Risk Factors for Axial Inflammatory Arthritis in Patients with Psoriatic Arthritis

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ABSTRACT. ***Objective.*** Axial involvement is an important manifestation of psoriatic arthritis (PsA). We aimed to identify risk factors associated with the presence of axial PsA (AxPsA) in patients with PsA.

Methods. Patients with AxPsA (bilateral sacroiliitis ≥ grade 2/unilateral sacroiliitis ≥ 3 and inflammatory neck/back pain or limited spinal mobility) at first clinic visit were identified from the University of Toronto PsA clinic database. Risk factors associated with the presence of AxPsA were determined. Subsequently, patients without AxPsA at first clinic visit were identified. Under a multistate framework, the proportion of patients with PsA who subsequently developed AxPsA was estimated robustly using marginal methods and a Markov model. Risk factors at baseline that were associated with future development of AxPsA were identified through multiplicative time-homogeneous Markov models.

Results. Our study included 206 patients. Fifty patients had AxPsA at first clinic visit. HLA-B*27, radiographic damage to peripheral joints, and elevated erythrocyte sedimentation rate (ESR) increased odds of having AxPsA, while family history of PsA decreased the odds. One hundred fifty-six patients did not have AxPsA at first clinic visit. On followup, 28 developed AxPsA, and 11 died. We estimated that after 10 years of followup, 15% would develop AxPsA. Nail dystrophy, number of radiographically damaged joints, periostitis, and elevated ESR increased the risk of developing AxPsA, while swollen joints decreased the risk.

Conclusion. These results suggest that severe peripheral arthritis and HLA-B*27 are risk factors for AxPsA. (First Release March 15 2010; J Rheumatol 2010;37:809–15; doi:10.3899/jrheum.091059)

Key Indexing Terms:
PSORIASIS SPONDYLITIS HLA-B*27 PERIOSTITIS MULTISTATE MODEL

Psoriatic arthritis (PsA) is defined as an inflammatory arthritis associated with psoriasis, usually seronegative for rheumatoid factor[1]. PsA affects peripheral and/or axial joints and inflammatory axial disease is an important manifestation[1]. Axial inflammation is characteristic of ankylosing spondylitis (AS), the prototype spondyloarthritis (SpA). AS is classified according to the modified New York criteria and is strongly associated with HLA-B*27[2]. Although the inflammatory axial disease in PsA may be indistinguishable from AS, it may also differ from AS in several respects. These differences were originally described by McEwen, *et al* in 1971, subsequently in 1993 by Gladman, *et al*, and most recently in 1998 by Helliwell, *et al*[3-5]. HLA-B*27 is associated with PsA, but the association is not as strong as that with AS[4,6]. In cross-sectional studies, HLA-B*27 was shown to be associated with earlier age of psoriasis and arthritis onset, bilateral sacroiliitis, and male gender, but an association with axial PsA (AxPsA) was not always found[7,8]. These inconsistencies could be due to the fact that these studies may have included patients with classical AS and psoriasis, as well as those with AxPsA having the distinguishing features described first by McEwen, *et al*[3].

We have noted that patients with PsA develop new-onset axial inflammatory arthritis on longitudinal followup[9,10]. We therefore aimed to identify factors associated with the presence of AxPsA at first clinic visit, to determine the proportion of patients newly developing AxPsA after clinic entry, and to identify risk factors at first clinic visit for future development of AxPsA in patients with peripheral PsA.

MATERIALS AND METHODS

We conducted our study at the University of Toronto PsA clinic. In this clinic, we assess patients every 6–12 months according to a standard protocol that includes history, assessment of comorbidities, pharmacotherapy,

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examination (including detailed assessment of peripheral joints, spine, and extraarticular features), laboratory evaluation including HLA-B*27 typing, radiographic evaluation of hands, feet, pelvis, cervical, thoracic and lumbar spine (every 2 years), and patient questionnaires on function, fatigue, and quality of life[11]. Data are tracked on a computerized database. The study is approved by the Research Ethics Board of the University Health Network, Toronto, Ontario, Canada.

