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COMPARAISON DES CRITERES DE CLASSIFICATION PEDIATRIQUE ET ADULTE DANS LES ARTHRITES JUVENILES IDIOPATHIQUES A LA TRANSITION DES SOINS PEDIATRIQUES AUX SOINS ADULTES

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Service de Rhumatologie

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THESE

préparée sous la direction du Docteure Berengère Aubry-Rozier
avec la collaboration du Professeur Michaël Hofer

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

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Comparaison des critères de classification pédiatrique et adulte dans les arthrites juvéniles idiopathiques à la transition des soins pédiatriques aux soins adultes

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de la Faculté de Biologie et de Médecine

Monsieur le Professeur John Prior
Vice-Directeur de l'Ecole doctorale

Comparaison des critères de classification pédiatrique et adulte dans les arthrites juvéniles idiopathiques à la transition des soins pédiatriques aux soins adultes

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RESUME

Résultats. Cent-trente patients ont été inclus: 13,9% avec une AJI systémique, 22,3% avec une AJI polyarticulaire, 22,3% avec une AJI oligoarticulaire, 34,6% avec une AJI associée aux enthésites (ERA) et 6,9% avec une AJI psoriasique. Parmi eux, 13,1% ont souffert d'uvéite. Les atteintes structurales étaient représentées par 14,5% d'érosions et de carpite, principalement observées dans les AJI psoriasiques, polyarticulaires ou systémiques. Dans le groupe ERA, 37,5% des patients présentaient une sacro-iliite radiologique.

En comparant les AJI aux rhumatismes adultes, nous avons trouvé que: 66,6% des patients avec une AJI systémique remplissaient les critères de MSA, 87,5% et 9,5% des AJI polyarticulaires, respectivement avec et sans facteur rhumatoïde, remplissaient les critères de PR et 34,5% des AJI oligoarticulaires remplissaient les critères de spondyloarthrite. Enfin, 77,7% des patients avec une ERA remplissaient les critères de spondyloarthrite et 100% des patients avec une AJI psoriasique remplissaient les critères de rhumatisme psoriasique.

Conclusion. Les AJI oligoarticulaires et polyarticulaires sans facteur rhumatoïde semblent être des entités pédiatriques, tandis que les autres types d'AJI remplissent les critères de classification des rhumatismes adultes correspondants.

Objectifs. Déterminer les caractéristiques des patients avec une arthrite juvénile idiopathique (AJI) vus à la transition dans le but de comparer les critères de classification pédiatrique et adulte.

Méthodes. Les patients avec une AJI définie par la classification ILAR vus en consultation de transition entre 2010 et 2017 ont été inclus dans une étude rétrospective bi-centrique (Lyon, Lausanne). Les critères de classification des AJI ont été comparés aux critères ACR/EULAR de 2010 de la polyarthrite rhumatoïde (PR), aux critères de Yamaguchi pour la maladie de Still de l'adulte (MSA), aux critères ASAS de spondyloarthrite et CASPAR du rhumatisme psoriasique.

Mots clés: Arthrite juvénile idiopathique, transition, critères de classification.

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Original article

Comparison of paediatric and adult classification criteria in juvenile idiopathic arthritis during the transition from paediatric to adult care

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ABSTRACT

Objectives: To determine the characteristics of juvenile idiopathic arthritis (JIA) patients seen during the transition period in order to compare paediatric classification criteria with those for adults.
Methods: Patients with JIA according to the ILAR classification and who had a consultation at transition between 2010 and 2017 were included in a retrospective bi-centre (Lyon, Lausanne) study. JIA classification criteria were compared to ACR/EULAR 2010 criteria for rheumatoid arthritis (RA), Yamaguchi criteria for adult-onset Still's disease (AOSD), ASAS criteria for spondyloarthritis and CASPAR criteria for psoriatic arthritis.
Results: One hundred and thirty patients were included: 13.9% with systemic JIA, 22.3% with polyarticular JIA, 22.3% with oligoarticular JIA, 34.6% with enthesitis-related arthritis (ERA) and 6.9% with psoriatic arthritis; 13.1% had suffered from uveitis; 14.5% of patients had erosions or carpitis, mainly those with psoriatic arthritis, polyarticular or systemic JIA; 37.5% of patients with ERA displayed radiological sacroiliitis. When comparing paediatric JIA criteria with adult classifications, we found that: 66.6% of patients with systemic JIA fulfilled the criteria for AOSD, 87.5% of rheumatoid factor-positive polyarticular JIA and 9.5% of rheumatoid factor-negative polyarticular JIA met the criteria for RA, and 34.5% of oligoarticular JIA fulfilled the criteria for spondyloarthritis. Finally, 77.7% of patients with ERA met the criteria for spondyloarthritis, and 100% of patients with psoriatic arthritis JIA met the criteria for psoriatic arthritis.
Conclusion: Oligoarticular JIA and rheumatoid factor-negative polyarticular JIA seem to be paediatric entities, whereas the other types of JIA tended to meet the respective adult classification criteria.

