Risk factors and predictors of psoriatic arthritis in patients with psoriasis[*]

Fatores de risco e preditivos do desenvolvimento de artrite psoriásica em pacientes portadores de psoríase

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Abstract: Given the potential consequences of joint damage for patients with psoriatic arthritis, we believe that the optimization of screening methods and the investigation of arthritis in patients with psoriasis are a medical priority. It is very useful to identify predictors of arthritis in patients with psoriasis. In fact, there is a consensus among doctors that the large gap between the diagnosis of psoriasis and that of psoriatic arthritis should be narrowed. In order to better manage patients with psoriasis, the authors review and discuss recent publications on the evidence of current predictors of arthritis in patients with psoriasis.
Keywords: Arthritis, psoriatic; Predictive value of tests; Psoriasis; Risk factors

Resumo: Em virtude das potenciais sequelas envolvidas no dano articular da artrite psoriásica, configura-se em uma prioridade médica a otimização dos métodos de rastreio e investigação de artrite nos pacientes com psoría-se. Identificar preditores de artrite em pacientes com psoriase é fundamental para a prática clinica, além disso há um reconhecimento de que o grande intervalo entre o diagnóstico de psoríase e o diagnóstico de Artrite psoriá-sica em sua fase inicial deve ser reduzido. No sentido de contribuir com uma melhor abordagem de pacientes com psoríase, os autores revisam e discutem recentes publicações com evidencias de alguns fatores preditores de inicio de artrite nestes pacientes.
Palavras-chave: Artrite psoriásica; Fatores de risco; Psoríase; Valor preditivo dos testes

INTRODUCTION

Psoriasis (Pso) is an immune-mediated skin disease that results in epidermal hyperproliferation. The association of psoriatic lesions with typical joint involvement is called Psoriatic Arthritis (PsA). Data from large epidemiological studies show that the prevalence of patients with PsA within samples of patients with psoriasis varies from 2-26%.[1-7] Other studies have reported higher numbers of patients with psoriasis and joint manifestations suggestive of PsA, as much as 48%.[8] Most often, in the natural history of the disease, skin manifestations precede joint manifestations in up to 67% of cases.[9]

Recently, genetics has revealed that these two diseases share some genes of the Major Histocompatibility Complex and cytokine-encoding genes.[10-12] Similarities aside, the mechanisms of both diseases are not completely correlated, probably due to various etiopathogenic factors.[13] However, because of the potential consequences of joint damage, the optimization of screening methods and the investigation of arthritis in patients with psoriasis have become a medical priority. This is also justified by the large gap between diagnosis of Pso and that of the early stages of PsA. This "diagnostic gap" ranged on aver-

age from <3months up to 5 years, but it can certainly be narrowed with the development of a clinical educational program targeted to rheumatologists and dermatologists.[14,15]

In view of all this and seeking to improve investigation results about the development of arthritis in patients with Pso, we conducted a brief review of the predictive factors involved in disease diagnosis and progression. We did not intend to address factors that cause each disease, which involve complex associations between predisposing genetic and environmental factors such as minor trauma, infections, emotional stress, medication and habits, such as smoking and alcoholism.[16] Our main objective was to analyze the best evidence in the medical literature regarding predictors of PsA in patients with Pso. Assessment of these factors may be especially relevant for the clinical practice of dermatologists, since in the group of patients with PsA the skin tends to be affected before the joints.[17]

From Genetics to Environmental risk

It is clear that studies of risk factors paved the way for disease prevention. Cohort and case-control studies have been frequently used for this purpose. For example, most evidence in this review was extracted from case-control studies of patients with Pso.

Some genes that are also associated with increased susceptibility to both diseases are recognized as risk factors for the development of PsA. Genes such as HLA-Cw * 0602, HLA-B27, HLA-B38, HLA-B39, HLA-DR4, IL-23R, IL-12R, and TNF-238A * TNIP1 are found in different cohorts. However, larger studies with a better description of the psoriatic population are still needed.[18]

In 2002, Thumboo et al. reported an increased risk of arthritis in patients with Pso using corticosteroids (odds ratio (OR) 4.33, 95% CI 1:34 to 14:02) and a reduced risk in pregnant women (odds ratio 0.19, 95% CI 0.04-0.95), all in the same cohort.[19]

In 2008, despite a selection bias, Pattinson et al. described the risk factors for the development of PsA: trauma requiring medical intervention (OR 2.53, 95% CI 1.1-6.00), changes of residence (OR 2.29 95% CI 1:21 to 4:40); rubeolla vaccination (OR 12:40, 95% CI 1.20-122.14) and fertility treatment (OR 0.17, 95% CI 0.04-0.79).[20] In fact, this last factor was negatively correlated with the development of PsA. Interestingly, it can be associated with pregnancy as a protective factor in the study by Thumboo et al.[19]

Wilson et al. reported intergluteal or perianal psoriasis (hazard ratio (HR) 2.35, 95% CI, 1:32 to 4:19); psoriasis affecting three different sites (HR 2.24, 95% CI 1:23 to 4:08), nail dystrophy (HR 2.93, 95% CI 1.68-

