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Characteristics That Predict Psoriatic Arthritis by the Classification Criteria for Psoriatic Arthritis in Patients With Juvenile Idiopathic Arthritis 18 Years After Disease Onset

Agnes Szentpetery,[1] Mia Glerup,[2] Kristiina Aalto,[3] Ellen D. Arnstad,[4] Anders Fasth,[5] Troels Herlin,[2] Charlotte Myrup,[6] Ellen Nordal,[7] Suvi Peltoniemi,[8] Marite Rygg,[9] Veronika Gjertsen Rypdal,[7] and Lillemor Berntson[10]

Objective. The purposes of this study were to assess the clinical characteristics of patients with juvenile idiopathic arthritis (JIA) who fulfill the ClASsification criteria for Psoriatic ARthritis (CASPAR) 18 years after disease onset in a population-based setting and to identify features likely to predict psoriatic arthritis (PsA).

Methods. Patients with JIA from defined geographic regions of Denmark, Finland, Norway, and Sweden with disease onset from 1997 to 2000 were enrolled prospectively and followed up for 18 years. Clinical, laboratory, and heredity data for psoriasis were collected. Patients were classified according to the International League of Associations for Rheumatology (ILAR) criteria at baseline, and we applied ILAR and CASPAR criteria at 18 years. Logistic regression was performed to study the effects of JIA-related characteristics and heredity for psoriasis on being classified for PsA.

Results. Among the 510 patients enrolled, 434 participated in the 18-year follow-up, 28 (6.5%) met the ILAR criteria, and 41 (9.4%) fulfilled the CASPAR criteria. Patients with wrist or subtalar joint involvement at onset had higher odds of being classified with PsA at 18 years (odds ratio [OR] 3.3, $P = 0.02$ and OR 12.9, $P = 0.01$, respectively). Presence of psoriasis, nail abnormalities, or dactylitis showed significant association with development of PsA (OR 20.2, $P < 0.001$; OR 11.6, $P = 0.002$; and OR 43.4, $P < 0.001$, respectively).

Conclusion. CASPAR criteria identify more patients with PsA compared with ILAR criteria and may better capture the heterogeneous nature of the disease. Presence of psoriasis and dactylitis at disease onset were the strongest predictors for the development of PsA. Further studies on the utility of CASPAR criteria in patients with JIA are needed.

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common chronic inflammatory rheumatic condition of childhood and encompasses all forms of arthritis of unknown origin with a duration of more than six weeks and onset before 16 years of age.[1] Juvenile psoriatic arthritis (JPsA) is one of the seven JIA categories outlined by the International League of Associations for Rheumatology (ILAR) classification for JIA.[2] JPsA is a rare condition because it represents 5% to 7% of the JIA population.[3–6] Children with JPsA present with heterogeneous clinical features[4] that can overlap with other categories of JIA.

Classifying patients with JPsA is often challenging because, in contrast to adult PsA, psoriasis may manifest up to 10 years after arthritis onset in children and may be prevented by the use of disease-modifying antirheumatic drugs.[3,5] The prevalence of nail involvement is also lower in children than in adults with PsA, and there is lack of supportive laboratory markers. Radiologic bone damage is reported in around 25% of juvenile patients with JPsA compared with 50% of adult patients with PsA, highlighting

[1]Agnes Szentpetery, MD, PhD: Uppsala University and Uppsala University Hospital, Uppsala, Sweden; [2]Mia Glerup, MD, PhD, Troels Herlin, MD, DMSci: Aarhus University Hospital, Aarhus, Denmark; [3]Kristiina Aalto, MD, PhD: New Children's Hospital, University of Helsinki, and Helsinki University Hospital, Helsinki, Finland; [4]Ellen D. Arnstad, MD, PhD: Norwegian University of Science and Technology, Trondheim, and Levanger Hospital, Nord-Trøndelag Hospital Trust, Levanger, Norway; [5]Anders Fasth, MD: Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden; [6]Charlotte Myrup, MD, PhD: Copenhagen University Hospital, Copenhagen, Denmark; [7]Ellen Nordal, MD, PhD, Veronika Gjertsen Rypdal, MD, PhD: University Hospital of North Norway and UiT The Artic University of Norway, Tromsø, Norway; [8]Suvi Peltoniemi, MD, PhD, Helsinki University Hospital and University of Helsinki, Helsinki, Finland; [9]Marite Rygg, MD, PhD, Norwegian University of Science and Technology and St. Olavs Hospital Trondheim University, Trondheim, Norway; [10]Lillemor Berntson, MD, PhD, Uppsala University, Uppsala, Sweden.

