

Evaluation of ILAR Classification Criteria for Juvenile Idiopathic Arthritis in Spanish Children

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ABSTRACT. *Objective.* To evaluate the proposed International League of Associations for Rheumatology (ILAR) classification criteria for juvenile idiopathic arthritis in a cohort of Spanish children.

Methods. One hundred twenty-five patients with chronic arthritis were categorized according to one of the traditional classifications and the proposed ILAR classification system after at least 6 months of disease. The traditional classifications included the European League Against Rheumatism (EULAR) criteria for pauciarticular, polyarticular rheumatoid factor (RF) negative, and systemic juvenile chronic arthritis (JCA), as well as for RF+ polyarthritis; the Vancouver criteria for juvenile psoriatic arthritis (JPsA); and the European Spondylarthropathy Study Group (ESSG) preliminary criteria for juvenile spondyloarthropathy (JSpA).

Results. The ILAR criteria classified 106/125 patients (84.8%). All patients with systemic and polyarticular JCA, RF+ polyarthritis, and definite juvenile psoriatic arthritis were reclassified in the corresponding ILAR category. In contrast, only 80% of pauciarticular JCA and 47% of JSpA patients could be allocated to the ILAR oligoarthritis (47/59 patients, 35 persistent and 12 extended) and enthesitis related arthritis (ErA, 8/17 patients) categories. Two children with probable PsA were reclassified in the RF- polyarthritis category. Nineteen patients (15.2%) were allocated to the ILAR "other arthritis" group, 13/19 because they did not fulfill criteria for any of the other categories (12 due to family history of psoriasis and one because of family history of HLA-B27 associated disease). The remaining 6 patients met criteria for 2 categories, RF- polyarthritis and either ErA (n = 5) or PsA (n = 1). No differences other than family history of psoriasis were found in any of the variables studied between pauciarticular JCA patients classified in the oligoarthritis (n = 47) and those in the "other arthritis" (n = 11) ILAR categories.

Conclusion. The proposed ILAR criteria allocated 84.8% of the patients classified by traditional criteria. Family history of psoriasis (n = 12) and polyarticular onset of disease in patients with ErA (n = 5) were responsible for most of the exclusions from other ILAR categories. (J Rheumatol 2002;29:2731-6)

Key Indexing Terms:

CHILDHOOD ARTHRITIS
CLASSIFICATION CRITERIA
JUVENILE SPONDYLOARTHROPATHY

JUVENILE IDIOPATHIC ARTHRITIS
JUVENILE CHRONIC ARTHRITIS
JUVENILE PSORIATIC ARTHRITIS

Chronic arthritis of childhood is a heterogeneous group of diseases classified according to certain clinical characteristics. The different classification criteria used around the world overlap and make comparability of genetic, serologic, epidemiologic, and therapeutic data difficult and less reliable.

The Classification Task Force of the Pediatric Standing Committee of the International League of Associations for Rheumatology (ILAR) proposed new classification criteria in Santiago, Chile, in 1994¹. The aim of the committee was to propose "a unified, internationally acceptable and applicable

set of classification criteria...to facilitate more meaningful research and better patient care"¹. In 1997 the criteria were reviewed in Durban, South Africa, and the term juvenile idiopathic arthritis (JIA) was adopted as an umbrella term². JIA indicates arthritis with onset before the 16th birthday, persisting for at least 6 weeks, and of unknown cause. Members of the ILAR classification committee have asked for international collaboration to evaluate the criteria in different patient populations³.

We evaluated the applicability of the ILAR criteria in a Spanish outpatient pediatric rheumatology clinic.

MATERIALS AND METHODS

The study included 125 consecutive patients followed at the pediatric rheumatology clinic of a tertiary center, University Hospital La Paz, who had arthritis for at least 6 months. The patients, identified retrospectively, were evaluated between January 1999 and March 2000. All patients had been classified according to one of the following traditional classification criteria: European League Against Rheumatism (EULAR) criteria⁴ for systemic, polyarticular, and pauciarticular juvenile chronic arthritis (JCA), as well as for rheumatoid factor (RF) positive polyarthritis; European Spondylarthropathy Study Group (ESSG) preliminary criteria for juvenile spondyloarthropathy

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Submitted November 30, 2000; revision accepted July 10, 2001.