5.12) and psoriasis involving the scalp (HR 3.89, 95% CI 2.18-6.94) as risk factors.[21]

In 2010, Soltani-Arabshahi et al. described the following variables associated with the risk of arthritis in patients with Pso: higher body mass index (BMI) at age 18 (OR 1.6, 95% CI 1:02 to 1:10), female patients (OR 1:45 , 95% CI 1.09-1.94), extension of body surface area affected (OR 1.01, 95% CI 1:00 to 1:01, Koebner phenomenon (OR 1:59, 95% CI 1:17 to 2:14 and nail involvement (OR 1.76, 95% 1:25 to 2:47).[22] However, the authors acknowledged the existence of several biases in their samples, many of which associated with different degrees of severity and extent of skin disease. The study also found that a high BMI is correlated with a shorter interval of time for the onset of PsA in patients with Pso.

In 2010, Tey et al. also conducted a retrospective study about the possible risk factors for the development of PsA in patients with Pso.[23] In their study, no statistical significance involving gender, ethnicity, age of onset of Pso, family history of Pso, smoking and alcohol consumption was found. However, significant values were checked for Maximum Surface Involved (p = 0.05 / OR 2:52, 95% CI 1.33-4.75) and family history of PsA (p <0.001 / OR 5.20, 95% CI 2.49-169.10).

In 2011, Eder et al. found that cumulative survey of> = 100pounds/hour (OR 2.8, 95% CI 1:51 to 5:05), trauma (OR 2.1, 95% CI 1:11 to 4:01), and infections requiring antibiotic therapy (OR 1.7, 95% CI 1.00-2.77) were significant risk factors for the development of PsA.[24] No correlation was found for alcohol use, immunizations, psychological stress and female hormonal exposures. There was an inverse correlation between the development of PsA and smoking (OR 0.6, 95% CI 0.36-0.89). The authors stressed the fact that this possible "protective effect" of smoking was similar to data found in other studies, including a value close to that found by Pattinson et al. (OR 0.68, 95% CI 0:39 to 1:17), but this is statistically less significant.[20] In an interesting study by Rakkhit et al., the authors reported that smoking accelerates the onset of PsA in patients without Pso, whereas it slows the emergence of PsA in patients with Pso.[25]

Tinazzi et al. published one of the latest works about risk factors.[26] It was a longitudinal study in which patients with joint complaints without Pso were investigated, by ultrasound, for the presence of subclinical enthesitis and subsequently monitored for the diagnosis of PsA. The GUESS (Glasgow Ultrasound Enthesitis Scoring System) index was used to confirm entheses inflammation. The initial scores of patients with Pso who later developed PsA or osteoarthritis were significantly higher than those of patients who did not develop joint disease (9.54 ± 2.2 vs. 6.61 ± 3.60, respectively, p = 0.0127). However,

after the monitoring period, comparison of GUESS scores did not reach statistical significance (9.14 ± 3.2 vs. 7.72 ± 3.94, p = 0.4115). Interestingly, thinning of the quadriceps tendon was reported as an independent predictor for the development of PsA (p = 0.029), whereas involvement of the Achilles and patellar tendons showed no correlation. The nails are affected in approximately 40-45% of cases of psoriasis without joint involvement. However, in cases of psoriasis complicated by arthritis, the nails are affected in 87% of cases.[23] Jamshidi et al. found a prevalence of 96.5% of nail involvement in patients with PsA, and a prevalence of 73.1% in patients with only Pso.[27]

Many studies have correlated familial history of Pso or PsA as a risk factor for the development of PsA. Rahman et al. found a prevalence rate of familial history of Pso in first-degree relatives of probands carrying PsA 19 times greater than that found in the general population.[28]

CONCLUSION

Joint involvement in PsA often leads to deformities and severe limitations, even in the early stages of the disease. Therefore, studies that correlate clinical risk factors with the development of arthritis in patients presenting exclusively with skin disease are essential to clinical practice. However, the existing risk study designs still have many methodological limitations that make their external validation difficult.

It is also important to better characterize potential risk factors with the onset of each of the five subtypes of PsA, since polyarthritis mutilans and axial disease are usually related to a worst functional outcome.

Some studies have confirmed well-known risk factors for the development of PsA, while others have reported new possible risk factors that have not yet been investigated.[29] Among the risk factors most widely accepted and of easy characterization in clinical practice, presence of nail lesions, greater extent of skin involvement and familial history of PsA are the most relevant and should be investigated by all clinicians taking care of patients with psoriasis.

Unfortunately, more data are needed to better qualify the available evidence regarding genetic factors in clinical practice, especially those related to the frequency of HLA class I and II alleles.

Further investigations in cohorts involving a larger number of patients with psoriasis might better indicate which factors discussed so far are most useful to the early detection of joint involvement in patients with Pso. These results could be an appropriate reference to dermatologists to rheumatologists, thus helping patients due to a more adequate management of the disease and individualized care. ❑

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