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Factors associated with severity of disease in psoriatic arthritis: a cross-sectional study

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ABSTRACT

Objectives. The objectives of this study were to evaluate the prevalence of disease severity in PsA and to assess the factors that might explain it.
Methods. This was a cross-sectional study of unselected PsA patients. Severity was defined according to GRAPPA criteria of severity. Factors potentially associated with severity (demographical, clinical, laboratory variables, treatment related factors and comorbidities) were assessed by uni- and multivariate logistic regressions.
Results. A total of 129 PsA patients were analysed: 77 (59.7%) women, mean±standard deviation age 53.5±11.8 years, and mean disease duration 7±7.4 years. Twenty-for patients (18.6%) had severe PsA. In the univariate regression, disease severity was associated with psoriasis duration, PsA duration, current moderate/severe skin disease, nail disease, history of corticotherapy, and total number of previous synthetic and biologic DMARDs. In the multivariate analysis, PsA severity was explained by the presence of current moderate/severe psoriasis – odds ratio 5.88 (95% confidence interval 1.39; 25.00) and history of corticosteroids – 4.65 (1.13; 18.87).
Conclusion. PsA severity is best explained by the presence of moderate or severe psoriasis and past treatment with corticosteroids, but further longitudinal studies are needed to identify predictive factors.

Keywords: psoriatic arthritis, disease severity, moderate/severe psoriasis, corticotherapy

BACKGROUND

Psoriatic arthritis (PsA) is a heterogeneous inflammatory arthritis associated with psoriasis. In the past, PsA was considered a mild, non-progressive form of arthritis, with less long-term disability compared to rheumatoid arthritis (RA) (1). However, it is now known that PsA is associated with increased mortality (2) and considerable morbidity (3-6).

There is no universal definition for disease severity neither for psoriatic arthritis nor for other chronic inflammatory arthritis, e.g., spondyloarthritis or RA. Structural damage, disability and impaired quality of life were used as surrogates for disease severity.

Radiological damage in PsA was shown to be less pronounced (7) or equal to RA (7, 8), depending on the scoring system. Nonetheless, PsA is considered a severe disease, with patients progressing to erosive disease and structural damage (3-5). Patients with PsA and patients with RA have similar functional and quality of life impairments (7). However, arthritis is associated with a higher impact on physical function, fatigue and pain, whilst psoriasis affects mostly the mental and social domains (9).

Data from longitudinal cohort studies have identified predictors for disease severity. A high erythrocyte sedimentation rate (ESR) and the presence of joint swelling at baseline are considered the most important predictors of future clinical and radiological joint damage (10-12). Additional predictive factors include genetic factors such as HLA-B27, HLA-B39, or HLA-DQw3 (13) and other clinical variables, for example dactylitis or axial disease (14, 15). Disease burden and impact on quality of life in PsA is predicted by skin and nail disease (16,17), but also comorbidities (18).

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The objectives of this study were to evaluate the prevalence of disease severity in PsA and to identify the factors associated with a more severe course of the disease.

METHODS

Study design and patients

This was a cross-sectional study which included unselected, consecutive adult patients with definite PsA according to the physician, with a range of disease manifestations and treatments. Patients were recruited from the Rheumatology department of "Sf. Maria" Hospital, Bucharest, during the 2014-2016 timeframe. Most of them fulfilled the CASPAR classification criteria for PsA (19). All patients gave a written informed consent and the protocol of the study was approved by the local ethics committee.

Data collection

Descriptive data of the population were collected. Patient-related features included age, gender and disease duration for both PsA and psoriasis. Disease-related characteristics included swollen joint count, SJC (0-66), tender joint count, TJC (0-68), current moderate or severe psoriasis, i.e., more than 5% body surface, nail disease, other activity such as dactylitis, enthesitis and axial involvement, and acute phase reactants, e.g., C-reactive protein (CRP) and ESR, structural damage and coxitis. Data regarding treatment included current and past non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, synthetic and biologic disease modifying drugs (sDMARDs, b DMARDs, respectively). Data on comorbidities were also collected, according to the recent European League Against Rheumatism (EULAR) recommendations on reporting, screening and preventing comorbidities in chronic inflammatory rheumatic diseases (20). This included cardiovascular diseases, i.e., history of myocardial infarction, pectoris angina, stent, stroke, transient ischemic attack, heart failure and lower limb peripheral arterial disease, malignancies, i.e., any history of malignancy, infections, i.e., history of tuberculosis, of serious infections, opportunistic infections and chronic viral infections, gastro-intestinal diseases, i.e., history of peptic ulcer, osteoporosis and depression. Risk factors and current treatment for comorbid conditions were also collected.

Severity of the disease

Severity of the disease was defined according to the Group of Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) severity criteria (21). Severity was defined as the presence of at least one of the following features: more than 5 affected joints, severe damage on x ray, loss of physical function, severe impact on quality of life, or severe patient evaluation for peripheral arthritis, body surface area more than 10% for skin disease, failure of response for spinal disease, loss of function, more than 2 sites affected or failure of response for enthesitis and failure of response for dactylitis.

