA, a number of patients remain erosion-free despite years of disease while other patients develop erosions during the course of the disease.

In our study, we aimed to determine (1) the prevalence, characteristics, and predictors of erosion-free patients (EFP) as compared with erosion-present patients (EPP) among those with PsA, and (2) the predictors of development of erosions and the time to development of erosions.

MATERIALS AND METHODS

Patient selection. This was a retrospective analysis conducted on all patients with PsA with at least a 10-year period of followup in the University of Toronto PsA cohort. The study was approved by the research ethics board of the University Health Network, and all patients gave written informed consent that was obtained according to the Declaration of Helsinki. The ClASsification for Psoriatic ARthritis (CASPAR) criteria for PsA were fulfilled by 98% of patients[9,10].

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Study definitions. EPP were patients with any peripheral joints with a modified Steinbrocker score[11] ≥ 2 either at baseline or during followup in the clinic. EFP could not have any peripheral joint erosions at baseline (first visit to clinic) or over the course of followup.

Demographic data. Demographics on all patients were collected during each clinic visit. Patients with adult PsA were evaluated in the PsA clinic by rheumatologists according to a standard protocol, which included a clinical assessment and laboratory evaluation at 6–12-month intervals and radiographic assessment at 2-year intervals[9]. Employment status was categorized as employed or unemployed.

Clinical assessment: PsA (peripheral and axial) and psoriasis activity. Baseline refers to the first clinic visit for each patient in the Toronto PsA cohort. At each baseline and followup visit, symptoms were reported (joint pain as present or absent), and physical examination (including complete musculoskeletal examination) with joint counts (68 joints for tenderness and 66 joints for swelling) was performed. The number of actively inflamed joints was recorded. An "actively inflamed" joint was defined as the presence of joint tenderness and/or effusion. Clinically damaged joints (68 assessed joints) were defined by the presence of limitation of range of movement of > 20% not related to the presence of joint effusion, joint deformity, subluxation, loosening, or ankylosis. Inflammatory spinal pain attributed to PsA was determined based on physician clinical judgment as concluded from subjective and objective data collected during a visit and was reported as present or absent. Psoriasis severity was assessed by the Psoriasis Area and Severity Index (PASI)[12]. At each visit, detailed information on current use of medications [nonsteroidal antiinflammatory drugs (NSAID), DMARD, and biologic drugs] was collected.

Laboratory and radiological assessment. Routine laboratory tests were collected and recorded at each visit. Radiographs were performed at 1- or 2-year intervals and scored according to the modified Steinbrocker method[11]: 0 = normal, 1 = soft tissue swelling/osteopenia, 2 = erosions, 3 = erosion and joint space narrowing, and 4 = total joint destruction.

Statistical analyses. Baseline descriptive statistics were computed for continuous variables [mean (SD)] and categorical variables [frequencies (%)]. The employment status as a binary outcome (employed/not employed) was further studied in EPP and EFP at baseline and the last followup visit in accordance to the region of joint involvement by PsA. Upper joint involvement was defined as active joints and damaged joints (clinically or radiologically) in the shoulders, elbows, wrists, or hands. Lower joint involvement was defined as active joints and damaged joints (clinically or radiologically) in the hips, knees, ankles, or feet. Comparison between EFP and EPP at baseline and followup were conducted using the Student t test, chi-square test, and Fisher's exact test.

Baseline characteristics were used to predict the development of erosions with logistic regression models (reduced model using stepwise selection). To examine the effect of time-varying covariates, we fit Cox regression models for the time to first development of erosions.

In the group of patients who did not have erosion at baseline and developed it later, the distribution of the time to development of erosion was estimated using the Kaplan-Meier method.

RESULTS

Characteristics of the patient population. Patients' characteristics are represented in Table 1. Among 290 patients with at least 10 years of followup, 36 were EFP (12.4%) and 254 were EPP (87.6%). At baseline, EFP were diagnosed with psoriasis at a younger age compared with EPP, 22.5 ± 14.7 versus 27.6 ± 12.1 years, respectively.

EPP. At baseline, of the 254 EPP, 176 (69.3%) had peripheral involvement, 6 (2.4%) had axial involvement, and 72 (28.4%) had both peripheral and axial involvement; 98 patients did not have peripheral erosion at baseline but developed it during the study period. At followup, of the 254 EPP, 176 (69.3%) had peripheral involvement and 103 (40.6%) had both peripheral and axial involvement.

Table 1. Characteristics of the 290 patients at baseline. Values are % or mean (SD).

Table 1A. Demographic characteristics.

