Original article

Psoriatic arthritis epidemiology, comorbid disease profiles and risk factors: results from a claims database analysis

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Abstract

Objective. Psoriasis is a systemic inflammatory disease often accompanied by comorbidities, including metabolic syndrome, cardiovascular diseases and depression. Up to 41% of psoriasis patients develop psoriatic arthritis (PsA), making it one of the most relevant manifestations. A large health claims data set was analysed to determine the rate of PsA development in psoriasis patients. Furthermore, comorbid disease profiles of psoriasis patients with or without PsA were compared, and potential risk factors for the development of PsA were identified.

Methods. This was a non-interventional, retrospective analysis of anonymized insurance health claims data using a subset of the Institute of Applied Health Research Berlin (InGef) database. The primary outcome was the prevalence and incidence of diagnosed PsA among psoriasis patients in Germany. Risk factors for the development of PsA in psoriasis patients were determined by conditional logistic regression analysis.

Results. The cumulative percentage of patients with existing psoriasis developing concomitant PsA over 4 years was 3.44%, with a mean time to diagnosis of PsA of 1.5 years. Psoriasis patients diagnosed with acute rheumatism (odds ratio: 2.93, 95% CI = 1.76, 4.86; $P < 0.001$) or pain in unspecific joints (odds ratio: 1.74, 95% CI = 1.01, 2.99; $P = 0.047$) showed an increased risk for development of PsA later on. Interestingly, fewer than half of the patients with concomitant PsA consulted a rheumatologist.

Conclusions. Unspecific arthritic symptoms are likely to precede PsA diagnoses and can develop soon after onset of psoriasis, with accumulating risk over time. There is a high unmet need for early rheumatological assessment of psoriasis patients.

Key words: PsA, psoriasis, comorbid disease, incidence, epidemiology, risk factors, insurance health claims data

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Key messages

- Development of concomitant PsA starts soon after diagnosis of psoriasis
- Unspecific arthritic symptoms are risk factors for the development of PsA, preceding its diagnosis
- Even after diagnosis, PsA patients are not routinely seen by rheumatologists

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CLINICAL SCIENCE

Introduction

Psoriasis is a chronic inflammatory skin disease, which is prevalent in ∼3% of the population in industrialized countries, affecting women and men equally [1, 2]. Psoriasis, which is aggravated by the association with multiple coexisting conditions, including metabolic syndrome, cardiovascular disease and psychiatric disorders, gravely affects patients' quality of life (QoL) [3–6]. In particular, concomitant psoriatic arthritis (PsA), one of the most relevant clinical manifestations, presents in >40% of psoriasis patients, severely impairing physical functioning, ability to work and QoL [6–11]. PsA can lead to joint damage and deformities. Owing to increased impairment of QoL and risk of a potentially destructive disease course of PsA, early diagnosis and therapeutic intervention are crucial for optimal patient care. PsA has been reported to be diagnosed 5–12 years after the first appearance of skin symptoms [12–15]. Subclinical inflammatory lesions detected by magnetic resonance imaging (MRI) were, however, found to be present in patients with cutaneous psoriasis preceding the development of PsA [16]. Diagnosis and consecutive treatment of PsA are often delayed owing to its diverse clinical features and the physician specialty consulted [17]. It is hypothesized that unspecific arthritic symptoms precede the development of PsA, emphasizing the importance of screening psoriasis patients for potential joint symptoms from the time of diagnosis [18–20]. It is estimated that ∼15% of psoriasis patients have undiagnosed PsA, despite guidelines, such as the German S3 guideline for therapy of psoriasis, recommending specific rheumatological evaluation of every psoriasis patient [9, 21, 22].

For both psoriasis and PsA, an increasing prevalence has been reported over the last 30 years [23–26], yet the incidence of PsA in newly diagnosed psoriasis patients (referred to here as psoriasis–PsA) and comorbid disease profiles are only described in part in the German population [9, 27, 28]. In this study, German health claims data were analysed to determine the incidence rate of PsA in psoriasis patients. Furthermore, comorbid disease profiles of psoriasis patients with or without concomitant PsA were compared, and potential risk factors for the development of PsA were assessed.