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Author correspondence via email to Agnes Szentpetery, MD, PhD, at agnes.szentpetery@medsci.uu.se.

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SIGNIFICANCE & INNOVATIONS

- ClASsification criteria for Psoriatic ARthritis (CASPAR) criteria identified more patients with psoriatic arthritis (PsA) compared with the International League of Associations for Rheumatology criteria in the Nordic cohort of 434 patients with juvenile idiopathic arthritis (JIA) 18 years after disease onset.
- Patients who met the CASPAR criteria had worse self-reported functional health status at 18 years compared with other categories of JIA.
- Presence of psoriasis and dactylitis at disease onset were the strongest predictors for development of PsA, whereas wrist or subtalar joint involvement, nail psoriasis, and heredity for psoriasis among first- or second-degree relatives also predicted PsA.

the severity of the disease also in children.[5,7] Many children with enthesitis and axial involvement are likely to be classified as enthesitis-related arthritis (ERA) or undifferentiated JIA rather than JPsA when applying the ILAR criteria. A retrospective study on patients with JPsA who met the Vancouver[8] or ILAR criteria showed that one-third of children were diagnosed with another JIA category based on clinical findings, despite some who had a family history of psoriasis.[9] The ILAR criteria for JPsA do not contain enthesitis and inflammatory back pain even though 33% of patients are reported to have enthesitis in a large cohort,[5] and axial disease is present in up to 25% of patients with JPsA.[10] In contrast, the adult ClASsification criteria for Psoriatic ARthritis (CASPAR)[11] take into account both psoriasis and heredity for psoriasis and include peripheral arthritis, axial manifestations, enthesitis, and radiographic features.[11]

It has been proposed that patients who are not classified as having JPsA by pediatric rheumatologists might be offered different treatment options than those labeled as having JPsA/PsA.[5] Observational data in the Nordic JIA cohort showed that children with JPsA develop more severe disease over time compared with other forms of JIA as they accumulate more inflamed joints and are less likely to achieve sustained remission.[12] Misclassification of children with JPsA therefore potentially carries the risk of not receiving tailored treatment and consequently a more severe disease outcome. It has recently been suggested that JPsA is the childhood counterpart to PsA[13]; however, studies describing the characteristics of patients with JPsA and long-term outcomes of the disease are still scarce. The majority of children diagnosed with JPsA will eventually carry the diagnosis of PsA in adulthood.[14] Applying CASPAR criteria in children with JIA has already been proposed; however, it has been scarcely studied, especially for the long-term disease course.[10,14] The objectives of our study were to assess the clinical characteristics of patients with JIA who fulfill the CASPAR criteria as young adults 18 years after disease onset in a population-based setting and to identify features likely to predict PsA, including characteristics related to JPsA and family history of psoriasis.

PATIENTS AND METHODS

Study design and patients. Data were obtained from the database of the Nordic JIA study, which is a prospective, multicenter, population-based study from specific geographic areas of Denmark, Finland, Norway, and Sweden.[15] In total, 510 consecutive patients with an onset of JIA between 1997 and 2000 were included at baseline within six months after disease onset, and 434 patients took part in the 18-year follow-up study.[16] Patients were classified according to the ILAR criteria at baseline and at the 18-year follow-up.[2] For this study, we applied the CASPAR criteria 18 years after disease onset.[11] To meet the CASPAR criteria, a patient must have inflammatory articular disease (joint, spine, or entheseal) with three or more points from the following five categories: 1) evidence of current psoriasis (two points), a personal history of psoriasis, or a family history of psoriasis in a first- or second-degree relative (one point); 2) typical psoriatic nail dystrophy including onycholysis, pitting, and hyperkeratosis observed on current physical examination (one point); 3) a negative test result for the presence of rheumatoid factor (RF) (one point); 4) either current dactylitis, defined as swelling of an entire digit, or a history of dactylitis recorded by a rheumatologist (one point); and 5) radiographic evidence of juxta-articular new bone formation on plain radiographs of the hand or foot (one point). Because we did not have radiographs, juxta-articular new bone formation was not considered for the classification.

Definitions of psoriasis and enthesitis. A patient was considered to have psoriasis if a dermatologist made that diagnosis. In cases when the skin assessment was performed by a rheumatologist, psoriasis was diagnosed if the rash likely represented psoriasis and was recorded in the patient's medical records at two or more occasions or if the patient had a positive family history in a first-degree relative. Psoriasis-like lesions that developed under anti–tumor necrosis factor therapy (paradoxical psoriasis) were not considered for CASPAR classification (n = 2).

