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ORIGINAL ARTICLE

Using the Juvenile Arthritis Disease Activity Score Based on Erythrocyte Sedimentation Rate or C-Reactive Protein Level: Results From the Portuguese Register

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Objective. **Our aims were to evaluate the correlation between Juvenile Arthritis Disease Activity Score 27-joint reduced count (JADAS27) with erythrocyte sedimentation rate (ESR) and JADAS27 with C-reactive protein (CRP) scores and to test the agreement of both scores on classifying each disease activity state. We also aimed at verifying the correlation of the 2 scores across juvenile idiopathic arthritis (JIA) categories and to check the correlation between JADAS27-ESR and clinical JADAS27 (JADAS27 without ESR).**

Methods. **A nationwide cohort of patients with JIA registered in the Portuguese Register, Reuma.pt, was studied. JADAS27-CRP was adapted by replacing ESR with CRP level as the inflammatory marker. JADAS27-CRP was calculated similarly to JADAS27-ESR as the simple linear sum of its 4 components. Pearson's correlations and K statistics were used in the analyses.**

Results. **A total of 358 children had full data to calculate JADAS27; 65.4% were female and the mean ± SD disease duration was 11.8 ± 9.1 years. The correlation coefficient between JADAS27-ESR and JADAS27-CRP was 0.967 ($P < 0.0001$), although the correlation coefficient between ESR and CRP level was 0.335 ($P < 0.0001$). The strong correlation between JADAS27-ESR and JADAS27-CRP was maintained when compared within each JIA category. The agreement between JADAS27-ESR and JADAS27-CRP across the 4 activity states was very good, showing 91.1% of the observations in agreement; K = 0.867 (95% confidence interval 0.824–0.91). The correlation between JADAS27 with ESR and JADAS27 without ESR was high (r = 0.97, $P < 0.0001$).**

Conclusion. **JADAS27 based on CRP level correlated closely with JADAS27-ESR across all disease activity states and JIA categories, indicating that both measures can be used in clinical practice. Moreover, the correlation of JADAS27 with and without ESR was also high, suggesting that this tool might be useful even in the absence of laboratorial measures.**

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common arthritis of childhood. It is a heterogeneous disease group of unknown etiology with distinct presentation, clinical features, immunopathogenesis, and genetic background (1). In fact, some of the categories of JIA may represent different diseases. Evaluation of disease activity is a crucial

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Significance & Innovations

- Juvenile Arthritis Disease Activity Score (JADAS) is a valid instrument for assessment of disease activity in juvenile idiopathic arthritis.
- JADAS based on erythrocyte sedimentation rate (ESR) correlated closely with JADAS based on C-reactive protein level.
- The correlation of JADAS with and without ESR is also high, suggesting that this tool might be useful even in the absence of laboratory measures.

component of the clinical assessment of children with JIA because persistently active disease plays a major role in causing joint damage and physical disability (2).

Recently, a composite score named Juvenile Arthritis Disease Activity Score (JADAS) was found to be a valid instrument for assessment of disease activity (2). JADAS consists of 4 components: physician global assessment of disease activity, parent/patient global assessment of well-being, number of joints with active disease, and an inflammatory marker (2). The clinical measures included in JADAS are part of the American College of Rheumatology (ACR) pediatric core set of outcome variables (3). A major advantage of JADAS when compared to ACR pediatric measures of improvement criteria is the ability to assess disease activity at a single visit and also to compare disease activity between individuals or groups. There are no perfect instruments and the major caveat of JADAS is that systemic features are not contemplated, limiting its use in systemic JIA. According to the authors who validated JADAS (2), the statistical performance of the JADAS 27-joint reduced count (JADAS27) was comparable with that provided by the JADAS71. However, assessment of 27 joints is more feasible and less tedious than evaluation of 71 joints. The simplest, 10-joint reduced count revealed the best discriminating validity, responsiveness (although not in nonresponder patients), and distribution, but had a somewhat poorer construct validity. The greater responsiveness of this joint count may be explained by most JIA patients having few joints involved. Use of this reduced count, which does not enable a precise assessment of joint disease and may limit the ability to detect new joint involvement over time, is advised only for use in retrospective studies, when the total number of involved joints is known, but no information on the individual affected joint is available (2).