Methods

Study design and data source

This was a non-interventional retrospective analysis of insurance claims data using the Institute of Applied Health Research Berlin (InGef) database [29]. The InGef database is a complete, longitudinal claims data set of 7 million individuals (10% of the statutory insured population of Germany) between 2012 and 2017. Approximately 85% of the German population (∼70 million individuals) are insured by the statutory health insurance (SHI) system. For the purpose of this study, InGef provided a representative subset of anonymized claims based on 4 million members of the SHI in Germany, which allows extrapolation of these epidemiological findings to the overall German adult population [29]. All patient-level data in the InGef research database were de-identified. Use of this study database for health services research was therefore fully compliant with German federal law and, accordingly, ethical approval and informed consent were not needed. Besides information on demographic characteristics of insured individuals, the database provides patient data, including diagnostic codes, outpatient care, pharmacotherapy and medical devices, at an anonymized individual level [30].

Patient selection and evaluation parameters

Individuals included in this study were continuously insured from 1 January 2012 until 31 December 2017 and had a diagnosis of psoriasis vulgaris and/or PsA (hospital main or secondary discharge diagnosis and/or outpatient diagnosis verified in at least two quarters within a rolling window of three quarters; M2Q criterion). Owing to data protection directives, the time period of consecutive observation is limited to 6 years. International Statistical Classification of Diseases and Related Health Problems (ICD) codes (10th revision, German modification) were used to identify a diagnosis (psoriasis vulgaris: L40.0; PsA: M07.0, M07.1 and M07.3).

Patients were classified as psoriasis or PsA prevalent if they were diagnosed with psoriasis or PsA between 1 January 2012 and 31 December 2017 and the diagnosis was verified within a rolling year window. Patients were classified as psoriasis incident in 2014 if they had a diagnosis (M2Q criterion) of psoriasis between 1 January 2014 and 31 December 2014. In addition, a diagnosis-free period of 1 year was defined to assure appropriate sensitivity in detection of psoriasis and PsA incidence. The consecutive observation period in our analysis was therefore limited to a window of 5 years. Likewise, incident PsA, concomitant with psoriasis, was determined by excluding patients who had a PsA diagnosis at least one quarter before their first diagnosis of psoriasis. Patients with a diagnosis of psoriasis between 1 January 2012 and 31 December 2013 or a diagnosis of PsA between 1 January 2012 and the quarter before the first diagnosis of psoriasis were excluded. These diagnosis-free intervals were set to minimize overestimation of the incidence by accounting for physician documentation, different patient behaviours and the nature and stage of the disease.

Patient characteristics [age, sex, PsA subtypes (M07 Distal interphalangeal PsA; M07.1 arthritis mutilans; M07.3 Other PsA)] were analysed in the population of prevalent psoriasis with and without concomitant PsA diagnosis from 2012 until 2017.

An exploratory analysis of the most frequently coded comorbid diseases (categories include psychiatric, metabolic, cardiovascular, skin, rheumatic, hepatic, renal, ophthalmological or other) was performed based on the diagnoses from the ICD-10-GM catalogue in the inpatient and outpatient sector. The number and proportion

of selected comorbid diseases were analysed from the index quarter in 2012 until the end of the observation period. In addition, the number of patients treated by each physician specialty in the respective year was counted and reported for the year with the highest prevalence of psoriasis–PsA (2017).

Identification of risk factors

Risk factors for the development of PsA in psoriasis patients were determined by conditional logistic regression analysis in sex- and age-matched populations using nearest neighbour matching in a ratio of one to four (psoriasis to PsA conversion to psoriasis without PsA conversion) [31]. Using a multivariate regression model, risk factors for development PsA within 4 years of the first psoriasis diagnosis (from first psoriasis diagnosis in 2014 until 31 December 2017) were evaluated. Patients were separated into two groups: patients developing PsA by 31 December 2017 after the first psoriasis diagnosis were assigned to the PsA group (psoriasis–PsA), and patients who did not develop PsA by 31 December 2017 after first diagnosis of psoriasis were assigned to the control group (psoriasis only). Risk factors for the development of concomitant PsA were identified and their effect size was quantified. All potential risk factors before the first diagnosis of PsA were considered. For the multivariate model, parameters such as the P-value for every individual comorbidity, odds ratio, relative risk, 95% CIs, goodness of fit (pseudo-R^2) and percentages of the comorbid diseases in each group were calculated.

