Prevalence of undiagnosed psoriatic arthritis among psoriasis patients: Systematic review and meta-analysis

Axel Patrice Villani, MD,a Marie Rouzaud, MD,b Morgane Sevrain, MD,c Thomas Barnetche, PhD,d Carle Paul, MD, PhD,e Marie-Aleth Richard, MD, PhD,f Marie Beylot-Barry, MD, PhD,g Laurent Misery, MD, PhD,h Pascal Joly, MD, PhD,i Michel Le Maitre, MD,j Selim Aractingi, MD, PhD,k François Aubin, MD, PhD,l Alain Cantagrel, MD, PhD,m Jean-Paul Ortonne, MD, PhD,n and Denis Jullien, MD, PhDa

Lyon, Bordeaux, Brest, Mortagne-sur-Sèvre, Toulouse, Marseille, Rouen, Caen, Paris, Besançon, and Nice, France

Background: Skin psoriasis precedes the onset of psoriatic arthritis (PsA) in 84% of patients with psoriasis. Dermatologists have an important role to screen psoriasis patients for PsA. The efficiency of PsA screening remains unknown.

Objective: We sought to determine the point prevalence of undiagnosed PsA in patients with psoriasis using a systematic search of the literature and meta-analysis.

Methods: PubMed, Cochrane, and Embase database searches yielded 394 studies for review. No study aimed to determine the prevalence of undiagnosed PsA in patients with psoriasis. We assumed that the prevalence of newly diagnosed PsA in patients with psoriasis at the time they seek medical care could be a sound estimate of this value. Seven epidemiological studies and 5 studies on PsA screening questionnaires allowed us to clearly identify patients with newly diagnosed PsA and were selected for review.

Results: The prevalence of undiagnosed PsA was 15.5% when all studies were considered and 10.1% when only epidemiological studies were considered.

Limitations: Data were obtained from studies not designed to address the question at hand. Heterogeneity was high (I² = 96.86%), and therefore a random effects model was used.

Conclusion: The high prevalence of undiagnosed PsA in patients with psoriasis adds to the recommendation that dermatologists need to screen all patients with psoriasis for PsA. (J Am Acad Dermatol 2015;73:242-8.)

Key words: cutaneous psoriasis; dermatologists; early detection; prevalence; psoriatic arthritis; systematic review.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease the prognosis of which depends on the severity of cutaneous involvement and on the existence of psoriatic arthritis (PsA). According to a systematic review, PsA prevalence among psoriasis patients ranges from 7% to 26%.1 A recent study conducted in European and North American dermatology...
clinics found a higher value (30%), with 41% of these patients ignoring that they had PsA.2 PsA is a progressive disease, and a subgroup of patients develops progressive damage and loss of function in the first few years of the disease.3,4 The burden of illness associated with PsA in patients with psoriasis has been reviewed.5 Given the poor outcomes associated with PsA, the benefit of the use of early and intensive treatment in PsA is being evaluated. Early results suggest that tight control of PsA disease activity using a treat-to-target approach significantly improves joint and skin outcomes for patients with newly diagnosed PsA.6 This makes early detection of PsA a key issue and gives dermatologists an important role in the detection and management of PsA. Indeed, in the majority of patients (~75-84%), skin lesions precede arthritic involvement, with a lag time of about 7 to 12 years.6,7 A high prevalence of undiagnosed PsA in patients with psoriasis would further support effort to improve screening procedures in this population as recommended by the American Academy of Dermatology in the United States8 and the National Institute for Health and Care Excellence in the United Kingdom.9 The aim of this study was to estimate the point prevalence of undiagnosed PsA in the general population of patients with psoriasis.

METHODOLOGICAL

Two investigators (A.V. and D.J.) independently searched published studies indexed in MEDLINE, EMBASE, and the Cochrane database between January 1980 and February 2013 using terms from the Medical Subject Heading (MeSH): “arthritis, psoriatic/epidemiology” and “prevalence.” No studies aimed to determine the prevalence of undiagnosed PsA in the general population of patients with psoriasis, and we therefore made the assumption that the prevalence of newly diagnosed PsA in patients with psoriasis at the time they seek medical care could be a sound estimate of this value. A manual search of references of selected retrieved articles, including reviews, was also performed. It pinpointed studies regarding PsA screening questionnaires that were not initially retrieved because they were not associated with the MeSH term “prevalence.” An independent search on PsA screening questionnaires was conducted and 5 studies that matched the inclusion criteria were also considered. The inclusion criteria were observational studies (cross-sectional and cohort) published as original studies to evaluate the prevalence of psoriatic arthritis in patients with skin psoriasis or those that provided data that allowed accurate calculation of this prevalence.