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JADAS was developed using the erythrocyte sedimentation rate (ESR) because C-reactive protein (CRP) values were not available in all databases used to validate the tool (2). However, as the authors of the JADAS highlighted, CRP level is a direct measure of the acute-phase response and is less confounded by other factors when compared to ESR. In rheumatoid arthritis (RA) the performance of the Disease Activity Index of 28 joints (DAS28) based on CRP level has been shown to have a similar profile to DAS28 based on ESR (4,5). Similarly, Nordal et al recently compared in a Nordic population the JADAS based on CRP level with the JADAS based on ESR and concluded that these instruments correlated closely, indicating that both scores can be recommended for assessing disease activity in JIA (6). Recently, cutoff values for classifying distinct disease activity states were proposed for the JADAS-ESR (7).

The aim of our work was to evaluate the correlation between the JADAS27-ESR and the JADAS27-CRP and to test the agreement of both scores for classifying each disease activity state. We also aimed at verifying the correlation of the 2 scores across all JIA categories and to check the correlation between the JADAS27-ESR and the JADAS27 without ESR.

PATIENTS AND METHODS

Population and ethical considerations. A nationwide cohort of patients with JIA according to International League of Associations for Rheumatology (ILAR) criteria, registered in the Rheumatic Diseases Portuguese Register, Reuma.pt (8), was studied. Patients with a diagnosis of JIA were consecutively included in the study during the visit in which they completed all study protocol and all disease activity measures were available for JADAS27-ESR and JADAS27-CRP calculation. Clinical information, inflammation markers, and physician and parent/patient visual analog scales (VAS) on global health were collected according to the study protocol and inserted by physicians. Questionnaires on self-reported physical disability were also assessed, i.e., the Childhood Health Assessment Questionnaire (C-HAQ; where 0 = best and 3 = worst) for children age <18 years (9), and the Health Assessment Questionnaire (HAQ; where 0 = best and 3 = worst) (10) for participants age >18 years. JIA categories were classified according to the ILAR criteria (11).

Parents and children between ages 12 and 18 years gave informed consent, as well as patients age ≥18 years. Reuma.pt was approved by the National Board of Data Protection and local ethics committees. Research was carried out in compliance with the Declaration of Helsinki, and all the ethics committees of the participating hospitals and clinics approved the study.

JADAS calculation. JADAS consists of 4 components: physician global assessment of disease activity on a 10-cm VAS (where 0 = no activity and 10 = maximum activity), parent/patient global assessment of well-being on a 10-cm VAS (where 0 = very well and 10 = very poor), number of joints with active disease, and an inflammatory marker

(ESR) (2). We decided to use the 27-joint reduced count (JADAS27) due to its greater feasibility. This count has been found to be a valid surrogate for the whole joint count in JIA (12). The JADAS27 includes the following joints: cervical spine, elbows, wrists, metacarpophalangeal joints (from the first to third), proximal interphalangeal joints, hips, knees, and ankles. The ESR value was normalized to a 0–10 scale according to the following formula:

$$\frac{\text{ESR mm/hour} - 20}{10}$$

Before making the calculation, ESR values <20 mm/hour were converted to 0 and ESR values >120 were converted to 10 (2).

Similarly to Nordal et al, JADAS27-CRP was adapted by replacing ESR with CRP level as the inflammatory marker (6). CRP level was truncated to a 0–10 scale according to the following formula:

$$\frac{\text{CRP mg/liter} - 10}{10}$$

This is similar to the truncated ESR used in JADAS (2). Before calculation, CRP values <10 mg/liter were converted to 0 and CRP values >110 mg/liter were converted to 10. JADAS27-CRP was calculated similarly to JADAS27-ESR, as the simple linear sum of its 4 components, yielding a global score of 0–57, which is also similar to JADAS27-ESR.