Statistical analysis

Owing to data protection requirements, all analyses were conducted exclusively by employees of Elsevier Health Analytics using the central statistical software program SAS Enterprise Guide, v.9.2 and R v.1.1.383 [RStudio Team (2016). RStudio: Integrated Development for R. RStudio, Inc., Boston, MA, USA; available at: http://www.rstudio.com]. All psoriasis and psoriasis–PsA patients fulfilling the inclusion criteria were included in the analyses to obtain representative results for the German population. The estimation of the overall SHI population was based on the official statistics of individuals covered by SHI in the respective year (http://www.gbe-bund.de). The ratio of insured individuals in the official statistics to patients found in the age- and gender-stratified analytical database was used as a factor to extrapolate the total number of individuals under SHI coverage.

Results

Patient characteristics of the psoriasis–PsA cohort

The insurance health claims data of the InGef database contained 2.9 million adult individuals stratified by age and sex, based on the population structure of Germany. At the end of the observation period, 52 916 had a

diagnosis of psoriasis, equalling a point prevalence of 1.8%. Of these psoriasis patients, 4390 (8.3%) had a documented diagnosis of PsA (psoriasis–PsA), with 178 of these patients having the severe subtype, arthritis mutilans (Fig. 1). Psoriasis–PsA patients were slightly younger than psoriasis patients without concomitant PsA (mean age of psoriasis–PsA patients, 55.2 years; mean age of psoriasis patients, 58.0 years).

In 2014, 5760 individuals were incident for psoriasis. Notably, the mean age at first diagnosis of psoriasis was 5 years lower in patients who later developed concomitant PsA (psoriasis, 56.0 years; psoriasis–PsA, 51.1 years).

Comorbid disease profiles

Both patient groups displayed a similar comorbid disease profile, with a high frequency of metabolic syndrome-associated conditions (obesity, essential arterial hypertension, disorders of lipoprotein metabolism and other lipidaemias; Table 1). Although unspecific arthritic symptoms (other joint disorders, other soft tissue disorders and somatoform disorders) were more frequent in psoriasis–PsA patients, they were also present in patients with psoriasis alone (Table 1).

Incidence of PsA in psoriasis patients

The incidence of psoriasis was increased in patients >50 years old, independent of sex (Fig. 2; Supplementary Table S1, available at *Rheumatology Advances in Practice* online). To determine the incidence and mean time of PsA development in psoriasis patients, incident psoriasis patients with no PsA diagnosis were selected and followed for 4 years. The cumulative percentage of psoriasis patients developing PsA (4-year incidence) was 3.4%, an annual mean incidence (AMI) of 0.96%. The mean time to diagnosis of PsA within the observation window of 4 years was 1.5 years (data on file). Percentages of psoriasis–PsA patients were similar between age groups (Supplementary Table S1, available at *Rheumatology Advances in Practice* online). Males and females had a similar incidence of psoriasis–PsA (Supplementary Table S1, available at *Rheumatology Advances in Practice* online).

Ambulatory physician specialties consulted by patients

To determine whether psoriasis patients were sufficiently evaluated for their risk of development of PsA, we assessed which ambulatory physician specialties were consulted by psoriasis patients. After diagnosis, nearly 80% of all patients were seen by a general practitioner and nearly 60% by a dermatologist; however, only 4% of patients with psoriasis consulted ambulatory rheumatologists (Fig. 3).

To assess whether patients with a concomitant PsA diagnosis were monitored adequately, we also analysed which physician specialties were consulted most