(JSpA)⁵; and Vancouver criteria for juvenile psoriatic arthritis (JPsA)⁶. After at least 6 months of disease patients were reclassified according to the proposed ILAR criteria. Family history of psoriasis was confirmed by a dermatologist in all cases. Family history of HLA-B27 associated disease included SpA and inflammatory bowel disease, diagnosed by a rheumatologist and a gastroenterologist, respectively.

Comparisons between groups were calculated using the 2 tailed Mann-Whitney U test or Fisher exact test when appropriate. The chi-square test was used to compare categorical data. Statistical significance was set at 0.05 for all tests. All calculations were performed using the statistical package SPSS 8.0 for Windows (SPSS Inc.)

RESULTS

The characteristics of the patients are shown in Table 1. The proposed ILAR criteria classified 106 out of 125 (84.8%) patients. The remaining 19 (15.2%) patients were put into the "other arthritis" JIA category, indicating that they could either be allocated to more than one category (n = 6) or were not classifiable (n = 13). Patient categorization according to traditional classification criteria and the ILAR criteria is shown in Table 2.

All patients with systemic JCA (n = 18), polyarticular (RF-) JCA (n = 25), RF+ polyarthritis (n = 2), and definite PsA (n = 2) were classified in the corresponding ILAR categories.

However, of the 59 patients with pauciarticular JCA only 47 (80%) could be allocated to the oligoarthritis JIA category (35 persistent, 12 extended). A boy positive for HLA-B27 with onset of oligoarthritis at age 12 years categorized as pauciarticular JCA because he did not meet ESSG criteria for JSpA (he had "arthritis" without "spinal pain" or any other ESSG criteria) fulfilled criteria for the ILAR enthesitis related arthritis (ErA) category ("arthritis" plus "presence of HLA-B27" and "onset of arthritis in a boy after the age of 8 years"). Regarding the remaining 11 pauciarticular JCA patients, 10 were excluded from the oligoarthritis category because of family history of psoriasis (7 in second-degree relatives including a 9-year-old girl with a positive RF test) and one because of a family history of HLA-B27 associated disease in a second-degree relative. No patient excluded because of family history of psoriasis met the ILAR criteria for PsA.

Similarly, of the 17 children who fulfilled the ESSG criteria for JSpA only 8 (47%) were reclassified in the ErA category. A 10-year-old girl with polyarthritis and enthesitis had a family history of psoriasis in a second-degree relative, which excluded her from the ErA class; on the other hand, she could be classified in the polyarthritis (RF-) JIA group. The remaining 8 JSpA patients were allocated in the "other arthritis"

Table 1. Patient characteristics.

| | Female:Male | Median Age, yrs (range) | Median Disease Duration, yrs (range) | ANA Positive, n (%) | RF Positive, n (%) | HLA-B27 Positive, n (%) |
|----------------------------|-------------|-------------------------|--------------------------------------|---------------------|--------------------|-------------------------|
| ILAR categories | | | | | | |
| Oligoarthritis, n = 47 | 40:7 | 7.4 (1.4–19.2) | 3.9 (0.5–17.4) | 38 (81) | — | 5 (11) |
| Polyarthritis RF-, n = 28 | 22:6 | 9.2 (2.7–19.6) | 4.7 (0.7–8.9) | 16 (57) | — | 2 (7) |
| Polyarthritis RF+, n = 2 | 2:0 | 18.0 (17.9–18.2) | 6.7 (6.4–6.9) | 2 (100) | 2 (200) | — |
| Systemic, n = 18 | 9:9 | 11.8 (3.7–22.8) | 7.3 (3–20) | 1 (6) | — | — |
| ErA, n = 9 | 1:8 | 16.6 (6.6–21.4) | 4.6 (1.2–8.3) | — | — | 8 (89) |
| Psoriatic arthritis, n = 2 | 1:1 | 15.5 (14–16.9) | 7.6 (5.9–9.3) | 2 (100) | — | 1 (50) |
| Other arthritis, n = 19 | 10:9 | 10.6 (5.3–18.9) | 4.6 (0.7–8.7) | 8 (42) | 1 (5) | 7 (37) |

ANA: antinuclear antibodies; RF: rheumatoid factor; ErA: enthesitis related arthritis.