Cutoff values for inactive disease, minimal disease activity, acceptable symptom state, and active disease. Recently, Consolaro et al (7) defined, for all versions of JADAS-ESR (JADAS10, JADAS27, and JADAS71), the cutoff score for classifying a patient as having "inactive disease" as ≤1 for all JIA categories. The cutoff for classification of "minimal disease activity" was >1 and ≤2 for oligoarticular JIA and >1 and ≤3.8 for polyarticular JIA. Children with systemic arthritis, rheumatoid factor (RF)–positive polyarthritis, RF-negative polyarthritis, or extended oligoarthritis were included in the polyarthritis group. The oligoarthritis group included patients with persistent oligoarthritis. Patients with JIA classified in the remaining ILAR categories were assigned to the polyarthritis or oligoarthritis group based on the number of joints affected during disease course (>4 or ≤4, respectively). Cutoff values for JADAS for "parent's acceptable symptom state" was >2 and ≤3.2 for oligoarticular JIA and >3.8 and ≤5.2 for polyarticular JIA (7). Values above the cutoffs for "parent's acceptable symptom state" were considered as "active disease" state (JADAS >3.2 and JADAS >5.2 for oligoarticular and polyarticular JIA, respectively).

We analyzed the agreement of the classification of patients with the cutoffs of JADAS27 (using ESR) with the JADAS27-CRP classification using the categories of "inactive disease," "minimal disease activity," "parent's acceptable symptom state," and "active disease" to verify whether these 2 JADAS versions were classifying the patients similarly.

Statistical analysis. Descriptive statistics were used to summarize population characteristics. Correlations between the continuous variables were calculated and expressed as Pearson's coefficient correlation. Correlations were considered high, moderate, or weak at coefficients ≥0.7, 0.4–0.7, or ≤0.4, respectively. The Student's *t*-test and analysis of variance (ANOVA) were used to compare means between groups. ANOVA followed by Bonferroni analysis was used to compare the JADAS27-ESR and JADAS27-CRP across all JIA categories. Pearson's correlations and K statistics were used to assess the agreement between disease states set by JADAS27-ESR and JADAS27-CRP. Statistical analysis was performed using SPSS statistical software, version 20. Two-sided *P* values less than 0.05 were considered statistically significant.

RESULTS

From the 729 patients with JIA included in the Reuma.pt database, 358 children had full data to calculate JADAS27-ESR and JADAS27-CRP. Of these 358 patients, 65.4% were female. Mean ± SD disease duration was 11.8 ± 9.1 years and the mean ± SD age at the last visit was 18.5 ± 9.9 years. A total of 134 patients (37.5%) were classified as persistent oligoarticular, 53 patients (14.8%) as extended oligoarticular, 51 patients (14.2%) were polyarticular RF negative, 30 patients (8.4%) were polyarticular RF positive, 39 patients (10.9%) were systemic, 35 patients (9.8%) had enthesitis-related arthritis, 11 patients (3.1%) had psoriatic arthritis, and in 5 patients (1.4%) information was lacking on the category of JIA. The age, sex, disease duration, and JIA categories distribution of the selected patients (358 patients) was similar to the patients that were excluded due to insufficient data (371 patients).

The correlation coefficient at the last visit with all JADAS items available between JADAS27-ESR and JADAS27-CRP was 0.967 ($P < 0.0001$) (Figure 1), although the correlation coefficient between ESR and CRP level was 0.335 ($P < 0.0001$) (this correlation refers to the raw values of ESR and CRP level, not the truncated values used to calculate JADAS27). When comparing the JADAS27-ESR and JADAS27-CRP within each category of JIA, the strong

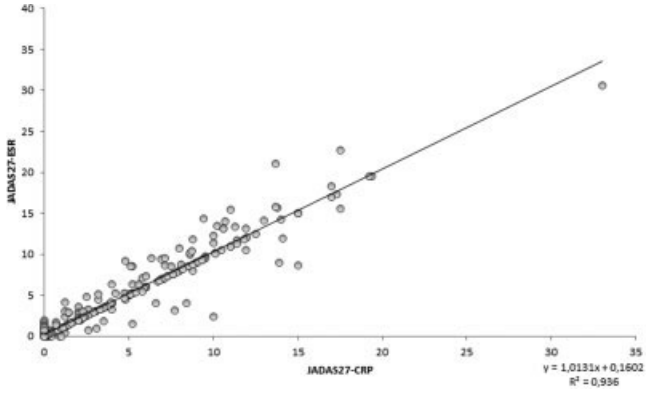

Figure 1. Correlation between Juvenile Arthritis Disease Activity Score 27-joint reduced count (JADAS27) based on erythrocyte sedimentation rate (ESR) and corresponding JADAS27 based on C-reactive protein (CRP) level in the Portuguese Reuma.pt cohort, at the same study visit (r = 0.967, $P < 0.0001$).