For our study, we classified patients as having AxPsA when the following criteria were fulfilled: (1) psoriasis, (2) bilateral sacroiliitis ≥ grade 2 or unilateral sacroiliitis ≥ grade 3 (New York radiographic criteria), and (3) inflammatory back/neck pain (low back pain or neck pain and stiffness for more than 3 months that improves with exercise but is not relieved by rest), or limitation in spinal mobility (qualitative restriction of cervical mobility, Schober's test < 5 cm, chest expansion < 5 cm)[12].

From the database, we identified patients who fulfilled criteria for AxPsA at first clinic visit. Factors associated with the presence of AxPsA were determined by comparison with those patients who did not have AxPsA at first clinic visit. We then identified patients who did not have AxPsA at first clinic visit. The proportion of patients from this group satisfying the criteria for AxPsA at various timepoints following entry to clinic was determined. Risk factors present at clinic entry associated with the future development of AxPsA were then identified. The risk factors studied included sex, age, ethnicity, family history of psoriasis and PsA, duration of psoriasis and PsA, number of joints actively inflamed, swollen, clinically damaged and radiographically damaged, presence of dactylitis, psoriatic nail dystrophy, radiographic periostitis, enthesitis, calcaneal spurs, prior nonsteroidal antiinflammatory agent use, prior disease-modifying antirheumatic drug use, smoking, hypertension (defined as systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mm Hg or treatment with antihypertensive medications), erythrocyte sedimentation rate (ESR), and HLA-B*27 status. Actively inflamed joints were defined as joints with swelling, stress pain, and/or joint-line tenderness (out of a total of 66 swollen and 68 tender joints scored according to protocol)[11,13]. The number of swollen joints was assessed specifically. Clinical damage was defined as the presence of joints with fixed deformities, flail joints, fused joints, or joints that had undergone surgery, and the total number out of a maximum of 68 was counted[11,13]. Radiographic damage was determined according to the modified Steinbrocker method, and the number of joints with at least stage 2 changes (presence of erosions) out of a maximum of 42 joints was assessed[14]. Dactylitis was defined as diffuse swelling of a whole digit[15]. Enthesitis was defined as tenderness at tendon/ligament insertion of Achilles tendon and plantar fascia. Periostitis was defined as ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of the hands or feet[16].

Statistical analyses. We first created a dataset with complete covariate information. We compared patients with and without AxPsA at first clinic visit and identified factors associated with the presence of AxPsA using logistic regression. To determine the proportion of patients newly developing AxPsA after clinic entry, and to identify risk factors at first clinic visit for future development of AxPsA in patients with peripheral PsA, we analyzed data in the framework of a 3-state illness-death model (alive with PsA, alive with AxPsA, and dead), where individuals in state 0 (PsA) can make transitions to either state 1 (AxPsA) or 2 (death), while individuals in state 1 can only make transitions to state 2. Thus, the event "death" is a competing risk event for the event "alive with AxPsA" (Figure 1)[17]. The data on the subsequent occurrence of AxPsA in patients presenting with peripheral PsA are examples of interval-censored data since the precise time of occurrence of the event of interest (AxPsA) following clinic entry is unknown, and is only known to have occurred between 2 timepoints when assessments were done. We obtained robust prevalence estimates (Pepe local likelihood) of AxPsA with the associated risk of mortality based on a difference in distribution functions of entry times[18,19]. We employed the local likelihood method with a nearest neighbor's bandwidth of 0.1, an Epanechnikov kernel, a locally constant approximation, and 400 grid points[19]. Ninety-five percent bootstrap CI were obtained by the nonparametric bootstrap method based on 500 bootstrap samples. We identified factors that affected the risk of transition between states through multiplicative time-homogeneous Markov models. We included univariate effects that were significant at the 0.25 level in a multivariate model. The model was then reduced by backward elimination until the remaining effects were significant at the 0.05 level. At that point, we tested all other effects for reentry to the model (no effects were added at this stage). We obtained estimates of regression coefficients from this final model.

RESULTS

The dataset created had 206 patients with complete covariate information. Of these patients, 50 had evidence of AxPsA at first clinic visit. The demographic and disease characteristics of these patients are given in Table 1. Table 2 shows the results of the logistic regression analyses on the factors associated with AxPsA at first clinic visit. HLA-B*27 (OR 5.75), the number of peripheral joints with radiographic damage (OR 1.12 for each damaged joint), and elevated ESR (1.02 for each 1 mm/h increase) were associated with increased odds of having AxPsA, while a family history of PsA (OR 0.1) decreased the odds.