FIG. 1 Prevalence of psoriasis and incidence of early PsA in psoriasis patients from the Institute of Applied Health Research Berlin database
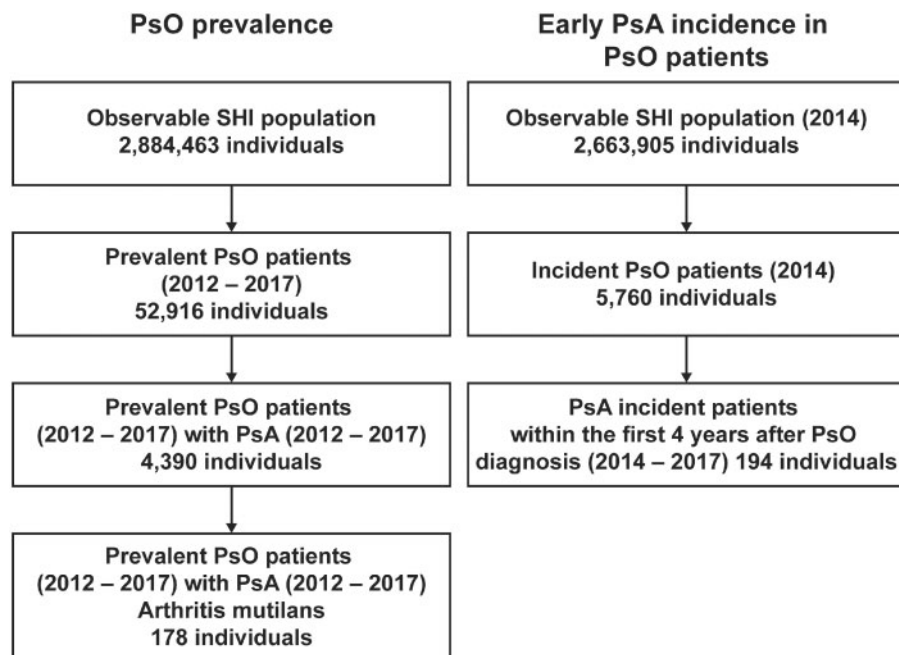
PsA: psoriatic arthritis; PsO: psoriasis; SHI: statutory health insurance.

TABLE 1 Frequencies of selected clinically relevant comorbid diseases of the psoriasis and psoriasis–PsA patient cohort[a]

| ICD-10 GM	Description	Percentage of patients with psoriasis (*n* = 48 526)	Percentage of patients with psoriasis–PsA (*n* = 4390)
M54	Dorsalgia	73.3	80.1
I10	Essential (primary) hypertension	62.1	64.3
M79	Other and unspecified soft tissue disorders not elsewhere classified	29.9	60.1
M25	Other joint disorder, not elsewhere classified	35.1	54.5
E78	Disorders of lipoprotein metabolism and other lipidaemias	50.4	50.7
J06	Acute upper respiratory infections of multiple and unspecified sites	46.2	50.5
M47	Spondylosis	35.7	45.7
F45	Somatoform disorders	33.7	41.7
M77	Other enthesopathies	28.5	39.6
E66	Overweight and obesity	30.7	38.6

[a]Population includes prevalent psoriasis in 2012–2017 without PsA [2012–2017 (psoriasis)] and prevalent psoriasis in 2012–2017 with PsA [2012–2017 (psoriasis–PsA)]. PsA: psoriatic arthritis;PsO: psoriasis; PsO–PsA: patients with both PsO and PsA.

frequently by psoriasis–PsA patients. Patients with or without PsA were seen by general practitioners (psoriasis, 74.9%; psoriasis–PsA, 77.4%) and dermatologists (psoriasis, 62.4%; psoriasis–PsA, 57.8%). Although more psoriasis–PsA compared with psoriasis patients consulted ambulatory rheumatologists (psoriasis, 4.4%; psoriasis–PsA, 50.0%), half of the patients with psoriasis–PsA were without rheumatological care (Fig. 3).

Risk factors for conversion of psoriasis to psoriasis–PsA

Psoriasis patients diagnosed with acute rheumatism (odds ratio: 2.93, 95% CI: 1.76, 4.86; $P < 0.001$) or pain in unspecific joints (odds ratio: 1.74, 95% CI: 1.01, 2.99; $P = 0.047$) showed a significantly increased risk of development of PsA in the future (Fig. 4). On the contrary, specific arthritic symptoms, such as Bouchard's nodes

FIG. 2 Age distribution of patients with psoriasis and incidence of psoriasis–PsA