Table 1. Pearson's correlation coefficients of JADAS27-ESR and JADAS27-CRP across the JIA categories*

	JADAS27-ESR, mean ± SD	JADAS27-CRP, mean ± SD	Correlation coefficient, r†	*P*
PsA	5.218 ± 4.61	4.855 ± 4.68	0.883	0.0003
ERA	3.731 ± 4.29	3.514 ± 3.87	0.973	< 0.0001
OligoE	3.128 ± 4.11	3.002 ± 3.93	0.976	< 0.0001
OligoP	2.569 ± 4.05	2.309 ± 3.66	0.970	< 0.0001
PolyRFneg	5.304 ± 6.88	4.878 ± 6.54	0.964	< 0.0001
PolyRFpos	6.217 ± 5.42	6.263 ± 5.46	0.964	< 0.0001
SoJIA	3.523 ± 3.68	3.464 ± 3.63	0.967	< 0.0001
All categories	3.661 ± 4.82	3.447 ± 4.58	0.967	< 0.0001

* JADAS27 = Juvenile Arthritis Disease Activity Score 27-joint reduced count; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; JIA = juvenile idiopathic arthritis; PsA = psoriatic arthritis; ERA = enthesitis-related arthritis; OligoE = oligoarticular extended; OligoP = oligoarticular persistent; PolyRFneg = polyarticular rheumatoid factor negative; PolyRFpos = polyarticular rheumatoid factor positive; SoJIA = systemic-onset JIA.
† Correlations were considered high when $r \geq 0.7$, moderate if $0.4 > r > 0.7$, and low if $r \leq 0.4$.

correlation was maintained (all correlation coefficients >0.8 and *P* values < 0.001) (Table 1).

JADAS27-ESR and JADAS27-CRP according to JIA categories are shown in Table 1. The mean JADAS27-CRP of the oligoarticular categories differed significantly from the mean JADAS27-CRP score of the polyarticular categories (persistent oligoarticular versus polyarticular RF positive [$P < 0.0001$], persistent oligoarticular versus polyarticular RF negative [$P = 0.010$], and extended oligoarticular versus polyarticular RF positive [$P = 0.03$]). The JADAS27-ESR also differed significantly between the oligoarticular and polyarticular categories of JIA (persistent oligoarticular versus polyarticular RF positive [$P = 0.003$] and persistent oligoarticular versus polyarticular RF negative [$P = 0.01$]).

From the 358 patients included in this study using the JADAS27-ESR, 160 (44.7%) patients were classified as having inactive disease, 42 (11.7%) had minimal disease activity, 45 (12.6%) had acceptable symptom state, and 111 (31%) patients had active disease. The classification was similar using the JADAS27-CRP: 166 (46.4%) patients were classified as having inactive disease, 41 (11.4%) had minimal disease activity, 39 (10.9%) had acceptable symptom state, and 112 (31.3%) patients