We then determined the incidence and risk factors for future development of AxPsA in patients who did not satisfy criteria for AxPsA at first clinic visit. The demographics and disease characteristics of the 156 patients who did not have AxPsA at clinic entry are also given in Table 1. After a median followup duration of 6.4 (range 0.5 to 31) years, 28 patients were observed to develop AxPsA, and 11 died. Table 3 shows the baseline characteristics of the 28 patients

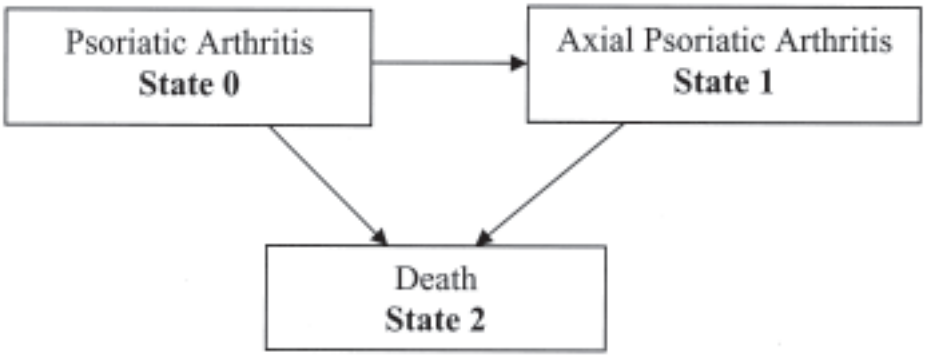

Figure 1. Three-state "Illness–Death" model for onset of axial psoriatic arthritis.

Table 1. Demographic and disease characteristics of patients at study entry.

Characteristic	Patients with AxPsA at First Clinic Visit, n = 50	Patients without AxPsA at First Clinic Visit, n = 156
Male/female	31/19	88/68
Age, yrs*	40.9 (11.9)	42.8 (12.7)
European ethnicity (%)	49 (98)	154 (99)
Duration of psoriasis, yrs*	13.6 (10.6)	13.5 (11.5)
Duration of PsA, yrs*	8.6 (7.9)	6.0 (6.9)
Family history of psoriasis (%)	17 (34)	63 (40)
Family history of PsA (%)	1 (2)	17 (11)
Prior NSAID use (%)	24 (48)	86 (55)
Prior DMARD use (%)	19 (38)	47 (30)
Smoker (%)	12 (24)	35 (22)
Hypertension (%)	3 (6)	16 (10)
No. of actively inflamed joints*	11.1 (8)	11.4 (9.6)
No. of swollen joints*	3.6 (3.5)	3.7 (4.6)
No. of clinically damaged joints*	10.1 (15.2)	2.8 (6.9)
Psoriatic nail dystrophy (%)	44 (88)	118 (76)
Dactylitis (%)	15 (30)	64 (41)
Enthesitis (%)	13 (26)	33 (21)
No. of radiographically damaged joints*	11.4 (12.5)	3.5 (5.8)
Periostitis (%)	10 (20)	22 (14)
Calcaneal spurs (%)	21 (42)	56 (36)
ESR*	38.8 (25.9)	25 (19.5)
Positive rheumatoid factor (%)	4 (8)	8 (5)
HLA-B*27 (%)	15 (30)	15 (10)

* Mean (standard deviation). AxPsA: axial psoriatic arthritis; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drug; ESR: erythrocyte sedimentation rate.

who developed AxPsA on followup, as well as the remaining 128 who were not observed to develop AxPsA. Figure 2 depicts the Pepe local likelihood estimates and the 95% CI of the prevalence of AxPsA from clinic entry. We estimate that after 10 years of followup, 15% of patients with PsA who did not have AxPsA at first clinic visit are alive with AxPsA (95% CI 0.06–0.22). The apparent dip in the prevalence of AxPsA around 10 years of followup is due to a rise in mortality in the cohort around that time period.