Variables	EFP, n = 36	EPP, n = 254^
Age at diagnosis of psoriasis, yrs	22.5 (14.7)	27.6 (12.1)
Age at diagnosis of PsA, yrs	34.1 (12.9)	34.3 (11.1)
Age at baseline, first visit to clinic, yrs	38.8 (12.1)	41.6 (11.7)
Duration of psoriasis, yrs	16.3 (12.3)	13.9 (11.5)
Duration of PsA, yrs	4.8 (6.6)	7.2 (8.1)
Male	58.3	58.7
White vs others	86.1	91.7
Employed, yes	100	69.8
Education status: college/university vs ≤ high school	90.9/9.1	60.0/40.0
Smoking status, ever/never	61.5/38.5	47.6/52.4
Alcohol status, ever/never	70.4/29.6	61.0/39.0

Table 1B. Clinical characteristics.

Variables	EFP, n = 36	EPP, n = 254^
Swollen joint count	3.2 (2.4)	4.6 (4.1)
Tender joint count	5.5 (5.1)	8.3 (7.6)
Active joints, yes	72.2	93.3
Active joint count	4.8 (5.3)	10.1 (9.1)
Damaged joints, yes	8.3	40.6
At baseline		
Peripheral disease only	24 (66.7)	176 (69.3)
Axial disease only#	5 (13.9)	6 (2.4)
Peripheral and axial disease	5 (13.9)	72 (28.4)
NA	2 (5.6)	0 (0)
At followup		
Peripheral disease only	19 (52.8)	176 (69.3)
Axial disease only#	2(5.6)	0 (0)
Peripheral and axial disease	0 (0)	103 (40.6)
PASI score	4.9 (4.2)	5.4 (7.2)
BMI	25.5 (7.9)	28.8 (5.6)
Rheumatoid factor		
< 40	28 (84.9)	185 (82.3)
≥ 40	1 (6.1)	21 (8.9)
≥ 70	1 (3.0)	13 (5.5)
≥ 140	2 (6.1)	8 (3.4)
CRP*	7.5 (8.4)	8.2 (10.5)
ESR*	13.4 (16.2)	17.8 (16.1)
Uric acid level*	274.9 (81.8)	317.1 (91.8)
NSAID	68.0	86.2
Sulfasalazine	0	38.1
Methotrexate	43.8	64.2

* Last available. # Axial disease if Grade 2 or more sacroiliitis. ^ Of the EPP (n = 254), 98 patients did not have peripheral erosion at baseline, but developed it during the study period. EFP: erosion-free patients; EPP: erosion-present patients; PsA: psoriatic arthritis; NA: not ascertained; PASI: Psoriasis Area and Severity Index; BMI: body mass index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; NSAID: nonsteroidal antiinflammatory drugs.

EFP. Of the 36 EFP, axial involvement was present in 5 patients (13.9%) at baseline and 2 (5.6%) at followup.

Clinical assessment. At baseline, 93% of the patients in the EPP group had actively inflamed joints as compared with 72% in the EFP group. EPP displayed a greater number of actively inflamed joints (10.1 ± 9.1) compared with EFP (4.8 ± 5.3). More EPP were receiving NSAID and sulfasalazine than EFP. Clinically damaged joints were found in 40.6% of the EPP group and in only 8.3% in EFP. EPP had a higher body mass index than EFP. EFP were all employed versus 69.8% of EPP (Table 1). There was no difference regarding the employment status in the EPP and EFP groups by region of joint involvement (data not shown).

At the last followup visit, similar to the baseline visit, differences in characteristics among EPP and EFP were also present. There were actively inflamed joints in 69.3% of the patients in the EPP group, compared with 52.8% in the EFP group. EPP displayed a similar number of actively inflamed joints [(4.7 ± 7.5) compared with EFP (4.7 ± 6.2)]. Clinically damaged joints were found in 87.4% of the EPP group and in 27.8% in the EFP group. EPP displayed a greater number of damaged joints (16.8 ± 15.2) compared with EFP (1.9 ± 1.3). The PASI scores were 5.3 ± 6.9 in the EPP and 5.6 ± 8.3 in EFP. EPP had a higher percentage of unemployment compared with EFP, 52% versus 25%, respectively. In the EPP group with upper and lower extremities involvement, unemployment was higher compared with employed (95% vs 86.7%), respectively. Employment status did not differ in patients with only upper or lower extremities involvement from PsA.

Predictors for development of erosions in EPP. The covariates included in our analysis were age, sex, race, duration of psoriasis, duration of PsA, actively inflamed joint count, damaged joint count, and medication use (0 = none, 1 = NSAID only, 2 = DMARD ± NSAID, 3 = biologics ± DMARD ± NSAID) at baseline.

Logistic regression analysis. The univariate analysis showed that actively inflamed joint count (OR 1.12, p = 0.001), damaged joint count (OR 2.35, p = 0.02), and use of DMARD/NSAID (OR 2.73, p = 0.02) were associated with the development of erosion.