Study eligibility was independently assessed by 2 investigators (A.V. and D.J.). It was not biased toward authors or journals, although these parameters were not blinded during the selection process. Diagnostic criteria for PsA were not limited to Classification Criteria for Psoriatic Arthritis (CASPAR) criteria because they were not available throughout the study period. Differing decisions were resolved by consensus with all other coauthors. Because a limited number of studies addressed the issue of the prevalence of PsA in patients with psoriasis, published conference abstracts on this topic were included. From each publication, 2 investigators (A.V. and D.J.) retrieved the following elements: author, year, inclusion period, country, type of database, number of skin psoriasis patients, number of newly diagnosed PsA patients, diagnostic criteria used for PsA (ie, CASPAR, Moll and Wright, or diagnosis by a specialist), patients’ background (ie, hospital recruitment, general population), and the prevalence of newly diagnosed PsA with 95% confidence intervals (CIs). Dr Villani collected all data elements from all identified publications; Dr Jullien independently cross-checked the data captured by Dr Villani. When the prevalence value was not readily available, it was calculated. This calculation was performed only if patients with newly diagnosed PsA were clearly identified in the study. We extracted from each study the number of patients who had newly diagnosed PsA as the numerator and the total number of patients with psoriasis as the denominator to estimate the prevalence of newly diagnosed PsA. When possible, a meta-analysis was performed (method of the inverse of the variance). Heterogeneity was estimated for each analysis (Q test, I²), and a random effects model was used if heterogeneity testing revealed significant results.

CAPSULE SUMMARY

- Published studies suggest that the prevalence of psoriatic arthritis among psoriasis patients ranges from 7% to 26%.
- We estimate that 15.5% of patients with psoriasis have undiagnosed psoriatic arthritis.
- This high estimated prevalence suggests that psoriasis patients should be thoroughly screened for psoriatic arthritis.
RESULTS

Our strategy yielded 394 potentially relevant articles. Three hundred fifty-four studies were excluded after title and abstract reading because they did not meet the inclusion criteria on basis of type of article, study design, population, or outcome of interest, and 55 were excluded after reading the full-length article for the same reasons as above or because they did not present sufficient data to accurately calculate the prevalence of newly diagnosed PsA. Five studies obtained from the additional literature search on PsA screening questionnaires were added, for a final selection of 12 studies (Table I; Fig 1)—7 epidemiological studies2,12-17 aimed at determining the prevalence of PsA in patients with skin psoriasis and 5 studies18-22 aimed at validating a PSA questionnaire.

In 7 of 12 studies, patients presented to a dermatologist first.2,12,15-17,21,22 Suspected arthritis was never mentioned to be a reason for presentation. In 7 of 12 studies, the final diagnosis was made by a senior rheumatologist2,12,15-17,21,22; in the 5 other studies, it was not stated who was responsible for the final diagnosis of PsA.13-14,18-20 CASPAR, GRAPPA, Moll and Wright criteria, as well as the rheumatologists’ assessments were used to make the final diagnosis of PsA (Table I). When considered, in 1 study,2 laboratory tests and imaging results did not markedly alter the prevalence of PsA based on the rheumatologists’ assessment of medical history and clinical examination alone. Data on PsA activity and/or extent were provided in 9 of 12 studies.2,13-18,21,22 Three studies16,18,21 provided data for patients with newly diagnosed PsA: in studies by Reich et al16 and Haroon et al,18 respectively, 41.3% and 69% of patients had nonpolyarticular disease.

The point prevalence of undiagnosed PsA varied from 4.2% to 33.6% across the 12 studies. In the metaanalysis of all 12 studies, the point prevalence estimate of PsA was 15.5% (95% CI, 11.5-19.5%; Fig 2). The high \( I^2 \) value (96.86%) showed that most of the variability across studies was caused by high heterogeneity. We therefore investigated the putative causes of heterogeneity through subgroup analysis of the studies according to methodologic, ethical, and clinically important parameters. When the analysis was restricted to studies using the CASPAR criteria for PsA diagnosis, the point prevalence of PsA was 14.9% (95% CI, 8.7-21.1%) and the heterogeneity remained high (\( I^2 = 94.43% \)). When only studies with patients from Europe or North America were considered, PsA prevalence increased slightly (17.4% [95% CI, 12-23%]) and heterogeneity remained high (\( I^2 = 97.2\% \)). Limiting further the selection to European or North American studies using CASPAR criteria did not change the results (PsA prevalence, 17.6% [95% CI, 9.1-26.2%] and \( I^2 = 92.16\% \)). Heterogeneity was not reduced when, in order to test the impact of severity of the skin disease, we restricted the analysis to studies that included patients with mean Psoriasis Area Severity Index (PASI) scores <10 (prevalence, 18.5% [95% CI, 9.9-27.1%] and \( I^2 = 97.5\% \)) or to studies that included patients who were seen in a hospital setting (prevalence, 17.5% [95% CI, 10.8-24.3%] and \( I^2 = 96.32\% \)). Excluding the 5 studies that were used to develop or assess PsA screening questionnaires to focus only on epidemiologic studies had no beneficial effect on heterogeneity; however, this approach generated a lower prevalence (10.1% [95% CI, 6.1-14.1%] and \( I^2 = 96.93\% \)). Complete results are presented in Table II.