We then identified risk factors at baseline associated with future development of AxPsA. Table 4 shows the results of this analysis. Male sex, family history of PsA, nail dystrophy, number of swollen joints, enthesitis, number of radiographically damaged joints, periostitis, calcaneal spurs, elevated ESR, and presence of hypertension were associated with the development of AxPsA in univariate analyses ($p < 0.25$). Nail involvement [relative risk (RR) = 7.07], periostitis (RR = 5.67), number of radiographically damaged joints (RR = 1.11 for each damaged joint), and ESR (RR = 1.03 for each 1-mm increase in ESR) were associated with increased risk of AxPsA. Swollen joints reduced the risk (RR = 0.83 for each swollen joint). Interestingly, HLA-B*27 was not identified as a risk factor.

It is recognized that the clinical criteria (inflammatory back pain, restricted spinal mobility) have poor sensitivity and specificity[20,21]. We therefore repeated the analyses after redefining the criteria for AxPsA. We redefined the criteria

Table 2. Risk factors associated with the presence of AxPsA at first clinic visit.

Covariate	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	p	OR	95% CI	p
Male	1.26	0.66–2.42	0.49			
European ethnicity	0.64	0.06–7.17	0.71			
Family history of psoriasis	0.76	0.39–1.48	0.42			
Family history of PsA	0.17	0.02–1.29	0.09	0.1	0.01–0.88	0.04
Age	0.99	0.96–1.01	0.35			
Duration of psoriasis	1.0	0.97–1.03	0.99			
Duration of PsA	1.05	1.00–1.09	0.03			
Prior NSAID use	0.75	0.4–1.42	0.8			
Prior DMARD use	1.42	0.73–2.77	0.3			
Smoker	1.09	0.52–2.31	0.82			
Hypertension	0.56	0.16–2.0	0.37			
No. of actively inflamed joints	0.99	0.96–1.03	0.86			
No. of swollen joints	0.99	0.93–1.07	0.91			
No. of clinically damaged joints	1.06	1.03–1.1	< 0.001			
Psoriatic nail dystrophy	2.36	0.93–5.97	0.07			
Dactylitis	0.62	0.31–1.22	0.17			
Enthesitis	1.31	0.63–2.74	0.47			
No. of radiographically damaged joints	1.1	1.06–1.15	< 0.0001	1.12	1.07–1.17	< 0.0001
Periostitis	1.52	0.67–3.48	0.32			
Calcaneal spurs	1.29	0.68–2.48	0.44			
ESR	1.03	1.01–1.04	< 0.001	1.02	1.01–1.04	0.003
Rheumatoid factor	1.61	0.46–5.59	0.45			
HLA-B*27	4.03	1.8–9.02	< 0.001	5.75	2.22–14.9	0.0003

AxPsA: axial psoriatic arthritis; NSAID: nonsteroidal antiinflammatory drug; DMARD: disease-modifying antirheumatic drug; ESR: erythrocyte sedimentation rate.

Table 3. Baseline characteristics of patients followed longitudinally (n = 156) who developed AxPsA (n = 28) and (n = 128) who did not develop AxPsA.

Covariate	Patients with AxPsA on Followup (n = 28)	Patients without AxPsA (n = 128)
Male/female	17/11	71/57
Age, yrs*	41.1 (12.8)	43.2 (12.7)
European ethnicity (%)	28 (100)	126 (98)
Duration of psoriasis, yrs*	11.9 (9.6)	13.9 (11.9)
Duration of PsA, yrs*	5.5 (4.9)	6.9 (7.3)
Family history of psoriasis (%)	12 (43)	51 (40)
Family history of PsA (%)	5 (18)	12 (9)
Prior NSAID use (%)	17 (61)	69 (54)
Prior DMARD use (%)	7 (25)	40 (31)
Smoker (%)	7 (25)	28 (22)
Hypertension (%)	5 (18)	11 (9)
No. of actively inflamed joints*	12.1 (11.7)	11.2 (9.1)
No. of swollen joints*	2.0 (3.1)	4.1 (4.8)
No. of clinically damaged joints*	3.4 (8.6)	2.7 (6.5)
Psoriatic nail dystrophy (%)	26 (93)	92 (72)
Dactylitis (%)	12 (43)	52 (41)
Enthesitis (%)	6 (21)	27 (21)
No. of radiographically damaged joints*	5.8 (8.4)	2.7 (4.9)
Periostitis (%)	6 (21)	16 (13)
Calcaneal spurs (%)	11 (39)	45 (35)
ESR*	32.8 (22.3)	23.3 (18.5)
Positive rheumatoid factor (%)	2 (7)	6 (5)
HLA-B*27 (%)	4 (14)	11 (9)

* Mean (standard deviation). AxPsA: axial psoriatic arthritis; NSAID: nonsteroidal antiinflammatory drug; DMARD: disease-modifying antirheumatic drug; ESR: erythrocyte sedimentation rate.