1. Introduction

Juvenile idiopathic arthritis (JIA) refers to a heterogeneous group of inflammatory arthritides affecting one or more joints and occurring for at least 6 weeks in a child younger than 16 years old. The International League of Associations for Rheumatology 2001 (ILAR) classification includes 7 subgroups: systemic JIA, rheumatoid factor positive (RF+) polyarticular JIA, rheumatoid factor negative (RF−) polyarticular JIA, oligoarticular JIA, enthesitis-related arthritis (ERA), psoriatic arthritis and undifferentiated arthritis [1].

JIA is the most common form of chronic inflammatory arthritis in children, and it tends to persist into adulthood [2]. It is associated with significant morbidity due to disease flare-ups, articular damage and extra-articular manifestations, which may lead to substantial physical disability and impaired quality of life [3–5]. This reinforces the importance of a well-prepared transition to adult rheumatology in order to enhance these patients' future care and well-being [6].

Transition is defined as an active process by which a young patient with a chronic disease develops skills and resources to gradually cope better and take control of his or her condition [7,8]. This

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phase should be structured because of a risk of failure in monitoring, leading to unfavourable outcomes. Transition can be challenging for both patients and doctors. Indeed, general medical approach differs between paediatricians and adults' rheumatologists, and differences in classification criteria in paediatric and adult rheumatology can also cause significant difficulty [9]. It is of particular importance that the diagnosis and consequently the approach to the management of the condition do not change between paediatric and adult departments.

The present study aimed at analysing the characteristics of young adults who had been diagnosed with JIA in childhood and who underwent transition consultation, in order to compare paediatric classification criteria with those of adults.

2. Methods

2.1. Patients

A bi-centre study was performed at the Lyon (France) and Lausanne (Switzerland) University Hospitals. According to the ILAR classification, patients with JIA, who had a consultation at transition between January 2010 and December 2017, were retrospectively included in the study. At transition, there was a joint consultation with both a specialist in adult rheumatology and the paediatrician who was in charge of the patient during childhood.

JIA classification criteria were compared to the ACR/EULAR 2010 criteria for rheumatoid arthritis (RA), the Yamaguchi criteria for adult-onset Still's disease (AOSD), the ASAS criteria for spondyloarthritis (SpA) and the CASPAR criteria for adult psoriatic arthritis [10–14]. Furthermore, we divided patients who fulfilled the ASAS criteria into 2 groups: firstly, patients with SpA with radiological [radiography or Magnetic Resonance Imaging (MRI)] sacroiliitis, and secondly, those with non-radiological (Nr) SpA, which corresponds to patients without radiological sacroiliitis responding to the ASAS criteria without meeting the CASPAR criteria.

The presence of other chronic inflammatory rheumatological conditions, such as systemic lupus erythematosus or other connective tissue disease, was an exclusion criterion. Moreover, patients who did not attend a rheumatology outpatient consultation during the transition period, due to spontaneous remission or loss of follow-up before the transition, were not included in the study. The study was approved by the local medical Ethics Committee of the Lyon University Hospital and by the cantonal medical Ethics Committee of the Lausanne University Hospital.

2.2. Data collection

The following variables were retrospectively assessed by medical records review using a standardised data collection form: demographics, gender, age at transition, disease duration, family and personal history of inflammatory rheumatic diseases, clinical presentation, peripheral and/or axial disease and extra-articular manifestations [uveitis, psoriasis, and inflammatory bowel disease (IBD)]. Laboratory results were documented: HLA-B27, RF, anti-citrullinated protein antibodies (ACPA), anti-nuclear antibodies (ANA), as well as radiological findings: erosions, carpitis and radiological sacroiliitis.