Statistical analysis

Patient and disease-related characteristics were compared according to the presence of disease severity using difference tests (t-Student, Mann Whitney or chi-square, depending on the type of variables).

Factors associated to disease severity were determined by performing univariate and multivariate logistic regressions. The variables tested were: age, gender, disease duration (for PsA and psoriasis), SJC, TJC, CRP, ESR, current moderate/sever psoriasis, nail disease, other activity (dactylitis, enthesitis, axial involvement), current NSAIDs, corticosteroids, sDMARDs and bDMARDs, history of corticotherapy, number of previous synthetic and biologic DMARDs and comorbidities and risk factors, as described above. Structural damage and coxitis and patient reported outcomes assessing functional status or quality of life were not included, since they were considered markers of severity. Only variables that were statistically significant associated with disease severity in the univariate logistic regression ($p<0.05$) were included in the multivariate analysis.

There was no imputation of missing data. Statistics were performed using SPPS for IBM, version 20.0.

RESULTS

Patient characteristics

In all, 129 PsA patients were analysed (Table 1). Mean ± standard deviation age was 53.5±11.8 years and most had long standing disease, with a mean disease duration of 7±7.4 years for PsA and 15.9±12.1 years for psoriasis; 77 (59.7%) were females. Only 24 (18.6%) presented current moderate/severe skin psoriasis. Most of them (79.1%) were treated with a

TABLE 1. *Characteristics of psoriatic arthritis patients, according to the severity of the disease*

Patient characteristics	All patients (N=129)	Patients with severe disease (N=24)	Patient with non-severe disease (N=105)
Females, N (%)	77 (59.7)	10 (41.6)	67 (63.8)
Age, years, mean (SD)	53.6 (11.8)	50 (12.1)	54.4 (11.6)
PsA disease duration, years, mean (SD)	7.0 (7.4)	11.9 (8.9)	6 (6.6)
Psoriasis disease duration, years, mean (SD)	15.9 (12.1)	20.6 (13.0)	14.8 (11.6)
Swollen joint count (0-66), median (range)	0 (0-9)	0 (0-9)	0 (0-8)
Tender joint count (0-68), median (range)	2 (0-22)	0 (0-22)	2 (0-14)
Current moderate/severe skin psoriasis, N (%)	24 (18.6)	13 (54.1)	11 (10.6)
Enthesitis, N (%)	18 (13.9)	3 (12.5)	15 (14.3)
Dactylitis, N (%)	33 (25.6)	4 (16.7)	29 (27.6)
Axial involvement, N (%)	53 (41.0)	14 (58.3)	39 (37.1)
Current corticotherapy, N (%)	20 (15.5)	5 (22.7)	15 (14.4)
History of corticotherapy, N (%)	25 (19.3)	9 (39.1)	16 (15.7)
Current sDMARD, N (%)	102 (79.1)	17 (70.8)	85 (80.9)
Number of previous sDMARDs, median (range)	0 (0-3)	1 (0-3)	0 (0-3)
Current bDMARD, N (%)	32 (24.8)	9 (37.5)	23 (21.9)
Number of previous bDMARDs, median (range)	0 (0-2)	0 (0-2)	0 (0-1)

PsA: psoriatic arthritis; SD: standard deviation; sDMARD: synthetic disease modifying drug; bDMARD: biologic disease modifying drug

synthetic DMARD and about a quarter (24.8%) with a biologic drug. Many patients had associated comorbidities, the cardiovascular diseases and risk factors being the most prevalent: dyslipidaemia 79.8%, hypertension 51.9%, obesity 34.1%, and cardiovascular events 32.6% (myocardial infarction, stroke, stent, peripheral arterial disease etc).

Disease severity and associated factors

There were 24 (18.6%) patients with severe disease, of which 11 (45.8%) were due to severe damage on x ray, mostly coxitis and 6 (25%) due to loss of physical function. Patients with more severe disease were preponderantly male, had a higher disease duration for both psoriasis and PsA and a higher number of previous synthetic and biologic DMARDs (Table 1); they also had a history of corticotherapy in a higher proportion compared to patients with non-severe PsA (Table 1). Except for body mass status (patients with a more severe disease had a higher body mass index), there was no difference regarding comorbidities in PsA patients according to disease severity (data not shown).