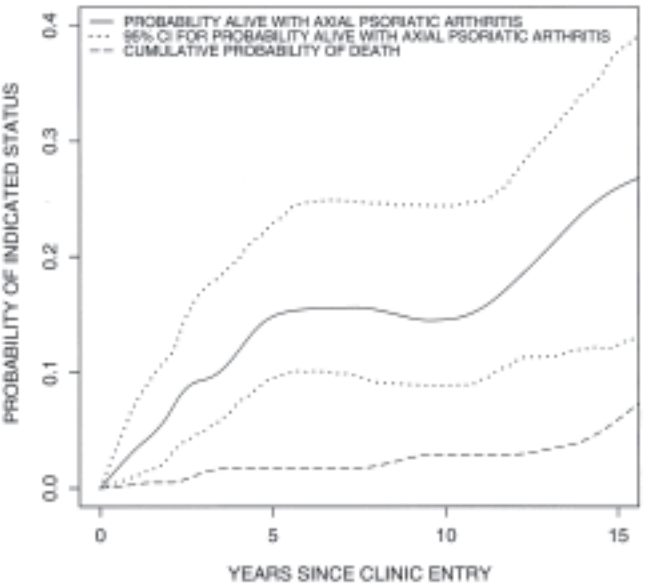

Figure 2. Robust estimates and 95% bootstrap CI of remaining alive and having axial psoriatic arthritis (AxPsA) over 15 years from clinic entry. The area between the dotted lines represents the 95% CI of the prevalence of AxPsA from clinic entry. We estimated that after 10 years of followup, 15% of patients with PsA who did not have AxPsA at first clinic visit are alive with AxPsA (95% CI 0.06–0.22). The lower broken line depicts the proportion of patients dying after study entry. The apparent dip in the prevalence of AxPsA around 10 years of followup is due to a rise in mortality in the cohort around that time.

basing it only on the New York radiographic criteria (AxPsA-R, i.e., psoriasis *and* bilateral sacroiliitis ≥ grade 2 or unilateral sacroiliitis ≥ grade 3)[12]. Male sex, radiographic joint damage, elevated ESR, and HLA-B*27 were associated with the presence of AxPsA-R at first clinic visit. In those without AxPsA-R at baseline, 23% were estimated to develop AxPsA-R after 10 years of followup. The risk factors at baseline that increased risk of future development of AxPsA-R were male sex, psoriatic nail dystrophy, periostitis, number of radiographically damaged joints, and elevated ESR (data not shown). Number of swollen joints no longer decreased the risk.

DISCUSSION

Axial inflammatory arthritis is an important manifestation of PsA. Most patients with AxPsA also have peripheral arthritis. Only 2% of patients have axial arthritis alone[1,21]. However, AxPsA has not been well defined. Patients with classical AS with psoriasis and those with axial arthritis with features that are different from classical AS have been included in this category[3,5]. The association of HLA-B*27 with AxPsA is not as strong as that with AS. That may be because the association is stronger in that subset of AxPsA that has features similar to AS. HLA-B*27 association is stronger in patients with younger age at onset who have disease features similar to classic AS (positive family history, bilateral sacroiliitis, isolated axial pattern, and enthesitis)[22].