Age distribution of PsO incident patients*

PsA incidence in PsO incident patients*
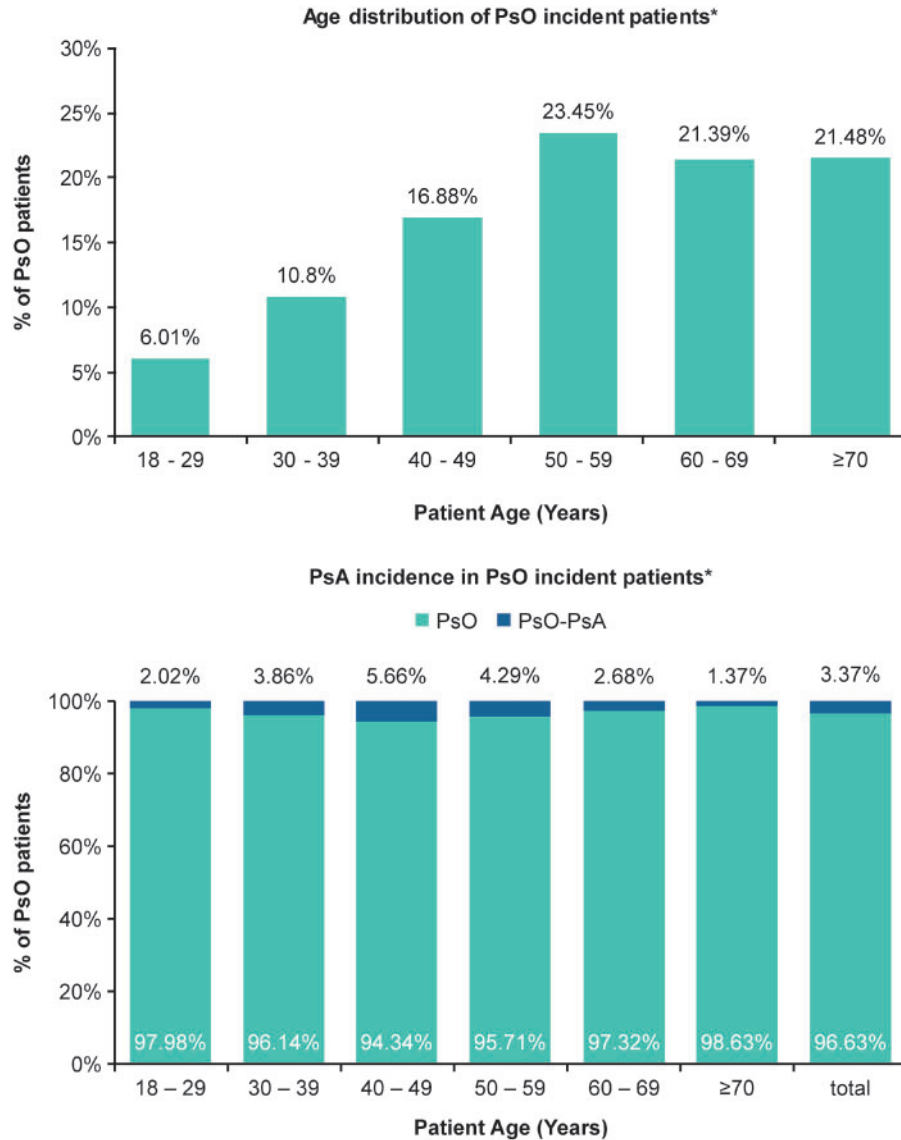
Population includes patients with psoriasis in 2014 (male, *n* = 2969; female, *n* = 2791), who were observed up to and including 2017 for PsA development. PsA: psoriatic arthritis; PsO: psoriasis; PsO-PsA: patients with both PsA and PsO.

and Heberden's nodes, did not confer a higher risk for development of PsA.

Discussion

In this study, the development of PsA in psoriasis patients in the first 4 years after diagnosis of psoriasis was assessed, and even in the early years after diagnosis of psoriasis, onset of PsA was observed. The mean time to PsA diagnosis of only 1.5 years demonstrated that the development of PsA can occur early after a diagnosis of psoriasis. Given that development of PsA drastically impairs the ability to work and QoL, these data reinforce the need to include rheumatologists early on for clinical decision-making for psoriasis patients. The prevalence of the severe subtype of arthritis mutilans (4.0% of PsA prevalent patients from 2012 to 2017) reveals that concomitant PsA is diagnosed too late or treated ineffectively in a significant number of patients. This suggests that there is an unmet need for rheumatological check-up in psoriasis patients soon after diagnosis of psoriasis; however, only a small percentage of patients with or without concomitant PsA consulted a rheumatologist. Furthermore, the cumulative incidence of psoriasis–PsA of 3.4% over the first 4 years after diagnosis of psoriasis suggests that disease progression can start early. The high frequency of unspecific

