

# Disease activity assessment for juvenile idiopathic arthritis in transitional care

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## SUMMARY

**Objective.** The indices to measure disease activity of chronic arthritis in adulthood and childhood are different. Therefore, assessing the status of the disease in young patients with juvenile idiopathic arthritis (JIA) can be tricky, especially when the transition to adult care is ongoing. The aim of our study was to assess the level of correlation between adult and juvenile scores in the measurement of disease activity in JIA patients during transitional care.

**Methods.** We estimated the disease activity by using the Juvenile Arthritis Disease Activity Score 71 (JADAS71), clinical JADAS, adult Disease Activity Score (DAS28), Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI) in JIA patients in transitional care. We enrolled patients older than 16 years at the time of the first transition visit, and disease activity was assessed at baseline and 12 months. Regression analyses were carried out to estimate the level of agreement among the different indices.

**Results.** We recruited 26 patients with JIA; 11 patients were polyarticular (42.3%) and 15 patients were oligoarticular (53.1%). The mean age at diagnosis was  $7.7 \pm 3.9$  years and the age at the first evaluation was  $20.9 \pm 3.7$  years. The correlation between JADAS71 and DAS28 was  $r^2=0.69$ ,  $r^2=0.86$  between JADAS71 and SDAI, and  $r^2=0.81$  between JADAS71 and CDAI.

**Conclusions.** SDAI and JADAS71 showed the best correlation, but a few patients were not captured at the same level of disease activity. New prospective studies with a larger number of patients will be needed in this field.

**Key words:** Transition, juvenile idiopathic arthritis, disease activity score, JADAS, SDAI.

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## INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease with persistent synovial inflammation and a widely variable clinical course and outcome (1). The objectives of JIA management are to improve symptoms, ameliorate quality of life, and prevent irreversible damage (2). The transition from pediatric to adult care is considered pivotal for correctly managing childhood-onset chronic illnesses, such as JIA (3-5). Transitional care is crucial, and there is evidence that morbidity and mortality increase following an inadequate transition from pediatric to adult care (3). Young patients are particularly vulnerable and can experience a worsening of their disease (5-7). A recent retrospective study has found that out of 58% of the patients who had ac-

tive disease at the time of transfer, 30% were hospitalized because of a disease flare in the year before, and 30% experienced an increase in disease activity the year after the transition (8). In our center, as indicated in the Delphi consensus survey among Italian pediatric and adult rheumatologists on transitional care of young people with JIA (6), the first two outpatient visits take place in the presence of pediatric and adult rheumatologists. One critical point in transitional care is the lack of a validated disease activity score that allows a homogeneous and continuum assessment of disease from adolescence to adulthood. Therefore, whether the scores to assess disease activity in rheumatoid arthritis (RA) can be employed and helpful to evaluate JIA turning into adult age is not clear.

The Juvenile Arthritis Disease Activity

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Score (JADAS) (9) includes the following items: physician's global assessment of disease activity, measured on a 0-10 visual analog scale (VAS), where 0 is no activity and 10 is maximum activity; parent/patient global assessment of child well-being, measured on a VAS 0-10, where 0 is very well and 10 is very poor; the erythrocyte sedimentation rate (ESR), normalized to a 0-10 scale; and count of joints with active disease developed in three versions depending on the number of joints assessed, 10 (JADAS10), 27 (JADAS27), or 71 (JADAS71), respectively (9). In adults with RA, the most common score is the Disease Activity Score based on 28 selected joints and their variations (DAS28), the Simplified Disease Activity Index (SDAI) (10), and the Clinical Disease Activity Index (CDAI) (11). In clinical practice, a patient with JIA who transfers to adult rheumatologists is evaluated with the disease activity scores validated for RA and not for JIA. The primary objective of the study was to identify the level of correlation between juvenile and adult scores in estimating the disease activity in JIA during transitional care.

## ■ MATERIALS AND METHODS

### *Study design*

Patients with JIA, oligo, and polyarthritis, in accordance with the International League of Associations for Rheumatology criteria (1), older than 16 years at the time of baseline visit, were recruited at the Rheumatology Unit of the Policlinic University Hospital of Bari, Italy, and retrospective data from all cases of JIA were collected. The data included: age, type of arthritis (oligoarticular or polyarticular), age at onset, age at diagnosis, positivity for antinuclear antibody (ANA), rheumatoid factor (RF), and anti-citrulline peptide, age at the time of visit, the time between last visit and baseline, type of treatments suggested; inflammatory marker at the time of visit (ESR in mm/hr, C-reactive protein in mg/dL); swelling joint count (SJC); tender joint count (TJC); active joint count (number of joints with pain and/or swollen), patient's global assessment of well-being, measured