Table 2. Classification of patients according to the proposed ILAR and traditional classification systems.

| | Proposed ILAR Classification Criteria | | | | | | |
|----------------------|---------------------------------------|------------------|-----------------|------------------|------------|------------|----------------------------------|
| | Oligo, n = 47 | Poly RF-, n = 28 | Poly RF+, n = 2 | Systemic, n = 18 | ErA, n = 9 | PsA, n = 2 | Other Arthritis* n = 13 n = 6 |
| Traditional criteria | | | | | | | |
| Pauci JCA, n = 59 | 47** | — | — | — | 1 | — | 11 |
| Poly JCA RF-, n = 25 | — | 25 | — | — | — | — | — |
| Poly RF+, n = 2 | — | — | 2 | — | — | — | — |
| Systemic JCA, n = 18 | — | — | — | 18 | — | — | — |
| JSpA, n = 17 | — | 1 | — | — | 8 | — | 2 |
| JPsA, n = 2 | — | — | — | — | — | 2 | — |
| Probable JPsA, n = 2 | — | 2 | — | — | — | — | — |

*19 Other arthritis: 13 did not fit any other category and 6 could be classified in more than one category. **47 Oligoarthritis: 35 persistent oligoarthritis and 12 extended oligoarthritis. JCA: Juvenile chronic arthritis; RF: rheumatoid factor; JSpA: juvenile spondyloarthropathy; JPsA: juvenile psoriatic arthritis; ErA: enthesitis related arthritis; PsA: psoriatic arthritis.

group. A boy positive for HLA-B27 with onset of polyarthriti-
tis, inflammatory spinal pain, and enthesitis at age 13 years
was excluded from the ErA category because of family history
of psoriasis. This patient, however, met the ILAR definition
criteria for both PsA (dactylitis and family history of psoriasis
in a first-degree relative) and polyarthritis (RF-) JIA cate-
gories. Another 5 patients with JSpA were allocated in the
"other arthritis" group because they satisfied the JIA defini-
tion criteria for both ErA and polyarthritis (RF-). It is remark-
able that those 5 patients were HLA-B27 positive, and all but
one, a boy with onset of arthritis after the age of 8 years, had
enthesitis; the 5 of them, however, had had polyarthritis at dis-
ease onset. The other 2 patients classified as JSpA were also
reclassified in the JIA-other arthritis category because of fam-
ily history of psoriasis, in second-degree relatives in both
cases.

There were 4 patients categorized as JPsA according to the
Vancouver criteria. The 2 children with definite disease by the
Vancouver criteria had arthritis and psoriasis, and they were
classified in the PsA ILAR category. The 2 patients with prob-
able disease by the Vancouver criteria were classified in the
polyarthritis (RF-) JIA group. They were a boy and a girl with
polyarthritis, dactylitis, and family history of psoriasis in sec-
ond-degree relatives. They did not fulfill ILAR criteria for
PsA because this category requires confirmation of psoriasis
in a first-degree relative. On the other hand, a family history
of psoriasis or HLA-B27 associated disease does not preclude
allocation of patients to the polyarthritis (RF-) category.

Therefore, 19 patients (15.2%) were classified in the "other
arthritis" JIA category. Twelve children (63%) were excluded
from other ILAR categories because of family history of pso-
riasis, in second-degree relatives in 9/12 (including a girl with
oligoarthritis and a positive RF test). Another patient was
excluded from the oligoarthritis category because of a family
history of HLA-B27 associated disease in a second-degree
relative. The remaining 6 patients fulfilled criteria for 2 cate-

gories (ErA and RF- polyarthritis in 5, PsA and RF- poly-
arthritis in one).

Considering the influence that family antecedents of pso-
riasis and HLA-B27 associated disease had on the ILAR classi-
fication system, we analyzed the distribution of the subjects
according to the proposed ILAR categories (Table 3). A fam-
ily history of psoriasis was recorded in 24 patients (19%)
across the JIA categories where it was allowed. Family histo-
ry of HLA-B27 associated disease was present in 9 children
(7%), including ankylosing spondylitis in 5, undifferentiated
SpA in one, and inflammatory bowel disease in 3.