Enthesitis evaluation was based on clinical examination. Enthesitis at sites included in the Leeds Enthesitis Index, Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index, and Maastricht Ankylosing Spondylitis Enthesitis Score[17] was recorded.

Data collection and clinical assessment. Data on demographics, joint involvement, use of conventional synthetic disease-modifying antirheumatic drugs (DMARDs) and/or biologic DMARDs, and disease activity were collected. Presence or history of psoriasis, nail pitting/onycholysis, dactylitis, enthesitis, uveitis, inflammatory back pain, and sacroiliitis on imaging were documented. The composite JIA disease activity score in 27 and

71 joints (JADAS-27 and JADAS-71) was used.[18] We applied the American College of Rheumatology provisional criteria for defining clinical inactive disease.[19] Remission was outlined according to Wallace's preliminary criteria.[20] The Juvenile Arthritis Damage Index was used to assess the articular and extra-articular damage.[21] Functional disability was evaluated using the Health Assessment Questionnaire (HAQ) by participants older than 18 years of age.[22] Heredity data on family history of psoriasis in first- and second-degree relatives were recorded.

Laboratory assessments. Normal erythrocyte sedimentation rate was defined as a velocity <20 mm/hour, and a normal C-reactive protein level was defined as <10 mg/liter. Immunofluorescent antinuclear antibody (ANA) tests using HEp-2 cells were performed using cutoff values for ANA according to the individual laboratories at each center. A positive ANA or RF test was defined as two positive tests a minimum of three months apart.[16] Human leukocyte antigen B27 was tested using standardized methods.

Ethical considerations. Approval from medical research ethical committees and data protection authorities was granted according to the regulations of each participating country. Ethical approval from the Swedish Ethical Review Authority was achieved in 2006 and 2007 (Dnr 639–96) and 2014 (Dnr 213–31). Written informed consent was obtained from parents of children aged younger than 16 years and from the patients aged at least 16 years according to the Declaration of Helsinki.

Statistical analysis. Statistical analysis was performed using IBM SPSS Statistics (version 28). Clinical characteristics of the study participants were reported as the mean or median (interquartile range) for continuous variables and number (percentage) for categorical variables. Mann–Whitney U tests and independent *t*-tests for continuous variables and Fisher's exact tests and chi-square tests for categorical variables were used to describe clinical characteristics of patients with JIA. Binary logistic regression (backward) was applied to identify JIA-related characteristics and heredity data for psoriasis associated with the fulfillment of CASPAR criteria for PsA. *P* values <0.05 were considered significant.

RESULTS

Components and fulfillment of CASPAR criteria across JIA categories at 18-year follow-up. Of the 434 patients assessed at the 18-year follow-up, 28 (6.5%) were classified into the JPsA category according to ILAR classification (Table 1). Thirty-two patients (7.4%) had psoriasis at the time of the visit, which was 78.6% of the JPsA group and 15.2% of the undifferentiated group. A personal history of psoriasis was reported in 9% of all participants. One patient in the ERA and one in the extended oligoarthritis group had a psoriasis-like skin rash, but it was not diagnosed as psoriasis at the time of the visit. Family history of psoriasis in first- or second-degree relatives occurred in all groups; the highest numbers were seen in the JPsA, undifferentiated, and ERA groups (67.9%, 63.6%, and 22.2%, respectively). Nail pitting or onycholysis was rare (4.4%) but present in 32.1% of participants with JPsA. Dactylitis occurred in 4.8% of all individuals and was seen in 21.4% of patients with JPsA.

Forty-one participants with JIA (9.4%) met the CASPAR criteria for adult PsA at the 18-year visit. None of the patients in the extended oligoarthritis, polyarticular RF-positive, and sJIA categories fulfilled the CASPAR criteria. Of the 41 patients who met the CASPAR criteria, 18 participants (44%) did not fulfill the ILAR criteria for JPsA. Ten patients (24.4%) met the CASPAR criteria without having psoriasis at any point during the disease course (five had heredity for psoriasis in second-degree relatives, four had it in first-degree relatives, and one had dactylitis and nail abnormalities). A total CASPAR score of 3 was achieved by 7.1% of the cohort, 4 points was reached only by participants with JPsA and undifferentiated arthritis, and 5 points was achieved exclusively by individuals with JPsA (Table 1). The majority of patients who fulfilled the CASPAR criteria for PsA at the 18-year follow-up were categorized as having JPsA or undifferentiated arthritis according to the ILAR criteria, whereas the distribution of participants with PsA across different ILAR categories were more widespread at baseline. Approximately one-third of the patients were classified with undifferentiated arthritis both at baseline and at the 18-year follow-up (Table 2).