The multivariate analysis in the reduced model showed that actively inflamed joint count (OR 1.09, 95% CI 1.02–1.17, p = 0.01) and damaged joint count (OR 2.43, 95% CI 1.14–5.17, p = 0.02) were predictive of the development of erosions, whereas a longer duration of psoriasis at baseline decreased the odds of developing erosion (OR 0.96, 95% CI 0.93–0.99, p = 0.03; Table 2).

Time-dependent analysis. The fixed covariates included in this model were sex, race, age, duration of psoriasis, and duration of PsA at baseline. The time-varying covariates were actively inflamed joint count, damaged joint count, and medication use (0 = none, 1 = NSAID only, 2 = DMARD ± NSAID, 3 = biologics ± DMARD ± NSAID). Male sex (HR 1.38, 95% CI 1.18–1.62), actively inflamed joints (HR 1.03, 95% CI 1.03–1.04), and damaged joints (HR 1.04, 95% CI 1.03–1.05) were predictors of development of erosions ($p < 0.0001$ for all). Medication use predicted erosions with HR of 1.14 and this result was likely attributable to "indication bias" confounding by the severity of the disease where it is expected that active patients with more severe disease would receive more medications (Table 3).

Time to development of erosions in the EPP (n = 254). At baseline of the EPP, 131 (52%) had peripheral erosion, and at followup, 254 (100%) developed peripheral erosion. The mean time to development of erosion was 6.8 ± 6.1 years (median 4.4; Figure 1).

DISCUSSION

The predictive role of several factors, including clinical and demographic characteristics, HLA antigens, biomarkers, medications, and others, on different domains (clinical, radiographic, quality of life, and others) of PsA disease state (progression, improvement, and remission) have been studied[13,14,15,16,17,18,19,20,21]. Our study focuses on the characteristics and predictors of EFP as compared with EPP among patients with PsA. We found that among patients with PsA

Table 2. Univariate and multivariate analysis of the baseline characteristics to predict the development of erosions in EPP.

Covariates	Univariate Model			Multivariate Model					
				Full Model			Reduced Model		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Age, 1-yr increase	1.02	0.99–1.05	0.19	1.02	0.98–1.07	0.31			
Sex, males vs females	1.01	0.50–2.06	0.97	1.09	0.49–2.44	0.84			
Duration of psoriasis, 1-yr increase	0.98	0.96–1.01	0.24	0.94	0.90–0.98	0.005	0.96	0.93–0.99	0.03
Duration of PsA, 1-yr increase	1.06	0.99–1.13	0.09	1.05	0.98–1.12	0.22			
Race, white vs other	1.78	0.63–5.07	0.28	2.02	0.64–6.43	0.23			
Active joint count, 1-unit increase	1.12	1.05–1.20	0.001	1.09	1.01–1.17	0.03	1.09	1.02–1.17	0.01
Damaged joint count, 1-unit increase	2.35	1.12–4.96	0.02	2.29	1.06–4.97	0.03	2.43	1.14–5.17	0.02
Medications*	1.65	1.09–2.48	0.02	1.18	0.74–1.89	0.48			

* Medications are defined as 0 = none, 1 = NSAID, 2 = DMARD ± NSAID, 3 = biologics ± DMARD ± NSAID. EPP: erosion-present patients; PsA: psoriatic arthritis; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs.

Table 3. Patient characteristics over time that affect the time to first erosions: results of time-dependent analyses (Cox regression analysis). Because the baseline means study entry visit to clinic, we did not model age at baseline in this model.

Covariates	Univariate Model			Reduced Model		
	HR	95% CI	p	HR	95% CI	p
Fixed covariates						
Sex						
Males vs females	1.43	1.21–1.68	< 0.0001	1.38	1.18–1.62	< 0.0001
Duration of psoriasis at baseline						
1-yr increase	0.99	0.99–1.00	0.12	—	—	—
Duration of PsA at baseline						
1-yr increase	1.01	1.001–1.02	0.03	—	—	—
Race						
White vs other	1.10	0.85–1.42	0.49	—	—	—
Time-dependent covariates starting from study entry visit to clinic						
Active joint count						
1-unit increase	1.03	1.03–1.04	< 0.0001	1.03	1.03–1.04	< 0.0001
Damaged joint count						
1-unit increase	1.04	1.03–1.05	< 0.0001	1.04	1.03–1.05	< 0.0001
Medications*	1.12	1.02–1.23	0.01	1.14	1.04–1.24	0.005

* Medications are defined as 0 = none, 1 = NSAID only, 2 = DMARD ± NSAID, 3 = biologics ± DMARD ± NSAID. PsA: psoriatic arthritis; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs.