Finally, we examined whether patients with pauciarticular
JCA reclassified in the ILAR oligoarthritis category (n = 47)
differed from those allocated to the "other arthritis" class (n =
11). We performed a statistical analysis on several demograph-
ic, clinical, and serological variables (Table 4). No significant
differences were found in any of the variables studied, with the
exception of family history of psoriasis. Children allocated to
the oligoarthritis category seemed to have an earlier onset of
disease, although this variable did not reach statistical signifi-
cance (p = 0.055). A similar analysis was not performed in
other JIA categories due to the size of our sample.

DISCUSSION

The number of patients uniquely classified by the ILAR crite-
ria in our Spanish population is very similar to that reported in
other series from Germany (87.6% of 97 patients)⁷ and
Canada (88.4% of 70 patients)⁸, despite the different tradi-
tional classification criteria used [EULAR in this study,
American College of Rheumatology (ACR) in the other 2]. To
our knowledge, this is the first report that reclassified patients
categorized by the EULAR criteria according to the ILAR
system. It should be kept in mind, however, that this study was
performed on a well defined population with longstanding
arthritis and not on newly diagnosed patients.

The proposed ILAR classification system allocated 106 of

Table 3. Family history of psoriasis and /or HLA-B27 associated disease in first or second-degree relatives in 125 patients with juvenile idiopathic arthritis.

| ILAR Categories | Family History of Psoriasis | | Family History of HLA-B27 Associated Disease | |
|-------------------------------------|-----------------------------|--------------------|--|-------------------|
| | 1st Degree, n = 8 | 2nd Degree, n = 16 | 1st Degree, n = 2 | 2nd Degree, n = 7 |
| Oligoarthritis, n = 47 | — | — | — | — |
| Polyarthritis RF-, n = 28 | 3 | 6 | — | — |
| Polyarthritis RF+, n = 2 | — | — | — | — |
| Systemic arthritis, n = 18 | 1 | — | — | — |
| Enthesitis related arthritis, n = 9 | — | — | 1 | 3 |
| Psoriatic arthritis, n = 2 | — | 1 | 1 | — |
| Other arthritis, n = 19 | | | | |
| Did not fit any category, n = 13 | 3 | 9 | — | 1 |
| Fit more than one category, n = 6 | 1* | — | — | 3* |

* A patient had family history of psoriasis in 1st degree and HLA-B27 associated disease in 2nd degree relatives.

Table 4. Comparison of pauciarticular JCA patients reclassified by the ILAR criteria in the oligoarthritis or the other arthritis diagnostic categories.

| | Oligoarthritis, n = 47 | Other Arthritis, n = 11 | p |
|--|---------------------------|----------------------------|-------|
| Age at onset, yrs, median (range) | 2.6 (0.8–13.8) | 4.9 (1.6–9.5) | 0.055 |
| Disease duration, yrs, median (range) | 3.9 (0.5–17.4) | 5 (0.9–8.6) | NS |
| Female, n (%) | 40 (85) | 8 (73) | NS |
| Pattern of arthritis (onset/course), % | | | |
| Involvement of small joints of the hands | 13/17 | 9/46 | NS/NS |
| Lower limb predominance | 75/68 | 64/55 | NS/NS |
| No upper or lower predominance | 21/30 | 36/27 | NS/NS |
| Symmetry of arthritis | 13/21 | 27/27 | NS/NS |
| Monoarthritis | 53/34 | 36/9 | NS/NS |
| Oligoarticular course | 74 | 55 | NS |
| Dactylitis, % | 4 | 18 | NS |
| Uveitis, % | 26 | 9 | NS |
| ANA+, % | 81 | 73 | NS |
| HLA-B27+ , % | 11 | — | NS |
| RF+ % | — | 9 | NS |

ANA: antinuclear antibody; RF: rheumatoid factor.

our 125 patients (84.8%) into distinct diagnostic categories, but 15.2% failed to be classified and fell into the ILAR category of “other arthritis.” Almost two-thirds of those children were allocated to this category only because of family history of psoriasis.