Baseline clinical characteristics and heredity for psoriasis. To find clinical features at the time of disease onset that distinguished the 41 participants who later fulfilled the CASPAR criteria for PsA from the rest of the JIA cohort, we compared baseline clinical characteristics, laboratory findings, and heredity for psoriasis between the two groups (Table 3). Because systemic juvenile idiopathic arthritis (sJIA) is considered fundamentally different from any other form of JIA based on its unique clinical appearance and genetic risk factors,[23] we excluded participants with sJIA from these analyses (n = 14). There was female predominance (68%) in both groups, and the median age of disease onset was also similar (6.95 vs 6.38 years). More patients with PsA had wrist (26.8% vs 13.8%; $P = 0.03$) and subtalar joint involvement (7.3% vs 1.3%; $P = 0.008$) than those who did not fulfill the CASPAR criteria. Median cumulative joint count was also higher in the PsA group (4 vs 3; $P = 0.046$). The number of individuals with arthritis in upper extremities tended to be higher in the PsA group (63.4% vs 43.4%; $P = 0.09$), and fewer patients had knee arthritis compared with the rest of the cohort (14.6 vs 26.7%; $P = 0.09$). Baseline disease activity measures and patient-reported outcomes, including the number of active small

Table 1. Components of the CASPAR criteria across JIA categories in the Nordic JIA cohort at 18-year follow-up*

	JPsA, n (%)	Enthesitis- related arthritis, n (%)	Extended oligoarticular, n (%)	Persistent oligoarticular, n (%)	Polyarticular RF negative, n (%)	Polyarticular RF positive, n (%)	Systemic arthritis, n (%)	Undifferentiated arthritis, n (%)	Total, n (%)
Total cohort	28 (6.5)	45 (10.4)	85 (19.6)	119 (27.4)	71 (16.4)	6 (1.4)	14 (3.2)	66 (15.2)	434 (100)
Current psoriasis[a]	22 (78.6)	0	0	0	0	0	0	10 (15.2)	32 (7.4)
Personal history of psoriasis[b]	23 (82.1)	1 (2.2)	1 (1.8)	0	0	0	0	14 (21.2)	39 (9)
Family history of psoriasis[c]	19 (67.9)	10 (22.2)	10 (11.8)	19 (16)	9 (12.7)	1 (16.7)	3 (21.4)	42 (63.6)	113 (26)
Current nail involvement	9 (32.1)	1 (2.2)	3 (3.5)	1 (0.8)	1 (1.4)	0	0	4 (6.1)	19 (4.4)
Dactylitis ever	6 (21.4)	1 (2.2)	0	5 (4.2)	6 (8.5)	0	0	3 (4.5)	21 (4.8)
RF negative	26 (92.9)	44 (97.8)	77 (90.6)	108 (90.8)	68 (95.8)	0	13 (92.9)	58 (87.9)	394 (91)
Patients with CASPAR score 3[d]	14 (50)	1 (2.2)	0	1 (0.8)	3 (4.2)	0	0	12 (18.2)	31 (7.1)
Patients with CASPAR score 4[d]	6 (21.4)	0	0	0	0	0	0	1 (1.5)	7 (1.6)
Patients with CASPAR score 5[d]	3 (10.7)	0	0	0	0	0	0	0	3 (0.7)
Fulfills CASPAR criteria	23 (82.1)	1 (2.2)	0	1 (0.8)	3 (4.2)	0	0	13 (19.7)	41 (9.4)

*CASPAR, ClASsification criteria for Psoriatic ARthritis; ILAR, International League of Associations for Rheumatology; JIA, juvenile idiopathic arthritis; JPsA, juvenile psoriatic arthritis; RF, rheumatoid factor.

[a] Current psoriasis is defined as psoriatic skin or scalp disease present at the final visit as judged by a rheumatologist or dermatologist.

[b] A personal history of psoriasis is defined as a history of psoriasis that may be obtained from a patient, family physician, dermatologist, rheumatologist, or other qualified health care provider.

[c] A family history of psoriasis is defined as a history of psoriasis in a first- or second-degree relative according to patient report.

[d] Patients with CASPAR score 3–5: number of patients achieved a total 3, 4, or 5 points out of 5 CASPAR criteria.