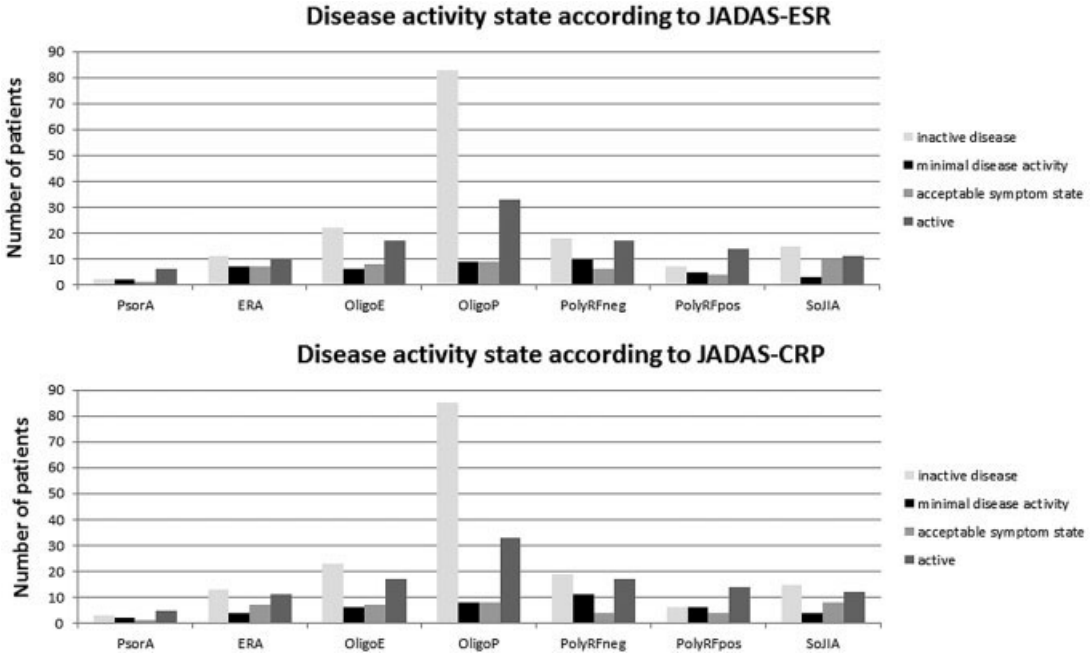

Figure 2. Disease activity state according to Juvenile Arthritis Disease Activity Score (JADAS) based on erythrocyte sedimentation rate (ESR) and JADAS based on C-reactive protein (CRP) level for the different juvenile idiopathic arthritis (JIA) categories at the study visit, in the Portuguese Reuma.pt JIA cohort. PsorA = psoriatic arthritis; ERA = enthesitis-related arthritis; OligoE = oligoarticular extended; OligoP = oligoarticular persistent; PolyRFneg = polyarticular rheumatoid factor negative; PolyRFpos = polyarticular rheumatoid factor positive; SoJIA = systemic-onset JIA.

Table 2. JADAS27-ESR and JADAS-CRP across JIA disease activity states and descriptive statistics of the components of JADAS27 (number of joints with active disease, parent/patient global assessment of well-being, physician global assessment of disease activity, and the inflammatory marker)*

	All activity states	Inactive disease	Minimal disease activity	Acceptable symptom state	Active disease
Patients, no. (%)	358 (100)	160 (44.69)	42 (11.73)	45 (12.57)	111 (31.01)
JADAS27-ESR					
Mean ± SD	3.71 ± 4.86	0.18 ± 0.31	1.78 ± 0.66	3.36 ± 0.97	9.67 ± 4.52
Median (minimum, maximum)	1.5 (0, 30.6)	0 (0, 1.1)	1.55 (1.1, 3.8)	3.3 (2, 5.4)	9 (3.6, 30.6)
JADAS-CRP					
Mean ± SD	3.50 ± 4.64	0.19 ± 0.42	1.76 ± 1.72	3.32 ± 1.56	9.01 ± 4.45
Median (minimum, maximum)	1.35 (0, 33)	0 (0, 3.1)	1.5 (0, 10)	3 (1.2, 8.4)	8.5 (1.2, 33)
JADAS-ESR vs. JADAS-CRP					
r	0.967	0.697	0.496	0.593	0.925
P	< 0.0001	< 0.0001	0.0008	< 0.0001	< 0.0001
ESR, mm/hour					
Mean ± SD	17.12 ± 17.16	9.74 ± 6.83	16.36 ± 12.7	19.49 ± 16.8	27.09 ± 23.11
Median (minimum, maximum)	12 (1, 120)	8 (1, 29)	14 (1, 44)	14 (1, 71)	20 (1, 120)
<20, %	74.02	91.88	66.67	68.89	53.15
CRP, mg/liter					
Mean ± SD	7.01 ± 14.24	3.04 ± 4.88	5.89 ± 11.43	10.78 ± 17.0	11.63 ± 20.2
Median (minimum, maximum)	2 (0, 156)	1 (0, 31.3)	2 (0, 51.9)	4 (0, 73.9)	4 (0, 156)
<10, %	81.84	91.88	92.86	73.33	66.67
Active joints					
Mean ± SD	0.39 ± 1.03	0 ± 0	0.12 ± 0.4	0.22 ± 0.56	1.13 ± 1.57
Median (minimum, maximum)	0 (0, 7)	0 (0, 0)	0 (0, 2)	0 (0, 3)	1 (0, 7)
PGA					
Mean ± SD	1.63 ± 2.32	0.10 ± 0.24	0.66 ± 0.61	1.53 ± 1.29	4.25 ± 2.42
Median (minimum, maximum)	0.4 (0, 10)	0 (0, 1)	0.7 (0, 2)	1.2 (0, 5.2)	4 (0, 10)
PhGA					
Mean ± SD	1.15 ± 1.7	0.04 ± 0.16	0.59 ± 0.56	0.97 ± 0.74	3.05 ± 1.86
Median (minimum, maximum)	0 (0, 9.3)	0 (0, 1.1)	0.5 (0, 2)	1 (0, 2.5)	2.9 (0, 9.3)