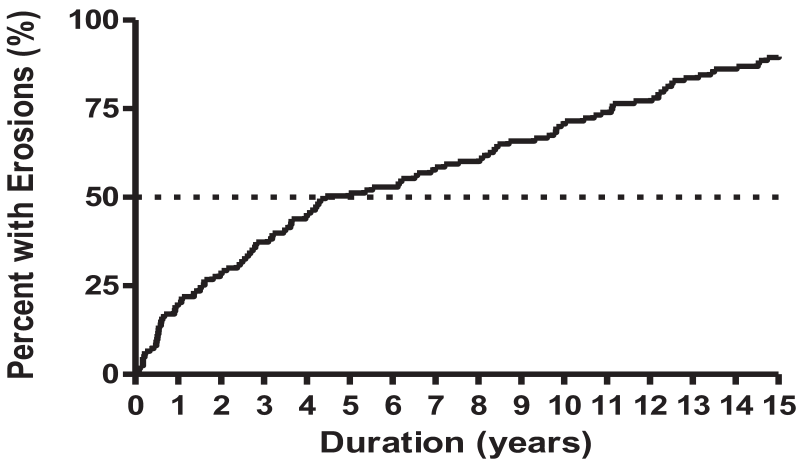

Figure 1. Time to development of erosions in EPP among those without erosions at baseline (n = 123).

followed for at least 10 years, 12% never developed erosions in the peripheral joints.

Our study confirms the results of previous studies that showed that PsA is a chronic and progressive disease, and that erosions continue to develop over time[1,2,4]. We have shown that 52% of patients already had at least 1 peripheral joint with an erosion at baseline and the mean time to the development of erosion in those without baseline erosions was 6.8 ± 6.1 years. A previous study showed that the mean time to detect erosions or joint space narrowing is 20 ± 4 months[3].

Our results confirm that a longer duration of psoriasis at baseline has a protective effect on the development of erosions, while male sex and the presence of actively inflamed and damaged joints at study entry predict the development of erosions. Gladman, *et al* showed that disease progression is more marked in patients presenting with established disease of more than 2 years' duration. These results suggest that patients with PsA should be treated earlier in the course of their disease[20]. Haroon, *et al* found that a diagnostic delay in PsA of more than 6 months results in poor radiographic and functional outcome, highlighting the importance of early management[22]. Queiro-Silva, *et al* found that a polyarticular onset, 5 or more swollen joints of PsA, is an independent predictor factor of erosive and deforming disease over time with an OR of 37[3]. Simon, *et al* found that during a 12-month followup of patients with PsA, progressive radiological damage was more frequent among patients with

an increasing swollen joint count than among those with a stable or decreased number of swollen joints[23]. Both joint tenderness and swelling of the specific joint are important predictors of joint damage in PsA[24]. Our results and those of previous studies are important in the identification of a subset of patients who require more aggressive therapies to prevent further development of erosion over time and eventually joint damage. The fact that patients continue to develop erosion up to 10 years in our study emphasizes the need for regular radiographs at 2-year intervals even in the EFP group. On the other hand, our paper documents that there are patients with PsA who do not develop erosions even after 10 years of followup. While these patients have less severe disease at presentation, we have not found other specific features that help identify those patients at presentation.

The association between the use of DMARD/NSAID and the development of erosion with an OR of 2.73 is attributable to indication bias or confounding by indication. Indeed, treatment with DMARD/NSAID is based on the disease severity. However, this association did not hold in the multivariate analysis. Previous studies demonstrated that treatment with biologic agents in patients with PsA yields sustained radiographic efficacy and inhibits radiographic progression in patients with PsA[15,25,26,27].

EPP are more often unemployed compared with EFP, which could be explained by more aggressive PsA in the EPP group. This is also an important reason to identify this group of patients early on to prevent further erosion development and thus unemployment in the long term. We also found that at their last followup visits, patients with upper and lower extremity involvement have a higher unemployment rate compared with patients with only upper or lower extremity involvement. The effect of having either upper or lower extremities erosions could not be further studied because of the small sample size of patients with both upper and lower extremities involved. Previous studies showed that patients with erosive and deforming disease had poorer functional performance than those without it as measured with the Health Assessment Questionnaire and with the classification of global functional status given by the American College of Rheumatology[3].

In our study, we selected patients with at least 10 years of followup, and this could have resulted in selection bias because patients with more severe disease are more likely to continue to be followed and meet this criteria. Thus, it is possible that the finding of 12.4% EFP underestimated the real percentage. On the other hand, in the group of EPP (n = 254), 123 patients did not have erosion at baseline visit, but developed it at a mean time of 6.8 ± 6.1 years.

Our results were persistent in both the regression analysis and the time-dependent analysis in predicting the development of erosions in peripheral joints over time. We found an association between the baseline patient characteristics and the development of erosion over time. The relationship between the development of erosion and inflammatory activity suggests that patients with PsA should be treated aggressively for their active joint disease as early as possible.

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