In our longitudinal observational cohort we have observed that patients have AxPsA at first assessment, or develop it on followup. We show that HLA-B*27, radiographic damage to peripheral joints, and elevated ESR increased odds of having AxPsA at first clinic visit, while family history of PsA decreased the odds. On followup, the presence of nail dystrophy, number of radiographically damaged joints, periostitis, and elevated ESR at baseline increased the risk of future development of AxPsA, while swollen joints decreased risk. Thus, severe peripheral arthritis in addition to HLA-B*27 is a risk factor for AxPsA. We also show that 15% of patients with peripheral PsA without axial involvement are expected to develop AxPsA over 10 years of followup. When the criteria for AxPsA were relaxed to include radiographic criteria alone (AxPsA-R), then male sex, number of radiographically damaged joints, and elevated ESR increased the odds of having AxPsA-R at first clinic visit and also increased the risk of future AxPsA-R in those patients who did not have AxPsA-R at first visit. Other risk factors showed a differential association; HLA-B*27 was associated with AxPsA only at first clinic visit, and pso-

Table 4. Risk factors at first clinic visit associated with future development of AxPsA .

Risk Factors	Univariate Analysis			Multivariate Analysis		
	RR	95% CI	p	RR	95% CI	p
Male	1.57	0.74–3.34	0.24			
European ethnicity	—	—	—			
Family history of psoriasis	0.91	0.43–1.92	0.81			
Family history of PsA	2.1	0.82–5.36	0.12			
Age	1.01	0.98–1.04	0.44			
Duration of psoriasis	0.99	0.96–1.03	0.79			
Duration of PsA	1.02	0.06–1.08	0.52			
Prior NSAID use	1.38	0.65–2.92	0.41			
Prior DMARD use	1.14	0.49–2.64	0.76			
Smoker	0.91	0.39–2.15	0.84			
Hypertension	2.95	1.12–7.79	0.03			
No. of actively inflamed joints	1.02	0.98–1.06	0.33			
No. of swollen joints	0.92	0.81–1.04	0.18	0.83	0.73–0.95	< 0.01
No. of clinically damaged joints	1.02	0.97–1.07	0.45			
Psoriatic nail dystrophy	4.6	1.09–19.38	0.04	7.07	1.56–32.04	0.01
Dactylitis	0.95	0.45–2.0	0.89			
Enthesitis	1.85	0.75–4.57	0.18			
No. of radiographically damaged joints	1.06	1.02–1.12	0.01	1.11	1.05–1.17	< 0.0001
Periostitis	3.26	1.31–8.14	0.01	5.67	2.11–15.27	< 0.0001
Calcaneal spurs	1.7	0.8–3.59	0.17			
ESR	1.01	0.99–1.03	0.09	1.03	1.01–1.05	0.001
Rheumatoid factor	1.33	0.32–5.42	0.69			
HLA-B*27	1.13	0.39–3.26	0.82			

AxPsA: axial psoriatic arthritis; NSAID: nonsteroidal antiinflammatory drug; DMARD: disease-modifying antirheumatic drug; ESR: erythrocyte sedimentation rate.

riatic nail dystrophy and radiographic periostitis increased the risk of future development of AxPsA-R.

Our study is unique in many respects. Our study has been possible because we collected data relevant to assessment of peripheral and axial arthritis regularly and performed radiographs of the spine even in the absence of symptoms or signs of axial arthritis in all patients with PsA. We have thus been able to detect radiographic changes in the spine in the absence of symptoms or signs, since it is recognized that a significant proportion of patients with AxPsA have silent axial involvement[23,24]. The various clinical, laboratory, and radiographic risk factors are recorded systematically in a longitudinal fashion, and tracked on a computerized database. HLA typing was done on all patients. The outcome (presence of AxPsA) was defined using strict definitions similar to the modified New York criteria for AS, and statistical analyses were done using robust methods. Drawbacks include small numbers of patients in the group presenting with peripheral arthritis alone who subsequently developed AxPsA, reflected in the wide CI of the estimate of AxPsA prevalence on followup (Figure 2). Moreover, this cohort of patients already had average disease duration of 6.6 years prior to clinic entry, and thus it was not an inception cohort. An inception cohort with disease duration < 1 year before clinic entry would be the ideal cohort for such studies.

One could argue that the definition of AxPsA that we used for this study does not reflect all manifestations of spinal involvement in PsA[5]. However, there is currently no validated or widely accepted definition for AxPsA[25]. We chose a rather strict definition based on criteria for AS, but recognize that this may not be adequate. Moreover, we repeated the analyses using radiographic criteria alone as the outcome measure. The results obtained were similar, except that family history of PsA and swollen joint count were no longer "protective" in the 2 AxPsA groups, respectively, and male sex and raised ESR were identified as additional risk factors.