2.3. Statistical analysis

Data are presented as numbers (percentages) for qualitative variables and as medians (minimum–maximum) or means (sd) for quantitative variables.

2.4. Role of the funding source

Not applicable.

3. Results

3.1. Patients' characteristics

A total of 130 patients, 92 in Lyon and 38 in Lausanne, were included in the study, whose main demographics and clinical features are shown in Table 1. Eighty-five were women and forty-five were men. The median age at the transition consultation was 19 years old. Only 33.1% of patients had a disease that lasted longer than 10 years. ERA, polyarticular and oligoarticular were the most prevalent subtypes of JIA, affecting 34.6%, 22.3% and 22.3% of our patients respectively.

3.2. Fulfilment of classification criteria for adult rheumatic diseases

To evaluate how JIA patients seen at transition fulfilled classification criteria for adult rheumatic diseases, we first assessed all the individual criteria used in these adults' classifications (Table 2). In terms of extra-articular manifestations, 13 patients had psoriasis, 3 had IBD and 17 patients had suffered from uveitis (8 with chronic asymptomatic anterior uveitis with a white eye and 9 with acute anterior uveitis causing a red painful eye). A family history of RA or connective tissue disease was seen in 5 patients (3 with ERA and 2 with polyarticular JIA), of SpA in 10 patients (7 with ERA), of psoriasis in 13 patients (5 with psoriatic arthritis), and one patient with ERA had a family history of IBD. Positive ANA was mainly found in patients with RF+ polyarticular JIA (5/7; 71.4%), with oligoarticular JIA (20; 69.0%), and with RF− polyarticular JIA (7; 33.3%). Twenty-seven out of 44 (61.4%) patients with ERA were HLA-B27 positive, and 7 (87.5%) of those with RF+ polyarticular JIA had positive ACPA. Seventeen patients (17/106; 16%) had radiological sacroiliitis at transition: 15 had ERA and 2 had oligoarticular JIA. In terms of peripheral structural damage, in our study, 44.4% of patients with psoriatic arthritis had erosions or carpitis, followed by those with RF+ polyarticular JIA (37.5%) and systemic JIA (26.7%) (Table 2).

When comparing paediatric classification criteria to those of adults, 12 (66.6%) patients with systemic JIA filled in the Yamaguchi criteria for AOSD. Seven (87.5%) patients with RF positive JIA met the ACR/EULAR criteria for RA. Ten (34.5%) patients with oligoarticular JIA filled in the ASAS criteria for SpA. Overall, 77.7% of ERA met the ASAS criteria for SpA (excluding cases of psoriatic arthritis). Fifteen (33.3%) ERA patients filled in the ASAS criteria for SpA with radiological sacroiliitis and 20 (44.4%) met the ASAS criteria for Nr-SpA. All patients with psoriatic arthritis in childhood kept that diagnosis as an adult, based on the CASPAR criteria. However, seventeen (80.9%) patients with RF− polyarticular JIA and seventeen (58.6%) with oligoarticular JIA did not fulfil any type of adult criteria (Table 2).

Interestingly, 10 diagnoses had been reviewed at transition or after. One patient with systemic JIA did not meet the Yamaguchi criteria for AOSD, but developed psoriasis after the musculoskeletal involvement, and consequently, met the CASPAR criteria for psoriatic arthritis. The diagnosis was unclear between systemic JIA and psoriatic arthritis until the patient had developed important synovitis of all the distal interphalangeal joints. Similarly, the diagnosis of two patients with oligoarticular JIA and one with ERA was reviewed to psoriatic arthritis. Two patients with oligoarticular JIA had their diagnosis reviewed to ERA as they finally were found to have sacroiliitis and fulfilled the ASAS criteria for

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Table 1
Patients' characteristics.