Fig. 3 Specialties of ambulatory physicians consulted by psoriasis and psoriasis–PsA patients
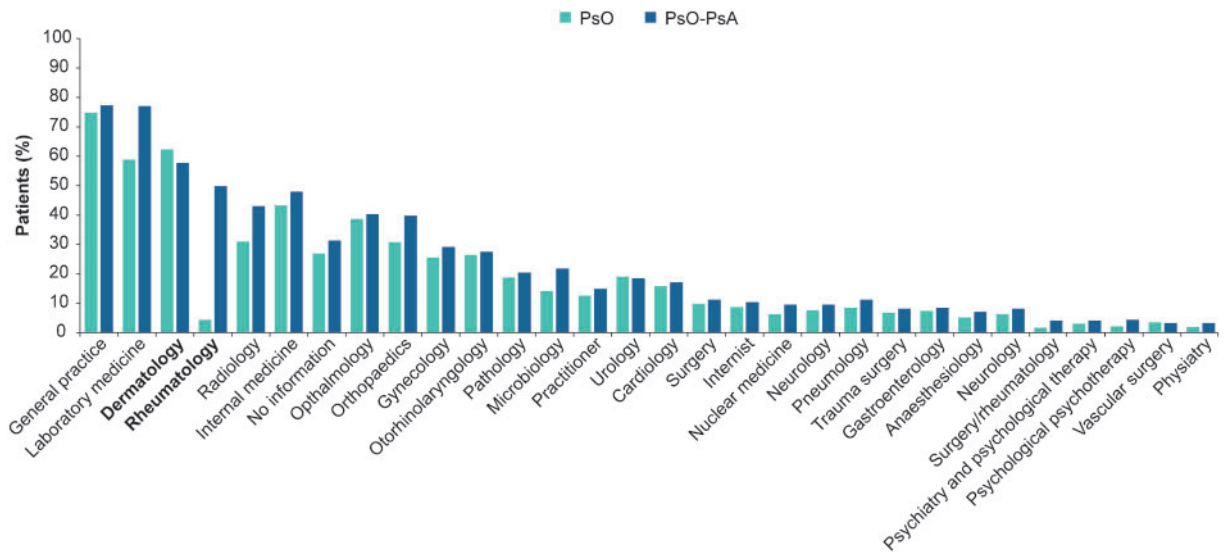
Top 30 ambulatory physician specialties consulted by psoriasis and psoriasis–PsA patients in 2017. Population includes prevalent psoriasis in 2017 without PsA [2017 (PsO)] and prevalent psoriasis in 2017 with PsA [2017 (PsO-PsA)]. PsA: psoriatic arthritis; PsO: psoriasis; PsO-PsA: patients with both PsA and PsO.

Fig. 4 Risk factors for the development of PsA in psoriasis patients
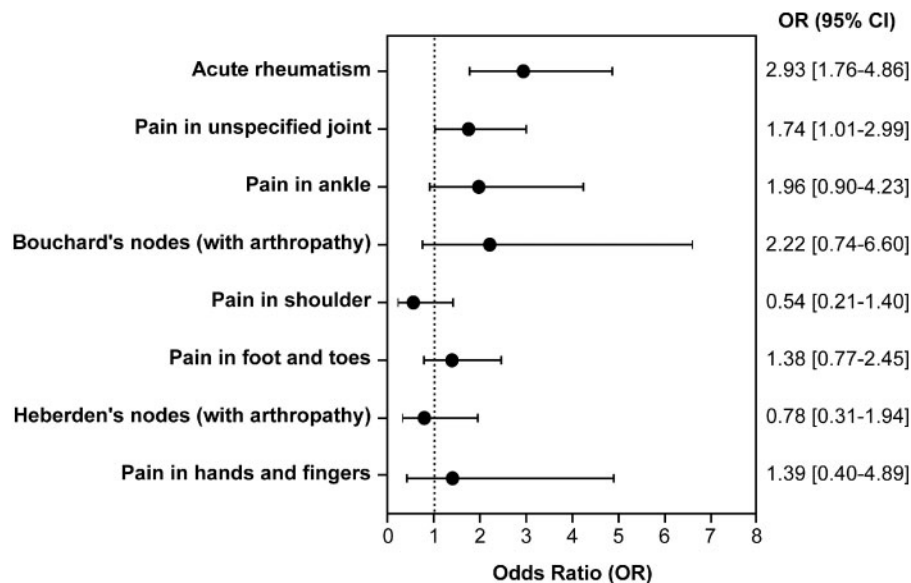
ORs (filled circle: OR point estimate; lines: 95% CI) of risk factors for developing PsA in patients with cutaneous psoriasis from a conditional logistic regression analysis, based on top 20. OR: odds ratio; PsA: psoriatic arthritis.