We demonstrate that severe peripheral arthritis as indicated by number of joints with radiographic damage and elevated ESR is associated with the presence of AxPsA at first clinic visit as well as future development of AxPsA. Thus, severe peripheral arthritis is a risk factor for AxPsA. With larger numbers and advanced statistical methods, these results robustly confirm reports of the association between peripheral arthritis and AxPsA[26,27]. The process of damage in the peripheral joints, particularly ankylosis, may reflect the same pathological process seen in the sacroiliac joints and syndesmophytes.

In patients presenting with peripheral PsA, in addition to the number of radiographically damaged joints and increased ESR, we identified psoriatic nail dystrophy and periostitis as risk factors associated with future AxPsA. Enthesitis has been proposed as a mechanism underlying psoriatic nail dystrophy[28]. Periostitis is a specific manifesta-

tion of PsA and indicates new bone formation[16,29]. Thus, these 2 markers together could indicate the presence of pathogenetic events that may occur in the spine leading to axial arthritis, since ankylosis in the spine is a reflection of both entheseal inflammation and new bone formation. These risk factors, thus, probably have biologic relevance. The presence of swollen joints was associated with reduced risk. Because swollen joints predict future peripheral joint damage, one would expect swollen joints to be a risk factor for AxPsA if damaged joints are, since swollen joints predict future peripheral joint damage[30,31]. It is possible that there is an inverse relationship between the degree and severity of inflammation in the peripheral joints and the spine. However, when we defined AxPsA based on radiographic criteria alone, swollen joints were no longer associated, and therefore this association may be due to problems in defining AxPsA.

Radiographic damage, nail dystrophy, and periostitis might indicate severity of the disease instead of being markers of pathogenic events. The more severe the disease, the more structures are involved. Thus, our data may also be interpreted as follows: patients with peripheral arthritis as well as axial arthritis, periostitis, and nail dystrophy have the complete disease spectrum, and the rest have incomplete PsA in an atypical and usually incomplete manifestation.

HLA-B*27 is associated with the presence of AxPsA at first clinic visit. This reflects shared genetic links between AxPsA and AS[32]. The association of HLA-B*27 with AxPsA is controversial. In SpA, HLA-B*27 is associated with the presence of spondylitis[33]. In cross-sectional studies in PsA, HLA-B*27 was shown to be associated with earlier age of psoriasis and arthritis onset, bilateral sacroiliitis, and male gender, but this association with AxPsA in PsA was not always found[7,8]. We have shown that HLA-B*27 is associated with AxPsA defined on the basis of presence of ≥ grade 2 sacroiliitis alone, or grade 1 sacroiliitis accompanied by presence of syndesmophytes and/or inflammatory back pain at first clinic visit[6]. In our study, we have demonstrated that HLA-B*27 is associated with AxPsA at first clinic visit but not with AxPsA that develops on followup. In addition to being associated with axial arthritis, HLA-B*27 may be associated with the severity of peripheral arthritis, since patients with AxPsA at first clinic visit also had severe peripheral arthritis (Table 1). We have shown that, when HLA-DR*07 was present, HLA-B*27 is associated with disease progression in PsA[34]. HLA-B*27 may be an important factor that helps distinguish AS from AxPsA.

There are few prospective longterm studies on SpA evaluating future development of definite spinal involvement (radiographic sacroiliitis and or fulfillment of diagnostic criteria for AS). Studies have been done on juvenile idiopathic arthritis (JIA) and undifferentiated SpA (USpA)[35-40]. In JIA, radiographically evident sacroiliitis developed in 6% of patients after median disease duration of 14.9 years[35]. HLA-B*27, absence of HLA-DPB1*02, late onset of disease, hip arthritis within the first 6 months, and elevated ESR for at least 6 months were found to be associated with the development of sacroiliitis[35,36]. In USpA, buttock pain and low-grade sacroiliitis were associated with future development of AS, and acute-phase reactant levels, juvenile onset, and HLA-B*27 showed a trend[37,40]. Our study shows similar results in patients with PsA.

Thus, we identified risk factors for AxPsA. Our results will need to be validated by studies in inception cohorts of patients with PsA.

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