* JADAS27 = Juvenile Arthritis Disease Activity Score 27-joint reduced count; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; JIA = juvenile idiopathic arthritis; PGA = parent/patient global assessment of well-being (on a 10-cm visual analog scale [VAS], where 0 = very well and 10 = very poor); PhGA = physician global assessment of disease activity (on a 10-cm VAS, where 0 = no activity and 10 = maximum activity).

had active disease. Figure 2 shows the disease activity states according to the different JIA categories based on JADAS27-ESR and JADAS27-CRP. The agreement between JADAS27-ESR and JADAS27-CRP across the 4 activity states assessed by K statistics was very good, showing 91.1% of the observations in agreement: K = 0.867 (95% confidence interval 0.824–0.91).

The correlation between JADAS27 with ESR and JADAS27 without ESR (clinical JADAS27) was high (r = 0.97, $P < 0.0001$), as well as the correlation between JADAS27-CRP and JADAS27 without CRP (r = 0.97, $P < 0.0001$). We analyzed separately the patients with higher values of ESR (≥20 mm/hour, n = 109) and increased CRP level (≥10 mg/liter, n = 70), and verified that the correlation between JADAS27-ESR and clinical JADAS27 was still high (r = 0.96, $P < 0.0001$), as well as between JADAS27-CRP and clinical JADAS27 (r = 0.93, $P < 0.0001$). We also assessed whether the correlation between clinical JADAS27 and the JADAS27 that included an inflammatory marker still remained high in the systemic subtype. The coefficient correlation with clinical JADAS27 was 0.96 and 0.94, respectively, for JADAS27-ESR and JADAS27-CRP. Table 2 shows the correlation between JADAS-ESR and JADAS-CRP across all JIA disease activity states.

Correlation between JADAS27-ESR and parent/patient global assessment of well-being was strong (r = 0.84, $P < 0.0001$) as well as the correlation between JADAS27-ESR and physician global assessment of disease activity (r = 0.88, $P < 0.0001$). We also tested the correlation between physician global assessment of disease activity (VAS) and parent/patient global assessment of well-being on a 10-cm VAS; the correlation coefficient was 0.64 ($P < 0.0001$). A moderate correlation (r = 0.49) was found between JADAS27-ESR and C-HAQ/HAQ ($P < 0.0001$).

DISCUSSION

Composite indices or pooled indices are useful tools for the evaluation of disease activity in patients with JIA. They allow the integration of various aspects of the disease into a single numerical value and may improve patient care. The JADAS is a new tool for the evaluation of disease activity in JIA that has been developed to provide physicians with a simple and useful instrument.