	Overall ($n = 130$)	Lyon ($n = 92$)	Lausanne ($n = 38$)
Sex ratio (M/F)	45/85 (34.6/65.4)	31/61 (33.7/66.3)	14/24 (36.8/63.2)
Age at transition (years)			
Median (min; max)	19 (17; 28)	19 (17; 28)	19 (17; 22)
Mean ± sd	19 ± 1.5	19 ± 1.6	19.1 ± 1.4
Disease duration (years)			
Median (min; max)	7 (1;24)	7 (1;24)	7 (3;17)
Mean ± sd	8.5 ± 5.1	8.7 ± 5.5	7.9 ± 3.9
JIA ILAR Classification			
Systemic JIA	18 (13.9)	13 (14.1)	5 (13.2)
Polyarticular JIA	29 (22.3)	21 (22.8)	8 (21)
RF+	8 (6.2)	7 (7.6)	1 (2.6)
RF-	21 (16.1)	14 (15.2)	7 (18.4)
Oligoarticular JIA	29 (22.3)	19 (20.7)	10 (26.3)
Persistent	9 (6.9)	4 (4.4)	5 (13.2)
Extended	20 (15.4)	15 (16.3)	5 (13.2)
ERA	45 (34.6)	30 (32.6)	15 (39.5)
Psoriatic arthritis	9 (6.9)	9 (9.8)	0

Values are *n* (%) unless otherwise specified. F: female; M: male; ERA: enthesitis-related arthritis; RF: rheumatoid factor; JIA: juvenile idiopathic arthritis.

Table 2
JIA classification according to adult rheumatic diseases.

	Systemic JIA ($n = 18$)	Polyarticular JIA RF+ ($n = 8$)	Polyarticular JIA RF− ($n = 21$)	Oligoarticular JIA ($n = 29$)	ERA ($n = 45$)	Psoriatic Arthritis ($n = 9$)	Total
Sex ratio (M/F)	6/12	1/7	6/15	4/25	24/21	4/5	45/85
Disease duration (years)	9.7	6.5	11.3	13.8	5.4	5.8	
Extra-articular manifestations							
White uveitis	0	0	1 (4.8)	7 (24.1)	0	0	8/130
Red uveitis	0	0	0	2 (6.9)	7 (15.6)	0	9/130
Psoriasis	1 (5.6)	0	0	1 (3.4)	2 (4.4)	9 (100)	13/130
IBD	0	0	0	2 (6.9)	1 (2.2)	0	3/130
Family history							
RA or connective tissue disease	0	2 (25.0)	0	0	3 (6.7)	0	5/130
Spondy-loarthritis	0	0	2 (9.5)	1 (3.4)	7 (15.6)	0	10/130
Psoriasis	1 (5.6)	0	2 (9.5)	1 (3.4)	4 (8.9)	5 (55.6)	13/130
IBD	0	0	0	0	1 (2.2)	0	1/130
Biology							
ANA+	3/15 (20.0)	5/7 (71.4)	7 (33.3)	20 (69.0)	7/27 (25.9)	1/5 (20.0)	43/104
RF+	0/15 (0.0)	8 (100.0)	0	0/26 (0.0)	0/26 (0.0)	1/4 (25.0)	9/100
ACPA+	0/12 (0.0)	7 (87.5)	1/14 (7.1)	0/17 (0.0)	0/12 (0.0)	0/4 (0.0)	8/67
HLA-B27 +	0/14 (0.0)	0	1/15 (6.7)	2/20 (10.0)	27/44 (61.4)	0	30/110
Structural damage							
Radiological sacroiliitis	0/17 (0.0)	0/4 (0.0)	0/19 (0.0)	2/17 (11.8)	15/40 (37.5)	0	17/106
Erosions, carpitis	4/15 (26.7)	3/8 (37.5)	4/20 (20.0)	1/23 (4.3)	1/42 (2.4)	4 (44.4)	17/117
Adult classifications							
AOSD	12 (66.6)	0	0	0	0	0	12
RA	1 (5.6)	7 (87.5)	2 (9.5)	0	0	0	10
SpA with sacroiliitis	0	0	0	2 (6.9)	15 (33.3)	0	17
Nr-SpA	0	0	1 (4.8)	8 (27.6)	20 (44.4)	0	29
Psoriatic arthritis	1 (5.6)	0	1 (4.8)	2 (6.9)	3 (6.7)	9 (100)	16
Unclassified	4 (22.2)	1 (12.5)	17 (80.9)	17 (58.6)	7 (15.6)	0	46

Values are *n* (%) unless otherwise specified. F: female, M: male, ACPA: anti-citrullinated protein antibodies, ANA: anti-nuclear antibodies, RF: rheumatoid factor, ERA: enthesitis-related arthritis, IBD: inflammatory bowel disease, JIA: juvenile idiopathic arthritis, RA: rheumatoid arthritis, SpA: spondyloarthritis.

axial SpA. One of them was HLA-B27 positive. Two patients with oligoarticular JIA had their diagnosis also reviewed to SpA as they developed IBD in the context of HLA-B27 positivity for one. Finally, the evolution of two patients with polyarticular JIA enabled to give a diagnosis of a mixed connective tissue disease with positive ANA.