DISCUSSION

The point prevalence of PsA in psoriasis patients varies notably across studies.1,2 Heterogeneity between studies18,22 in the diagnosis criteria for PsA may contribute to this variability. The Prevalence of Psoriatic Arthritis in Adults with Psoriasis: An Estimate from Dermatology Practice (PREPARE) study2 illustrates the extent to which the criteria used to diagnose PsA can impact the reported prevalence. Of 949 psoriasis patients seen at dermatologic centers in Northern America and Europe, PsA screening questionnaires detected probable PsA in 42.9% to 45.1%; when asked, 22.7% thought they had PsA; after rheumatologist assessment, 30% (95% CI, 27-33%) had PsA, and among those 41% (ie, 13.2% of the studied population) had not been previously diagnosed with PsA.

Our finding that up to 15.5% (95% CI, 11.5-19.5%) of psoriasis patients had undiagnosed PsA suggests that PsA prevalence in psoriasis patients may have been underestimated in some studies. The value we calculated provides an evaluation of the likelihood for a dermatologist to see a psoriasis patient with undiagnosed PsA at a dermatologic center. It does not reflect directly the prevalence of undiagnosed PsA in the general population of patients with psoriasis.
Higher skin disease severity might enhance the risk of PsA.16,23 Though controversial,24,25 this issue raises the possibility that PsA prevalence—and therefore the likelihood to observe undiagnosed PsA—may be increased in patients referred to hospital-based tertiary care because they are more likely to have a severe skin disease. Most of the studies reviewed here were conducted in tertiary care centers, and the reported prevalence of undiagnosed PsA may have therefore been overestimated. However, the data do not support this possible caveat. Haroon et al18 observed a high prevalence (29%) of undiagnosed PsA in patients attending dermatology clinics who had mild psoriasis (mean PASI score = 2.04 ± 1.15). In the PREPARE study,2 patients seen in dermatologic centers had moderate to severe psoriasis (mean PASI score = 6.1 ± 6.1).

### Table I. Psoriatic arthritis studies included in this meta-analysis

<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Country</th>
<th>Database</th>
<th>N</th>
<th>Criteria of PsA</th>
<th>Prevalence (%)</th>
<th>PASI * total/PsA Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reich et al16 (2009)</td>
<td>Germany</td>
<td>DI and DO</td>
<td>1511</td>
<td>Moll and Wright</td>
<td>17.6</td>
<td>12/14.3</td>
</tr>
<tr>
<td>Yang et al17 (2011)</td>
<td>China</td>
<td>DI</td>
<td>1928</td>
<td>CASPAR</td>
<td>5.34</td>
<td>6.27/9.7</td>
</tr>
<tr>
<td>Carneiro et al12 (2012)</td>
<td>Brazil</td>
<td>DI</td>
<td>133</td>
<td>CASPAR</td>
<td>12.78</td>
<td>NA/NA</td>
</tr>
<tr>
<td>Tinazzi et al21 (2012)</td>
<td>Italy</td>
<td>DI</td>
<td>228</td>
<td>CASPAR</td>
<td>31.14</td>
<td>6.13/6.7</td>
</tr>
<tr>
<td>Haroon et al18 (2013)</td>
<td>Ireland</td>
<td>DI and DO</td>
<td>100</td>
<td>CASPAR</td>
<td>29</td>
<td>2.04/2.4</td>
</tr>
<tr>
<td>Walsh et al22 (2013)</td>
<td>America</td>
<td>DI</td>
<td>189</td>
<td>Rheumatologist-diagnosed</td>
<td>33.6</td>
<td>NA/NA</td>
</tr>
<tr>
<td>Fernandez-Sueiro et al13 (2012)</td>
<td>Spain</td>
<td>DI</td>
<td>122</td>
<td>CASPAR</td>
<td>9.8</td>
<td></td>
</tr>
<tr>
<td>Henes et al19 (2011)</td>
<td>Germany</td>
<td>DI and DO</td>
<td>404</td>
<td>CASPAR</td>
<td>10.9</td>
<td>NA/NA</td>
</tr>
</tbody>
</table>

CASPAR, Classification Criteria for Psoriatic Arthritis; DI, dermatology inpatients; DO, dermatology outpatients; G, general; GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; NA, not available; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis.