Similar to the work of Nordal et al (6), in our study the JADAS27 based on ESR and on CRP level correlated closely, indicating that both measures can be used. In addition, we have tested the recently published cutoff

criteria for classification of inactive disease, minimal disease activity, parent's acceptable symptom state (7), and active disease to analyze whether patients were classified in the same state using either JADAS27-ESR or CRP. The criteria (i.e., cutoff values) were developed due to the need for identifying different states of JIA activity and may provide simple and intuitive reference values that can be used to monitor the disease course over time in an individual patient or to compare disease status across individual patients or patient groups (7). The agreement between JADAS27-ESR and JADAS27-CRP across the 4 activity states was very good, showing agreement in 91.1% of the observations, reinforcing that clinicians can use both measures to calculate the JADAS without changing the categories in which the patients are classified.

JADAS calculation may have had some limitations in our study population. Most of our JIA patients had inactive disease, which might have enhanced the results. However, when we performed the correlation of JADAS-ESR with JADAS-CRP according to the disease activity states (Table 2), the patients with active disease showed a high correlation ($r = 0.925$, $P < 0.0001$). Additionally, in patients with values of ESR ≥20 or CRP level ≥10 (i.e., converted values different than zero), the high correlation between the 2 scores was maintained ($r = 0.94$, $P < 0.0001$) (data not shown).

Another limitation of JADAS is that the conversion of the higher values of ESR and CRP level to 10 can mislead the results: a JIA patient with CRP level of 200 mg/liter obtains the same JADAS score as a patient with a CRP level of 110 mg/liter (both values of CRP are converted to 10).

Finally, as the authors of JADAS point out, although the score was designed to be robust enough to cover all categories of JIA, a thorough assessment of disease activity in children with systemic JIA requires quantification of extraarticular manifestations, particularly fever and rash (2).

Measurement of CRP level presents some advantages compared to ESR: CRP level is a direct measure of the acute-phase response and is less confounded by other factors, including comorbidities. Also, CRP level assessment is more rapid and the cost is comparable to ESR (4). Still, although the inclusion of CRP level and ESR is fully justified by their face and content validity, the delay associated with their assessment might be one reason why many physicians do not apply composite scores to guide their clinical decisions. In a study of RA, Aletaha et al concluded that acute-phase reactants add little to composite disease activity indices (13). These inflammatory parameters did not seem to contribute with sufficiently important information to composite scores to change judgment of disease activity, in addition to merely using clinical measures. Because laboratory tests are frequently missing at patient visits, we have also tested JADAS27 with and without ESR. The correlation between JADAS27 with ESR and JADAS27 without ESR (clinical JADAS) was high ($r = 0.97$, $P < 0.0001$), indicating that when ESR is not available JADAS27 can be calculated without this variable. The clinical JADAS27 can therefore be used to conduct a disease activity evaluation anytime and anywhere. Recently, McErlane et al concluded that for the majority of JIA categories, clinical applicability of JADAS would be improved by exclusion of ESR and that the amended score (JADAS3-71), which omits the ESR, correlates well with JADAS71 (14).

We have also tested the correlation between physician global assessment of disease activity (VAS) and parent/patient global assessment of well-being on a 10-cm VAS in order to see whether it would be possible to cut one of these components of JADAS27, similar to the DAS28 of 4 and 3 variables in RA (15). The correlation was moderate and insufficient to exclude a component from the tool. In fact, it is crucial to include these 2 scales in JADAS. Parent/patient global assessment is important because it is the only parameter that incorporates the parent's/patient's perception of disease activity. The physician global assessment is also relevant because it represents the most responsive measure in JIA (2).

As with Consolaro et al (2), in our study the correlation between JADAS27-ESR and functional impairment according to C-HAQ/HAQ was only moderate ($r = 0.499$, $P < 0.0001$). This moderate correlation was expected because C-HAQ/HAQ scores combine the effect of both disease activity and damage. The authors of JADAS decided not to include functional status assessment because it has been shown to be relatively insensitive to change in JIA (2).

In conclusion, in our study the JADAS27 based on CRP level and ESR correlated closely, and both classify patients similarly regarding disease activity state, indicating that both measures can be used interchangeably in clinical practice. In addition, clinical JADAS, a score that does not include laboratory measures, was also well correlated with JADAS-ESR and JADAS-CRP.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Mourão had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Acquisition of data. Mourão, Santos, Melo-Gomes, Martins, Costa, Ramos, Brito, Duarte, Figueira, Figueiredo, Furtado, Lopes, Oliveira, Rodrigues, Salgado, Sousa, Fonseca, Canhão.