One of the main purposes of the ILAR classification system is to create more homogeneous diagnostic categories than current classification systems by using a more restrictive set of criteria, particularly in certain categories. In this regard, the criterion “family history of psoriasis in second-degree relatives” is responsible for a relevant number of allocations to the other arthritis group^{7,8}. It represents an exclusion criterion for the oligoarthritis and ErA categories, but it does not allow reclassification in the PsA group. Considering the high frequency of psoriasis in the general population, it is not clear at this time whether this criterion will increase homogeneity within the categories or just interfere with the allocation of the patients. Indeed, our analysis of several variables in children with pauciarticular JCA reclassified in the oligoarthritis or in the other arthritis JIA categories revealed no differences other than family history of the disease. If the criterion “family history of psoriasis” was restricted to first-degree relatives, an additional 6 children would have been reclassified in the oligoarthritis and 2 in the ErA category. Therefore, 91% of the patients would have been classifiable by the ILAR system.

The current restrictiveness of the proposed ILAR criteria may have some unexpected effects, illustrated in the next 3 examples. First, a patient with polyarthritis, a family history of psoriasis in a second-degree relative, and either dactylitis or nail abnormalities suggestive of psoriasis cannot be classified in the PsA but rather in the polyarthritis (RF–) JIA category. This scenario is due to current ILAR definition of PsA that requires, in the absence of psoriasis, 2 of the following:

dactylitis, nail abnormalities, and family history of disease in a first-degree relative. In contrast, a family history of psoriasis or HLA-B27 associated disease does not interfere with the allocation of patients to the polyarthritis (RF–) category, defined by the presence of polyarthritis during the first 6 months of disease in the absence of RF or systemic symptoms.

The second example relates to a more frequent clinical situation. An HLA-B27 positive patient with polyarthritis, enthesitis, and inflammatory spinal pain fulfills criteria for both polyarthritis (RF–) and ErA categories. Accordingly, this patient will be placed in the “other arthritis” JIA category. This situation is possible because the ILAR system does not consider the definition criterion of ErA as exclusion criterion for the polyarthritis (RF–) category. This has been observed in other series^{7,9}.

Finally, the presence of psoriasis in a patient with polyarthritis or oligoarthritis results — if the patient with oligoarthritis does not have family history of the disease — in classification in the “other arthritis” JIA category because the patient fulfills definition criteria for 2 categories (PsA and polyarthritis or oligoarthritis, respectively)⁷.

The main strength of ILAR criteria is their potential to unify terms and concepts regarding idiopathic arthritides of childhood, avoiding the multiple, overlapping classification systems currently used. Those criteria, however, are undergoing evaluation to test their performance and their ability to classify more homogeneous groups of children with idiopathic arthritis.

The ILAR proposal includes definition criteria, i.e., the sets proposed by the ACR or EULAR, as well as exclusion criteria. The exclusion criteria would make the ILAR classification system more stringent than the others, at least a priori, resulting in a higher degree of homogeneity of children allo-

cated to a particular category. As discussed above, however, current criteria have not demonstrated that homogeneity has been achieved. Further interference with the homogeneity of the categories in our series includes the following considerations. First, the criterion “family history of psoriasis” is distributed across almost all ILAR categories, although it only excludes patients from the oligoarthritis and ErA groups. Second, RF– polyarthritis inclusion and exclusion criteria result in the classification of patients with SpA within the class. Third, patients with positive RF may end up classified in different categories depending on the number of joints involved at disease onset, despite future evolution.

The ILAR proposal represents a much needed effort to develop internationally accepted criteria that would facilitate communication among patients, physicians, and scientists and enable the identification of homogeneous groups of children with chronic arthritis. In light of this and other studies that have analyzed ILAR system performance, those criteria require further evaluation and revision.

ADDENDUM

During the review process of this manuscript other series and editorials addressing the performance of the ILAR classification criteria have been published^{10,11}.

ACKNOWLEDGMENT

The authors thank Dr. Daniel Lovell for his review of the manuscript.

APPENDIX. Classification systems used.