Table 2. JIA categories according to the ILAR classification of the 41 patients fulfilling the CASPAR criteria after 18 years of disease*

JIA categories according to ILAR criteria	At baseline, n (%)	At 18-year follow-up, n (%)
JPsA	7 (17.1)	23 (56.1)
ERA	1 (2.4)	1 (2.4)
Extended oligoarthritis	1 (2.4)	0
Persistent oligoarthritis	10 (24.4)	1 (2.4)
Polyarticular RF negative arthritis	8 (19.5)	3 (7.3)
Polyarticular RF-positive arthritis	0	0
Systemic arthritis	0	0
Undifferentiated arthritis	14 (34.1)	13 (31.7)

*CASPAR, ClASsification criteria for Psoriatic ARthritis; ERA, enthesitis-related arthritis; ILAR, International League of Associations for Rheumatology; JIA, juvenile idiopathic arthritis; JPsA, juvenile psoriatic arthritis; PsA, psoriatic arthritis; RF, rheumatoid factor.

and large joints, JADAS 27 and JADAS 71 results, and CHAQ scores, were similar in the two groups.

Notably, more individuals in the PsA group had psoriasis (22% vs 0.8%; $P < 0.001$), nail involvement (20% vs 1.3%; $P < 0.001$), and dactylitis (17.5% vs 1.3%; $P < 0.001$) at the disease onset as compared with those not classified as PsA. The number of patients with heredity for psoriasis among first- or second-degree relatives, or both, was significantly higher in the PsA group ($P < 0.001$).

Joint involvement, PsA-related characteristics, and heredity for psoriasis associated with later PsA classification. A binary logistic regression was performed to ascertain the effects of JIA-related clinical characteristics at baseline and heredity for psoriasis on being classified for PsA at the 18-year visit according to CASPAR criteria (Table 4). Binary variables that showed significant difference at baseline between the 41 individuals with PsA and the rest of the cohort were entered into the model. Participants with wrist and subtalar joint involvement had 3- and 13-times higher odds of being classified with PsA (odds ratio [OR] 3.3, 95% confidence interval [95% CI] 1.2–8.9, $P = 0.02$ and OR 12.9, 95% CI 1.8–91.3, $P = 0.01$, respectively). Presence of psoriasis and psoriasis-related nail changes at disease onset showed significant association with development of PsA (OR 20.2, 95% CI 4.6–89.3, $P < 0.001$ and OR 11.6, 95% CI 2.6–53, $P = 0.002$, respectively). Participants with dactylitis at disease onset showed the highest association with being classified as PsA at the 18-year visit (OR 43.4, 95% CI 9.1–206.2, $P < 0.001$).

Strong associations were found between family history of psoriasis among first- or second-degree relatives and classification of PsA (OR 3.4, 95% CI 1.0–11.6, $P = 0.048$ and OR 4.1, 95% CI 1.8–14.5, $P = 0.003$, respectively). An even sturdier association was observed for individuals with psoriasis in both their first- and second-degree families (OR 10.3, 95% CI 2.4–44.3, $P = 0.002$).

Clinical characteristics of patients classified as PsA at 18-year follow-up. Patients tended to have more severe disease in the PsA group compared with the rest of the cohort at the 18-year follow-up, as indicated by a higher number of patients with flare, continued disease activity, and higher number of cumulative joint counts. Patient-reported outcomes, in particular the HAQ score ($P = 0.03$), also reflected worse health status and function in the PsA group, and a similar trend was observed for pain, global health, and disease activity scores ($P = 0.05$, $P = 0.06$, and $P = 0.09$, respectively) (Supplementary Table 1). The presence of psoriasis at any point during disease course showed significant association with active disease and flare at the 18-year visit (OR 2.1, 95% CI 1.1–4.0, $P = 0.03$ and OR 2.3, 95% CI 1.2–4.6, $P = 0.02$, respectively).

DISCUSSION

In this study, we applied the CASPAR criteria to the entire Nordic JIA cohort to classify patients with PsA 18 years after disease onset. In contrast to the ILAR criteria, the CASPAR criteria were developed for adults and are more comprehensive regarding clinical features.[11] It has been proposed that pediatric rheumatologists currently do not diagnose JPsA in all children whose disease manifestations meet the CASPAR criteria.[5] In our cohort, the prevalence of JPsA 18 years after disease onset was 6.5% according to ILAR criteria, compared with 9.4% when applying the CASPAR criteria. Strikingly, about one-third of our patients with CASPAR-PsA were categorized as having undifferentiated arthritis by the ILAR criteria, leaving these individuals in a group considered to be highly heterogeneous and often excluded from clinical trials and consequently less accessible to targeted therapies.[24] One of the reasons why the application of the CASPAR criteria led to the identification of additional individuals who would be classified as having PsA by adult rheumatologists is that, in contrast to the ILAR criteria, CASPAR criteria include enthesitis and axial arthritis for PsA, which occurred in 7% and 20% of our CASPAR-PsA group, respectively. On the other hand, the diagnosis of JPsA by the ILAR criteria requires the presence of psoriasis or, if the rash is absent, the addition of two criteria, including a positive family history of psoriasis in a first-degree relative or presence of nail involvement or dactylitis, whereas the CASPAR criteria allow the diagnosis of PsA based on a second-degree relative. Indeed, 5 of 41 patients met the CASPAR criteria on the basis of family history for psoriasis in a second-degree relative. Applying CASPAR criteria to the Childhood Arthritis and Rheumatology Research Alliance JIA cohort also identified more patients with PsA compared with the number with JPsA diagnosed by their treating physicians.[5] Of the additional individuals, fewer had psoriasis, but more presented with manifestations of spondyloarthritides.[5] This further supports previous assumptions that the current ILAR criteria for JPsA are too stringent and result in missed JPsA