4. Discussion

In our study, ERA was the most frequent subtype of JIA (34.6%), followed by polyarticular (22.3%) and oligoarticular JIA (22.3%). The prevalence of these inflammatory joint diseases is not very well known, due to a lack of data in this field. Previous studies found

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slightly different results with oligoarticular and polyarticular JIA being the most predominent subtypes of JIA, followed by ERA [15]. Our study was targeted at patients at the age of transition, i.e. a mean age of 19 years old, and consequently, these two populations probably differ due to the inclusion in our cohort of patients with ERA diagnosed during their teenage years, as attested by the shortest disease duration since diagnosis (5.4 years), and the exclusion of some patients with oligoarticular JIA, whose follow-up had been interrupted before the age of transition due to a prolonged remission.

In our study, 9/29 (31.0%) patients with oligoarticular JIA suffered from uveitis: 7 white uveitis and 2 red uveitis. Four out of 9 (44.4%) had persistent oligoarticular JIA and 5/20 (25.0%) had extended oligoarticular JIA. Only two of these patients, one with white uveitis and the other with one red uveitis, had positive ANA. It should be noted however that in this category of patients, ANA may well disappear during the course of the disease. In addition, for those with red uveitis, the diagnosis of oligoarticular JIA had not been changed towards ERA. When occurring in oligoarticular JIA, uveitis tends to be asymptomatic, chronic, and not associated with ocular redness or pain; whereas uveitis tends to present as a red painful eye in patients with ERA. This is of particular importance as "white uveitis" is a sight-threatening condition, which may go unnoticed. It is therefore crucial for patients with JIA, and more especially with oligoarticular JIA, to attend regular ophthalmological consultations. In previous studies, the prevalence of uveitis in patients with JIA was only 12%, occurring mostly in oligoarticular JIA, with a prevalence of 25% in oligoarticular extended JIA and 16% in persistent oligoarticular JIA, which is lower than our findings [16,17]. Predictive factors for the occurrence of uveitis in oligoarticular JIA seemed to be an early age of onset of the disease and a positive ANA [18,19]. In patients with ERA, 7/45 (15.6%) suffered from red uveitis, and all of them were HLA-B27 positive. No case of white uveitis was observed. Interestingly, Ramanathan et al. had also found a higher prevalence of uveitis in patients with ERA who were HLA-B27 positive; however, the overall prevalence of uveitis in ERA patients in their study was higher than in our cohort, affecting one in three patients [20].

We found that one patient (2.2%) with ERA developed Crohn's disease, and another one experienced recurrent diarrhoea, without any element being found in favour of IBD on endoscopy. Previous research showed that 6.5% of patients with ERA developed IBD, but as high as 60% of patients with ERA had infraclinical intestinal symptoms [19]. Moreover, Stoll et al. found that the rate of faecal calprotectin was higher in patients with ERA, regardless of the non-steroidal anti-inflammatory drugs intake, which potentially suggests a narrow link between ERA and IBD [21]. In addition, the emergence of IBD in two patients diagnosed with oligoarticular JIA enabled us to reclassify them into a diagnosis of SpA at transition, highlighting the importance of the transition period to reconsider diagnosis.

All patients with psoriatic arthritis had cutaneous manifestations, one of them displaying palmoplantar and ungueal psoriasis. In general, 48% of patients experience joint involvement prior to cutaneous manifestations, whereas 41% have cutaneous psoriasis prior to presenting joint involvement. Nails are affected in 75% of patients [22]. When skin involvement follows musculoskeletal complaints, diagnosis can be challenging and can often be delayed. Consequently, in our study, 4 diagnoses have been changed to psoriatic arthritis during adulthood; nevertheless, 3 of these patients were on anti-TNF. This raises the question of whether we faced a true psoriatic arthritis with joint involvement prior to cutaneous manifestations or a paradoxical psoriasis on anti-TNF. One third of patients who undergo a change of diagnosis in favour of psoriatic arthritis have this modification occur after 4.2 years of disease evolution on average [23].