Analysis and interpretation of data. Mourão, Santos, Melo-Gomes, Martins, Branco, Fonseca, Canhão.

REFERENCES

1. Martini A, Lovell DJ. Juvenile idiopathic arthritis: state of the art and future perspectives. Ann Rheum Dis 2010;69:1260–3.
2. Consolaro A, Ruperto N, Bazso A, Pistorio A, Magni-Manzoni S, Filocamo G, et al, for the Paediatric Rheumatology International Trials Organisation. Development and validation of a composite disease activity score for juvenile idiopathic arthritis. Arthritis Rheum 2009;61:658–66.
3. Giannini EH, Ruperto N, Ravelli A, Lovell DJ, Felson DT, Martini A. Preliminary definition of improvement in juvenile arthritis. Arthritis Rheum 1997;40:1202–9.
4. Wells G, Becker JC, Teng J, Dougados M, Schiff M, Smollen J, et al. Validation of the 28-joint Disease Activity Score (DAS28) and European League Against Rheumatism response criteria based on C-reactive protein against disease progres-

sion in patients with rheumatoid arthritis, and comparison with the DAS28 based on erythrocyte sedimentation rate. Ann Rheum Dis 2009;68:954–60.
5. Crowson CS, Rahman MU, Matteson EL. Which measure of inflammation to use? A comparison of erythrocyte sedimentation rate and C-reactive protein measurements from randomized clinical trials of golimumab in rheumatoid arthritis. J Rheumatol 2009;36:1606–10.
6. Nordal EB, Zak M, Aalto K, Berntson L, Fasth A, Herlin T, et al. Validity and predictive ability of the juvenile arthritis disease activity score based on CRP versus ESR in a Nordic population-based setting. Ann Rheum Dis 2012;71:1122–7.
7. Consolaro A, Bracciolini G, Ruperto N, Pistorio A, Magni-Manzoni S, Malattia C, et al, for the Paediatric Rheumatology International Trials Organisation. Remission, minimal disease activity, and acceptable symptom state in juvenile idiopathic arthritis: defining criteria based on the Juvenile Arthritis Disease Activity score. Arthritis Rheum 2012;64:2366–74.
8. Canhao H, Faustino A, Martins F, Fonseca JE, and the Rheumatic Diseases Portuguese Register Board Coordination, Portuguese Society of Rheumatology. Reuma.pt: the rheumatic diseases Portuguese register. Acta Reumatol Port 2011;36:45–56.
9. Melo-Gomes JA, Ruperto N, Canhao H, Fonseca JE, Quintal A, Salgado M, et al, and the Paediatric Rheumatology International Trials Organisation. The Portuguese version of the Childhood Health Assessment Questionnaire (CHAQ) and the Child Health Questionnaire (CHQ). Clin Exp Rheumatol 2001; Suppl 23:S126–30.
10. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum 1980;23:137–45.
11. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, et al. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol 2004;31:390–2.
12. Bazso A, Consolaro A, Ruperto N, Viola S, Magni-Manzoni S, Malattia C, et al. Development and testing of reduced joint counts in juvenile idiopathic arthritis. J Rheumatol 2009;36:183–90.
13. Aletaha D, Nell V, Stamm T, Uffmann M, Pflugbeil S, Machold K, et al. Acute phase reactants add little to composite activity indices for rheumatoid arthritis: validation of a clinical activity score. Arthritis Res Ther 2005;7:R796–806.
14. McErlane F, Beresford MW, Baildam EM, Chieng SE, Davidson JE, Foster HE, et al. Validity of a three-variable Juvenile Arthritis Disease Activity Score in children with new-onset juvenile idiopathic arthritis. Ann Rheum Dis 2013;72:1983–8.
15. Van der Heijde DM, van 't Hof MA, van Riel PL, Theunisse LA, Lubberts EW, van Leeuwen MA, et al. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. Ann Rheum Dis 1990;49:916–20.