Table 3. Baseline characteristics of participants fulfilling the CASPAR criteria for PsA 18 years after disease onset compared with the rest of the JIA cohort (excluding participants with sJIA)*

Baseline characteristics	Numbers assessed	Fulfilling the CASPAR criteria (n = 41)	Numbers assessed	Not fulfilling the CASPAR criteria (n = 378)	*P* value
Demographics					
Female, n (%)	41	28 (68.3)	378	259 (68.5)	0.98
Age at onset, median (IQR)	41	6.4 (1–14.9)	376	5.5 (0.8–15.8)	0.29
Joint involvement					
Oligoarthritis, n (%)	41	24 (58.5)	378	254 (67.2)	0.20
Polyarthritis, n (%)	41	17 (41.5)	378	112 (29.6)	0.33
Small joint involvement, n (%)	41	21 (51.2)	378	140 (37.0)	0.26
Number of active small joints, mean ± SD	41	1.6 ± 2.5	367	1.2 ± 3.1	0.24
Large joint involvement, n (%)	41	35 (85.4)	378	336 (88.9)	0.35
Number of active large joints, mean ± SD	41	1.1 ± 1.4	367	1.2 ± 1.7	0.92
Arthritis in upper extremities, n (%)	41	26 (63.4)	378	164 (43.4)	0.09
Arthritis in lower extremities, n (%)	41	37 (90.2)	378	332 (87.8)	0.54
Shoulder, n (%)	41	1 (2.4)	378	2 (0.5)	0.17
Elbow, n (%)	41	2 (4.9)	378	28 (7.4)	0.55
Wrist, n (%)	41	11 (26.8)	378	52 (13.8)	0.03
Metacarpophalangeal joints, n (%)	41	4 (9.8)	378	33 (8.7)	0.83
Proximal interphalangeal joints, n (%)	41	6 (14.6)	378	42 (11.1)	0.50
Distal interphalangeal joints, n (%)	41	1 (2.4)	378	7 (1.9)	0.79
Hip, n (%)	41	3 (7.3)	378	17 (4.5)	0.42
Knee, n (%)	41	6 (14.6)	378	101 (26.7)	0.09
Ankle, n (%)	41	11 (26.8)	378	76 (20.1)	0.31
Tarsal, n (%)	41	2 (4.9)	378	9 (2.4)	0.34
Subtalar, n (%)	41	3 (7.3)	378	5 (1.3)	0.008
Metatarsophalangeal joint, n (%)	41	2 (4.9)	378	15 (4.0)	0.78
Proximal interphalangeal joints toe, n (%)	41	3 (7.3)	378	18 (4.8)	0.48
Active joint count, median (IQR)	41	2 (0–14)	367	1 (0–31)	0.26
Cumulative joint count, median (IQR)	41	4 (1–30)	367	3 (0–45)	0.046
JADAS-27, median (IQR)	41	1 (0–10)	367	1 (0–25)	0.58
JADAS-71, median (IQR)	41	2 (0–14)	367	1 (0–31)	0.35
CHAQ, median (IQR)	29	0.5 (0–1.9)	218	0.3 (0–2.5)	0.71
Pain CHAQ, median (IQR)	28	0.3 (0–1.8)	208	0.3 (0–2.6)	0.68
Spondyloarthritis-related features					
Psoriasis, n (%)	41	9 (22)	378	3 (0.8)	<0.001
Age at onset psoriasis, mean ± SD	20	11.8 ± 6.0	9	11.6 ± 4.2	0.95
Nail pitting/onycolysis, n (%)	40	8 (20)	378	5 (1.3)	<0.001
Dactylitis, n (%)	40	7 (17.5)	378	5 (1.3)	<0.001
Enthesitis, n (%)	41	4 (9.8)	364	28 (7.7)	0.41
Uveitis acute, n (%)	41	4 (9.8)	378	1 (0.3)	0.37
Chronic anterior uveitis, n (%)	41	4 (9.8)	378	31 (8.2)	0.5
Inflammatory back pain at 1 year, n (%)	41	2 (4.9)	366	6 (1.6)	0.18
Sacroiliitis on image at 1 year, n (%)	25	0	238	1 (0.4)	0.92
Laboratory findings					
ANA positive, n (%)	38	15 (39.5)	333	125 (37.5)	0.82
RF positive, n (%)	41	1 (2.4)	378	8 (2.1)	0.52
HLA-B27 positive, n (%)	41	10 (24.4)	360	80 (22.2)	0.75
Heredity for psoriasis					
Psoriasis in first-degree relatives, n (%)	41	15 (36.6)	329	39 (11.9)	<0.001
Psoriasis in second-degree relatives, n (%)	41	21 (51.2)	329	52 (15.8)	<0.001
Psoriasis ONLY in first-degree relatives, n (%)	41	8 (19.5)	329	31 (9.4)	0.04
Psoriasis ONLY in second-degree relatives, n (%)	41	14 (34.1)	329	44 (13.4)	<0.001
Psoriasis in first- and second-degree relatives, n (%)	41	7 (17.1)	329	8 (2.4)	<0.001
Psoriasis in first- or second-degree relatives, n (%)	41	29 (70.7)	329	84 (25.5)	<0.001