EULAR JUVENILE CHRONIC ARTHRITIS CRITERIA

1. Age of onset < 16 years
2. Arthritis in one or more joints
3. Duration of disease 3 months or longer
4. Type defined by characteristics at onset:
 - (A) Systemic: Arthritis with characteristic fever
 - (B) Pauciarticular: Arthritis in less than 5 joints
 - (C) Polyarticular: Arthritis in more than 4 joints, rheumatoid factor (RF) negative
 - (D) Juvenile rheumatoid arthritis: Arthritis in more than 4 joints, RF positive
 - (E) Juvenile ankylosing spondylitis
 - (F) Juvenile psoriatic arthritis

EUROPEAN SPONDYLARTHROPATHY STUDY GROUP CRITERIA

Inflammatory spinal pain, or synovitis (asymmetric or predominantly in lower limb) plus one of:

Positive family history

Psoriasis

Inflammatory bowel disease

Urethritis, cervicitis, or acute diarrhea within one month before onset of arthritis

Buttock pain alternating between the right and left gluteal regions

Enthesopathy

Sacroiliitis

VANCOUVER CRITERIA FOR JUVENILE PSORIATIC ARTHRITIS

1. Definite
 - (A) Arthritis and typical psoriatic rash or
 - (B) Arthritis with 3 of 4 minor criteria:
 - Dactylitis
 - Nail pitting or onycholysis

- Psoriasis-like rash
 - Family history of psoriasis in a first or second-degree relative
2. Probable: Arthritis with 2 of 4 minor criteria

ILAR SYSTEMIC ARTHRITIS CATEGORY

Arthritis with or preceded by daily fever of at least 2 weeks' duration, documented to be quotidian for at least 3 days, and accompanied by one or more of the following:

- (A) Evanescent, non-fixed, erythematous rash
- (B) Generalized lymph node enlargement
- (C) Hepatomegaly or splenomegaly
- (D) Serositis

ILAR OLIGOARTHRITIS CATEGORY

Arthritis affecting 1–4 joints during the first 6 months of disease

- (A) Persistent oligoarthritis: affects no more than 4 joints throughout the disease course
- (B) Extended oligoarthritis: affects a cumulative total of 5 joints or more after the first 6 months of disease

Exclusions:

1. Family history of psoriasis confirmed by a dermatologist in at least one first or second-degree relative
2. Family history of HLA-B27 associated disease in at least one first or second degree relative
3. Positive RF test
4. HLA-B27 positive male with onset of arthritis after 8 years of age
5. Presence of systemic arthritis as defined above

ILAR POLYARTHRITIS RF NEGATIVE CATEGORY

Arthritis affecting 5 or more joints during the first 6 months of disease.

Exclusions:

1. Presence of RF
2. Presence of systemic arthritis as defined above

ILAR POLYARTHRITIS RF POSITIVE CATEGORY

Arthritis affecting 5 or more joints during the first 6 months of disease, associated with positive RF tests on 2 occasions at least 3 months apart.

Exclusions:

1. Absence of positive tests for RF on 2 occasions at least 3 months apart
2. Presence of systemic arthritis as defined above

ILAR PSORIATIC ARTHRITIS CATEGORY

1. Arthritis and psoriasis, or
2. Arthritis and at least 2 of:
 - (A) Dactylitis
 - (B) Nail abnormalities (pitting or onycholysis)
 - (C) Family history of psoriasis confirmed by a dermatologist in at least one first-degree relative

Exclusions:

1. Presence of RF
2. Presence of systemic arthritis as defined above

ILAR ENTHESTITIS RELATED ARTHRITIS CATEGORY

1. Arthritis *and* enthesitis, or
2. Arthritis *or* enthesitis with at least 2 of:
 - Sacroiliac joint tenderness and/or inflammatory spinal pain
 - Presence of HLA-B27

Family history in at least one first or second-degree relative of medically confirmed HLA-B27 associated disease

Anterior uveitis that is usually associated with pain, redness, or photophobia
Onset of arthritis in a boy after the age of 8 years

Exclusions:

1. Psoriasis confirmed by a dermatologist in at least one first or second-degree relative
2. Presence of systemic arthritis as defined above

ILAR OTHER ARTHRITIS CATEGORY

Children with arthritis of unknown cause that persists for at least 6 weeks but that either:

1. Does not fulfill criteria for any of the other categories, or
2. Fulfills criteria for more than one of the other categories

Exclusions:

Patients who meet criteria for other categories

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