*If not available in the published article, the result was calculated with a weighted average.
Some studies assessing PsA screening questionnaires excluded patients with already known PsA.\textsuperscript{18,20,21} This selection bias means that PsA screening questionnaire studies may not reflect the true prevalence of undiagnosed PsA and may have contributed to an overestimate of PsA. When these studies were excluded, the prevalence was reduced to 10.1\% (95\% CI, 6.1-14.1\%). Therefore, although they contribute to highlighting the issue of undiagnosed PsA in patients with psoriasis, including these studies is questionable, and a prevalence of 10.1\% may be more accurate. When considering a prevalence of PsA among patients with cutaneous psoriasis of 26\%\textsuperscript{1} with $\leq$41\%\textsuperscript{2} of undiagnosed PsA among patients with PsA, the overall prevalence of undiagnosed PsA in cutaneous psoriasis would be 10.7\%, which is close to our result when not taking into account studies regarding PsA screening questionnaires (10.1\%).

The approximately 50\% difference we observed when considering all studies (15.5\%) versus only epidemiological studies (10.1\%) reflects the heterogeneity in studies that prevents us from providing a robust estimate of the true prevalence of undiagnosed PsA in patients with psoriasis.
Underestimation might be another caveat. Although in 1 study, patients had to be naïve of systemic treatment of their skin condition, in 3 studies, some patients were receiving disease-modifying antirheumatic drugs or biologic agents that are known to be effective in the treatment of PsA. Some of these patients may have had true PsA that remained undiagnosed because it was asymptomatic. These cases could contribute to the underestimate of prevalence of undiagnosed PsA in patients with psoriasis.

The reported prevalence of undiagnosed PsA among patients with psoriasis is based primarily on studies that did not use modern imaging techniques, thereby excluding patients with subclinical PsA. However, in the PREPARE study, only 2 of 183 patients that received ultrasound, magnetic resonance imaging scans, and radiographic imaging had their PsA diagnosis changed from negative to positive based on the imaging results.

Another important limitation to our study is the high heterogeneity ($I^2 = 96.86\%$). Many factors may account for this. The studied populations varied from inpatients seen at dermatology departments to virtual patients in databases or volunteers willing to fill in a questionnaire. CASPAR screening criteria were not available throughout the study period, and different criteria were used to define PsA. Studies were also conducted in several different countries with varying PsA prevalence in the general population. Limiting our analysis to prevalence studies only had no impact on the $I^2$ value.

Additional limitations that could have accounted to the observed heterogeneity are the complexity of PsA across the full spectrum of psoriasis, the genetic differences between psoriasis and PsA, the approximately 10-year delay in the presentation of PsA manifestations, and the suboptimal performance of the 3 major screening tools for PsA.

Because of these limitations, high heterogeneity, and the lack of appropriate serologic screening tests for definitive diagnosis of joint disease, the prevalence of undiagnosed PsA we found has to be considered with caution. Nevertheless, an important message from this study is that the prevalence of undiagnosed PsA is high and that dermatologists should be screening all patients with psoriasis for PsA on a systematic basis as recommended by the American Academy of Dermatology in their 2009 psoriasis guidelines.

PsA can be difficult to detect by physicians who are not trained to assess rheumatologic symptoms, such as dermatologists, and several questionnaires have been created. Among them, the Psoriasis and Arthritis Screening Questionnaire, Psoriasis Epidemiology Screening Tool, and Toronto Psoriatic Arthritis Screen have proven to be valuable tools, with acceptable sensitivity/specificity and good negative predictive value. These tools assist dermatologists in identifying patients with psoriasis without PsA and patients with possible PsA who needs further assessment. In the United Kingdom, psoriasis guidelines recommend that patient with psoriasis who do not have a diagnosis of PsA complete an annual Psoriasis Epidemiology Screening Tool questionnaire, notably within the first 10 years of onset of psoriasis.

The recent results of the Tight Control of Psoriatic Arthritis (TICOPA) protocol found that tight control of PsA disease activity using a treat-to-target approach significantly improves joint and skin outcomes for newly diagnosed PsA patients ($<24$ months’ symptom duration) when compared to a standard care protocol. This shows that early detection of PsA will improve the outcome of these patients. Dermatologists are at the front line to determine the presence of arthritis in psoriasis patients, and they should be sensitized to perform such evaluation.

In conclusion, between 10.1% and 15.5% of patients with psoriasis seen by dermatologists in hospital settings may have undiagnosed PsA. This value does not take into account patients with subclinical PsA that can only be detected with highly sensitive imaging techniques. Not all patients with arthritis experience an arthritic flare or active enthesitis at the time they are seen by a dermatologist. However, early detection of PsA is essential because tight control of inflammation in these patients may improve joint outcome. Dermatologists should therefore be able to determine whether a patient with psoriasis requires prompt referral to a rheumatologist. A tight collaboration between dermatologists and rheumatologists is essential to establish early detection of PsA and to ensure rapid PsA management.

REFERENCES