*The Mann–Whitney test and Kruskal–Wallis test were used for comparison of continuous variables, and Fisher's exact test and chi-square test were used for comparison of categorical variables. The heredity for psoriasis is based on cumulative data. ANA, antinuclear antibodies; CASPAR, ClaASsification criteria for Psoriatic ARthritis; CHAQ, Childhood Health Assessment Questionnaire; HLA-B27, human leukocyte antigen B27; IQR, interquartile range; JADAS-27/71 score, Juvenile Arthritis Disease Activity Score- 27/71 joints; PsA, psoriatic arthritis; RF, rheumatoid factor; sJIA, systemic juvenile idiopathic arthritis.

diagnoses.[10,25] None of our patients who were categorized into extended oligoarthritis, polyarticular RF-positive arthritis, and sJIA met the CASPAR criteria for PsA. This is perhaps not surprising in the light of recent genotypic data on HLA associations across each JIA category that has revealed that oligoarticular JIA genetically differs from polyarticular

Table 4. Associations between baseline characteristics and heredity for psoriasis, and fulfillment of CASPAR criteria for PsA after 18 years*

Baseline characteristics and heredity for psoriasis	Odds for fulfilling the CASPAR criteria after 18 years		
	OR	95% CI	P-value
Wrist joint involvement	3.3	1.2–8.9	0.02
Subtalar joint involvement	12.9	1.8–91.3	0.01
Psoriasis	20.2	4.6–89.3	<0.001
Nail pitting/onycolysis	11.6	2.6–53.0	0.002
Dactylitis	43.4	9.1–206.2	<0.001
Psoriasis only in first-degree relatives	3.4	1.0–11.6	0.048
Psoriasis only in second-degree relatives	4.1	1.8–14.5	0.003
Psoriasis in first- and second-degree relatives	10.3	2.4–44.3	0.002

*Binary logistic regression analyses. Complete data were available in 365 patients. CASPAR, ClASsification criteria for Psoriatic ARthritis; PsA, psoriatic arthritis; OR, odds ratio; 95% CI, 95% confidence interval.

RF-positive arthritis and JPsA and that HLA associations for sJIA are distinct from those seen in the other categories.[26]

The absence of overlapping nomenclature between juvenile and adult arthritis categories has significant implications for clinical care and research. Recent genetic data have further highlighted the need to reevaluate the current distinction between juvenile and adult arthritis.[27] In a study by Oliveira-Ramos et al aimed to determine how adult patients with JIA fulfill classification criteria of adult rheumatic diseases, patients with JPsA maintained PsA classification as per CASPAR criteria.[14] In our cohort, not all patients with JPsA fulfilled the CASPAR criteria as adults because some did not have psoriasis, nail changes, or dactylitis at the time of assessment.