In the univariate analysis (Table 2), PsA severity was associated with PsA disease duration (p=0.001), psoriasis disease duration (p=0.041), current moder-

TABLE 2. *Factors associated with disease severity in psoriatic arthritis: univariate and multivariate logistic regressions*

Variable	Univariate analysis β coefficient (p value)	Multivariate analysis Odds ratio (95% confidence interval) (p value)
PsA disease duration, years	0.302 (0.001)	1.03 (0.95; 1.12) (0.448)
Psoriasis disease duration, years	0.192 (0.041)	1.01 (0.95; 1.06) (0.725)
Current moderate/severe psoriasis, yes/no	0.436 (<0.001)	**5.88 (1.39; 25.00) (0.016)**
Nail disease, yes/no	0.256 (0.003)	0.42 (0.09; 1.81) (0.248)
History of corticotherapy, yes/no	0.227 (0.011)	**4.65 (1.13; 18.87) (0.032)**
Number of previous sDMARDs	0.229 (0.011)	1.36 (0.65; 2.87) (0.416)
Number of previous bDMARDs	0.237 (0.007)	1.29 (0.32; 5.27) (0.717)

PsA: psoriatic arthritis; sDMARD: synthetic disease modifying drug; bDMARD: biologic disease modifying drug
For the multivariate analysis, significant results are in bold type.

ate/severe skin psoriasis (p<0.001), nail disease (p=0.003), history of corticotherapy (p=0.011) and the number of previous sDMARDs and bDMARDS (p=0.011, and p=0.007, respectively). In the multivariate analysis, disease severity was explained by the presence of moderate or severe psoriasis – odds ratio, OR 5.88 (95% confidence intervals, 95% CI 1.39; 25.00) and history of treatment with corticosteroids – OR 4.65 (95% CI 1.13; 18.87).

DISCUSSION

This study confirms that PsA is a potentially severe disease, leading to major structural damage and loss of physical function. The severity of the disease was associated with disease duration, skin and nail involvement, treatment with corticosteroids and number of previous disease modifying drugs; it was best explained by the presence of moderate or severe psoriasis and history of corticotherapy.

In the present study less than a quarter of patients (18.6%) had severe PsA, mostly due to structural damage or loss of physical function. As far as we know, this is the first study to assess severity according to GRAPPA criteria (21), making it difficult to compare it to similar studies. However, previous studies have shown that between 11% and 42% of PsA patients have American College of Rheumatology grade III or IV functional impairment (3,22-24). Additionally, the burden of PsA on functioning and quality of life was shown to be as high as in RA or AS (7,9,25-28). Although there are few data on the prevalence of severe structural damage in PsA, it was shown that despite clinical improvement with current DMARD treatment, PsA results in radiological damage in almost half of the patients at 2 years (5,29). Moreover, radiological progression and damage in PsA is similar to RA (8).

Disease severity was associated in this study with disease duration, for both PsA and psoriasis, probably due to accrual damage. It is an intuitive finding, given the fact damage is irreversible and it tends to increase over time. Impaired quality of life and functioning as measured by the Health Assessment Questionnaire was proven to vary over time and to be associated with longer disease duration in PsA (30), as well as in RA (31,32). Moreover, structural damage was also shown to be related to longer duration of arthritis (33).

The number of previous DMARDs both synthetic and biologic was also associated with disease severity. This might reflect either a longer disease duration or a persistently active, non-responsive disease, thus a higher accrual damage.

Use of corticosteroids was associated in both logistic regressions with disease severity. As far as we know, in PsA there are few data regarding the relationship between corticotherapy and disease severity. One study showed that a high medication level at presentation to the clinic, particularly use of steroids is a predictor for progression of clinical damage (10). However, corticotherapy are not so often used as in RA where it is known to be associated with functional disability (34,35).

Moderate and severe skin involvement was also associated in both logistic regressions with disease severity. Previous studies have already demonstrated that psoriasis is associated with impaired quality of life and that the body surface area affected by psoriasis had the greatest association with decreased quality of life (16,17). Similarly, nail involvement which was found to be associated with PsA severity in the current study was also previously shown to have a high impact on quality of life in psoriasis and PsA (36-38).

The number of tender and swollen joints at baseline and initial ESR which are well-known predictors of structural damage and disability and impaired quality of life (10-12) were not associated to disease severity in the current study. However, they weren't measured at baseline, since it is a cross-sectional study. Comorbidities also failed to show an association with disease severity. In a cross-sectional on 631 PsA patients, comorbidities were proven to have an incremental effect on quality of life, which was more related to type of comorbidity than number of comorbidities (18). However, it only assessed their impact on quality of life and not disease severity as a whole.

There are further methodological issues that warrant consideration. Since the patients included in the study were all from a tertiary center, it might lead to a selection of more severe cases than in the general PsA population. However, the demographic characteristics, the severity of disease, prevalence of comorbidities and access to biologics was as expected. Further, the cross-sectional nature of the study does not allow identifying potential predictive factors for disease severity, but only associated variables. A longitudinal study would be necessary in this case; nevertheless, it is more difficult to perform one. Finally, there is no standard definition of disease se-

verity, making it difficult to compare across studies. Previous studies have assigned disability, structural damage or impaired quality of life to disease severity (10-18). To our knowledge, this is the first study to assess PsA severity according to GRAPPA criteria.

In conclusion, PsA is a potentially severe disease, leading to major structural damage and loss of physical function. PsA severity is associated with disease duration, skin and nail involvement, corticotherapy and number of previous disease modifying drugs; it is best explained by the presence of moderate or severe psoriasis and past treatment with corticosteroids. Further longitudinal studies are needed to identify predictive factors for disease severity in PsA.

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