Musculoskeletal symptoms, structural damage and response to treatments can be similar in patients with oligoarticular or polyarticular JIA and psoriatic arthritis, except for dactylitis, which is usually observed in psoriatic arthritis [23,24]. Many report that psoriatic arthritis tends to present in children in two different forms: one similar to oligo- and polyarticular JIA and one similar to SpA with sacroiliitis [25,26]. Sacroiliac involvement has been described in cases of psoriatic arthritis both in children and adults [27]; however, in our cohort, there was no sacroiliitis observed in these patients. Fifteen out of forty (37.5%) patients with ERA had sacroiliitis, and 27/44 (61.4%) were HLA-B27 positive. Data was missing for the remaining patients. In comparison, Pagnini et al. found that 30% of patients with ERA developed sacroiliitis on MRI within the first year of the disease [28]. Lin et al. found a higher prevalence, with 64% of patients with ERA having sacroiliitis on MRI, but only 40% of them were HLA-B27 positive. They also showed that hip involvement on MRI was a predictive factor of the occurrence of sacroiliitis [29].

After highlighting the characteristics of patients with JIA who were seen in a transition consultation, we focused on comparing paediatric and adult diagnostic classifications. Only 12 out of 18 patients (66.6%) with systemic JIA fulfilled the criteria for AOSD; however, data was missing from medical records. In a study conducted in 1990, Cabane et al. showed that systemic JIA and AOSD had the same presentation and clinical evolution, with joint involvement prevailing compared to systemic manifestations that tend to disappear with time. The revision project of the current JIA ILAR classification criteria by Martini et al. in the PRINTO consensus suggests "arthralgia" instead of "arthritis" in the diagnostic criteria for systemic JIA, and it keeps the duration of arthralgia the same as in the Yamaguchi criteria [30]. Therefore, we might find a higher percentage of patients diagnosed with systemic JIA based on these new criteria meeting the Yamaguchi criteria. These preliminary classification criteria, which consider systemic JIA equivalent to AOSD, still need to be formally validated with a dedicated project; therefore, our study still uses the accepted ILAR criteria. We found that 87.5% of patients with RF+ polyarticular JIA fulfilled the 2010 ACR/EULAR criteria for RA, against only 9.5% of patients with RF− polyarticular JIA. Other patients with RF− polyarticular JIA and 58.6% of patients with oligoarticular JIA did not meet any criteria for adult rheumatological disease, as in Oliveira-Ramos' study [31,32]. Therefore, these data support the previous hypothesis that oligoarticular JIA and RF-polyarticular JIA seem to be paediatric entities [9,26,30,33].

In patients with ERA, 77.7% fulfilled the ASAS criteria for either peripheral or axial SpA. Interestingly, ERA in the paediatric population tends to present differently to SpA in adults, as there is less axial involvement and more peripheral manifestations including enthesitis and hip arthritis in children [34]. Many juvenile forms of SpA have been classified as ERA according to ILAR. In comparison to adult classification criteria, the ILAR classification for ERA differs due to its exclusion criteria. Indeed, it does not take into account axial involvement, and it does not include a past medical history or a family history of psoriasis in a first-degree relative. Even though axial manifestations are less frequent than in adults, a significant number of patients with ERA fulfilled the criteria for axial SpA in our study. Taking this into consideration would facilitate communication and transition from paediatric to adult rheumatology [35].

All patients with psoriatic JIA fulfilled the ASAS criteria for peripheral SpA and the CASPAR criteria, and their diagnosis was therefore maintained in adult rheumatology, in accordance with the results from Oliveira-Ramos et al. [32].

Our study used JIA patients' characteristics to compare paediatric classification criteria to those of adults in the transition period. Indeed, enhanced understanding of the evolution of JIA subtypes in adulthood can lead to improved medical management of

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these patients in adulthood. Interestingly, the clinical evolution of patients with RF− polyarticular JIA remains unknown. Does this rheumatological disease evolve as adults' RF− RA or could it be a precursor to connective tissue diseases or other systemic diseases with joint involvement? Data is lacking on this matter and further research is needed.

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Disclosure of interest

The authors declare that they have no competing interest.

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