rheumatological comorbid diseases, such as other joint disorders and other soft tissue disorders, or associated conditions, such as somatoform disorders, shows that subclinical inflammatory PsA lesions might already be present in a significant proportion of psoriasis patients at the time of diagnosis of psoriasis. Taken together, this emphasizes the need to monitor psoriasis patients closely for symptoms indicative of early arthritis. In Germany, the limited availability of rheumatologists results in prolonged waiting times for appointments. The ability of German dermatologists to diagnose PsA on their own is improving with the use of the GErman Psoriasis ARthritis Diagnostic questionnaire (GEPARD) or Psoriasis Epidemiology Screening Tool (PEST), and

these patients should be presented to a rheumatologist along with their clinical characteristics (e.g. arthritis, swollen joints, tendon pain) [32].

The frequent comorbid diseases and risk factors found in our study are consistent with PsA being characterized by locally unspecific arthritic symptoms and with the hypothesis that early subclinical arthritic joint inflammation precedes manifestation of PsA in psoriasis patients [16]. These results suggest that psoriasis patients who will develop PsA soon after diagnosis of psoriasis could be identified by unspecific arthritic symptoms and should therefore receive rheumatological care. Recent evidence suggests that early intervention treatment of PsA with biologic disease-modifying anti-rheumatic drugs (DMARDs) halts the progression of bone changes and decreases synovial inflammation [33, 34].

Christophers *et al*. [35], in a questionnaire-based cross-sectional observational study, showed that after 20 years of follow-up, the incidence of psoriasis–PsA in Germany was 13% (AMI of 0.65%). This is slightly lower than the incidence of psoriasis–PsA observed in our study, although the AMI of psoriasis–PsA worldwide varies depending on the size of the study. In Italy, an AMI of 1.7% was observed in patients from outpatient dermatology clinics [36], whereas a Canadian study reported an incidence of 3.2% over a 4-year observational period (AMI 0.79%) [24]. The mean time to diagnosis of PsA (1.5 years) constitutes approximately half of the observational period, reflecting a constant probability to develop the disease over a 4-year period, which is consistent with these studies [24, 36]. Variation in the reported incidence rates of psoriasis–PsA might be attributed to the lack of widely accepted diagnostic criteria for PsA, different study designs, geographical variations, different study inclusion criteria (e.g. data obtained from registries, hospitals) and ICD coding system biases. Furthermore, the methods for diagnosis of PsA vary between studies (e.g. self-reported questionnaire, rheumatological assessment). In studies that rely on specific ICD coding, the incidences are likely to be underestimated owing to unrecognized, milder forms of PsA without careful rheumatological assessment.

Both male and female psoriasis patients showed a similar risk for development of PsA. Consistent with the mean age of psoriasis diagnosis, the incidence of psoriasis was increased after 50 years of age. Psoriasis–PsA developed consistently over time, which supports previous studies and meta-analyses [14].

In the present study, unspecific arthritic symptoms, such as acute rheumatism and pain in unspecified joints, were risk factors for conversion of psoriasis to psoriasis–PsA. This supports the hypothesis that unspecific arthritic symptoms and manifestations such as dactylitis and enthesitis are early indicators of the development of PsA, whereas specific arthritic symptoms, such as pain in the ankle, pain in the shoulder, pain in the foot and toes, pain in the hand and fingers, Bouchard's nodes and Heberden's nodes, are associated with RA [16].

This study was restricted to the 4-year observation period after diagnosis of psoriasis. Another limitation was that the influence of the severity of psoriasis on both the development rate and mean time to diagnose PsA could not be assessed. The higher PsA rates in published hospital studies could be attributed to a population with more severe psoriasis [35, 37].

PsA is also currently rather narrowly limited to joint involvement (peripheral joints, large joints and axial joints), yet enthesitis and dactylitis are characteristic manifestations of PsA. In ICD coding analysis, these PsA might therefore be underestimated. These data on PsA epidemiology, development and risk factors are of high clinical relevance and could therefore be of interest to the rheumatology community, especially in other countries with a similar demographic structure, e.g. within Europe.

Acknowledgements

Supplementary data

Supplementary data are available at *Rheumatology Advances in Practice* online.

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