We studied clinical characteristics and heredity data that may differentiate PsA from other categories of JIA at disease onset. More patients with CASPAR-PsA had wrist and subtalar joint involvement and a higher cumulative joint count compared with those that did not meet the CASPAR criteria. These results are in line with previous studies that detected more involvement of the wrists and small joints of the hands and feet in patients with JPsA.[28,29] We found that significantly more individuals with CASPAR-PsA had psoriasis, nail involvement, and dactylitis at disease onset compared with the rest of the cohort; however, these features were present in only about 20% of the patients at onset. In contrast, around 70% of the children had heredity for psoriasis among first- or second-degree relatives. Although dactylitis is a well-recognized distinguishing feature from other categories of JIA, whether psoriasis serves as a reliable indicator for JPsA is unclear because psoriasis in children is less prevalent at onset compared with adults, and its manifestations are often atypical.[4,25] Butbul et al suggested that the presence of psoriasis may have little clinical relevance in the outcome and response to therapy of children with JIA and therefore may be considered as an extra-articular manifestation in JIA.[9] In contrast, we previously reported that children with psoriasis have higher risk of not being in remission 8 years after arthritis onset[12] and found that the presence of psoriasis at any point during the disease course of JIA was associated with active disease even 18 years after disease onset.

With regression analysis, wrist or subtalar joint involvement at disease onset, presence of psoriasis, nail changes, dactylitis, or family history of psoriasis in first- or second-degree relatives showed significant associations with development of PsA, with dactylitis and psoriasis as the strongest predictors. These observations are in agreement with previous studies; Shore et al found that presence of nail pits, a family history of psoriasis, and a cumulative asymmetric arthropathy are predictive of JPsA before psoriasis onset,[30] whereas in a study by Flatø et al, predictors of PsA within the first six months were psoriasis, heredity in a first-degree relative, dactylitis, and arthritis in ankles or toes.[31] To our knowledge, second-degree heredity for psoriasis in itself has not been reported yet as a predictor for PsA in JIA. This might be of importance because, in contrast to CASPAR criteria, second-degree heredity for psoriasis is not incorporated in the current classification of JIA, and children who have not yet developed psoriasis might not be recognized as having JPsA early in their disease course.

The new provisional Pediatric Rheumatology International Trials Organization classification criteria for JIA suggest that the number of joints involved and the presence of psoriasis may not represent reliable criteria for JIA classification.[32] We do not share this view because our data indicate that psoriasis at disease onset is not only predictive for development of adult PsA, but its presence during disease course associates with severe outcome. We believe that psoriasis is a reliable criterion and therefore should be included in any forthcoming JIA classification. We also showed that individuals who met the CASPAR criteria had worse self-reported functional health status after 18 years as reflected by inferior HAQ scores compared with other categories of JIA.

Dactylitis associates with more erosive forms of PsA, and it is currently considered both a marker of disease activity and severe prognosis in adults.[33,34] We showed that children with dactylitis at disease onset had an extremely high probability of exhibiting PsA as adults, which not only highlights the importance of early recognition of this feature, but also supports preserving JPsA as a distinct diagnostic entity in the ongoing debate about the classification of JIA.

The strength of our study is the population-based, nonselective, and longitudinal design. We used validated and multidimensional outcome measures. The novelty in applying CASPAR criteria on a large, clinically well-described cohort that was observed for up to 18 years is a major strength.

A limitation of our study is that we did not collect radiographic data at the 18-year visit. We potentially could have identified more

patients fulfilling the CASPAR criteria if we had radiographic information on new bone formation. Another limitation is the small sample size of individuals with JPsA, which may bias the prediction results.

In conclusion, we found that the CASPAR criteria identify more patients with PsA compared with the ILAR criteria because they are less stringent and may better capture the heterogeneous nature of the disease. The presence of psoriasis and dactylitis at disease onset were the strongest predictors for the development of PsA, whereas wrist or subtalar joint involvement, nail changes, and family history of psoriasis in first- or second-degree relatives were also associated with PsA. Our data suggest that having psoriasis or dactylitis during the disease course may predict negative disease outcome in young adults with JIA. Our study is a contribution to the ongoing debate about the classification and rationale of JPsA and highlights the importance of early recognition of features associated with PsA. Further studies on the utility of the CASPAR criteria in patients with JIA are needed to potentially recognize more patients with JPsA early in the disease course and ultimately to provide better care and more favorable long-term outcome for children with JPsA.

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AUTHOR CONTRIBUTIONS

All authors contributed to at least one of the following manuscript preparation roles: conceptualization AND/OR methodology, software, investigation, formal analysis, data curation, visualization, and validation AND drafting or reviewing/editing the final draft. As corresponding author, Dr Szentpetery confirms that all authors have provided the final approval of the version to be published and takes responsibility for the affirmations regarding article submission (eg, not under consideration by another journal), the integrity of the data presented, and the statements regarding compliance with institutional review board/Helsinki Declaration requirements.

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