on a VAS 0-100 (VAS GH); physician's global assessment of disease activity on a VAS 0-10 (VAS Ph); patient's assessment of disease activity, on a VAS 0-10 (VAS Pt); patient's pain scale on a VAS 0-10; Health Assessment Questionnaire (HAQ) 0-3. The baseline was considered the first visit by a rheumatologist of the adults, and the data were collected at baseline and after 12 months of follow-up. Since JADAS10 and JADAS27 may have a joint count lower than the real number of active joints in patients with polyarticular JIA, JADAS71 and clinical-JADAS71 (cJADAS71) as juvenile and DAS28, SDAI, and CDAI as adult measures have been taken into account for this analysis. Disease activity status was stratified according to the standard thresholds for each score defining the state of remission: low, moderate, and high disease activity (10-13).

### *Statistical analysis*

Continuous variables were expressed as mean  $\pm$  standard deviation and range, while discrete variables were expressed in the form of absolute and percentage values. The analysis of variance for repeated measurements was used to demonstrate the presence of significant variations between the variables studied and to identify the levels of agreement. The linear regression model was applied to continuous variables, whose correlation has been defined by the R-square value: the strength of correlation is poor between 0 and 0.4, fair between 0.4 and 0.6, good between 0.6 and 0.8, and excellent between 0.8 and 1. For the discrete variables, instead, Kendall's tau test was used, whose cutoff to define the correlation is the same as for R-square in the linear regression analysis. We performed a multiple regression analysis to evaluate the level of association between a series of variables (single and composite) and the level of disability perceived by the patient as measured by the HAQ disability index. Therefore, we built a model including ESR, VAS GH, VAS Ph, VAS Pt, TJC, SJC, and JADAS71. C-JADAS71, DAS28, CDAI, and SDAI. The tests were considered statistically significant at  $p < 0.05$ .

## ■ RESULTS

We recruited 26 patients: 18 females and 8 males. The mean age at diagnosis was  $7.7\pm 3.9$  years, and the age at the first evaluation was  $20.9\pm 3.7$  years. Based on the subset of arthritis, 11 patients were polyarticular (42.3%) and 15 patients were oligoarticular (53.1%). Moreover, they were stratified based on the positivity of ANA (12 pts, 46.1%), RF (4 pts, 15.4%), and anti-citrullinated protein antibodies (3 pts, 11.5%). At baseline, 6 patients were taking prednisone (mean dose at baseline  $8.9\pm 8.2$  mg), and 15 were on therapy with the disease-modifying anti-rheumatic drugs (DMARDs) methotrexate (n=13) and sulfasalazine (n=2). All 26 patients were treated with biological DMARDs (bDMARDs): abatacept (n=2), adalimumab (n=7), anakinra (n=1), certolizumab (n=1), etanercept (n=13), rituximab (n=1) and tocilizumab (n=1). After 12 months, they were still on bDMARDs, but with some changes: 2 were treated with abatacept, 6 with adalimumab, 1 with canakinumab, 2 with certolizumab, 14 with etanercept, and 1 with tocilizumab. No patient was lost during the follow-up. Figure 1 shows the diagrams of the distribution of the different disease activity scores at the baseline and 12-month assessments. The linear regression analysis expressed as R-square was 0.690 for the correlation between JADAS71 and DAS28 (discrete concordance); 0.865 for the correlation between JADAS71 and SDAI (excellent concordance); and 0.809 for the correlation between JADAS71 and CDAI (good concordance). The Kendall's tau test was 0.797 for the correlation of JADAS71 with DAS28 and 0.788 between cJADAS71 and DAS28 (good concordance); 0.831 for the correlation with SDAI both for JADAS71 and cJADAS71 (excellent concordance); and 0.831 for the correlation of JADAS71 with CDAI and 0.813 between cJADAS71 and CDAI (excellent concordance).

Figure 2 shows the linear regression of the correlation between the continuous variables. By evaluating the degree of dispersion of the points in the graph of oligoarticular and polyarticular JIA patients, it

was possible to understand the type of correlation (whether positive or negative) and the strength of the correlation between the various indices examined, according to the cut-off of each score. Despite the strength of the correlation, some patients, mainly those with oligoarticular JIA, are estimated to have low disease activity when ranked with SDAI but high or moderate disease activity if scored with JADAS71. Finally, a multiple regression analysis to evaluate the level of association between the baseline model and the disability index shows that SJC (0.001), CDAI (0.005), and SDAI (0.001) are the most significant variables associated with HAQ.

## ■ DISCUSSION AND CONCLUSIONS

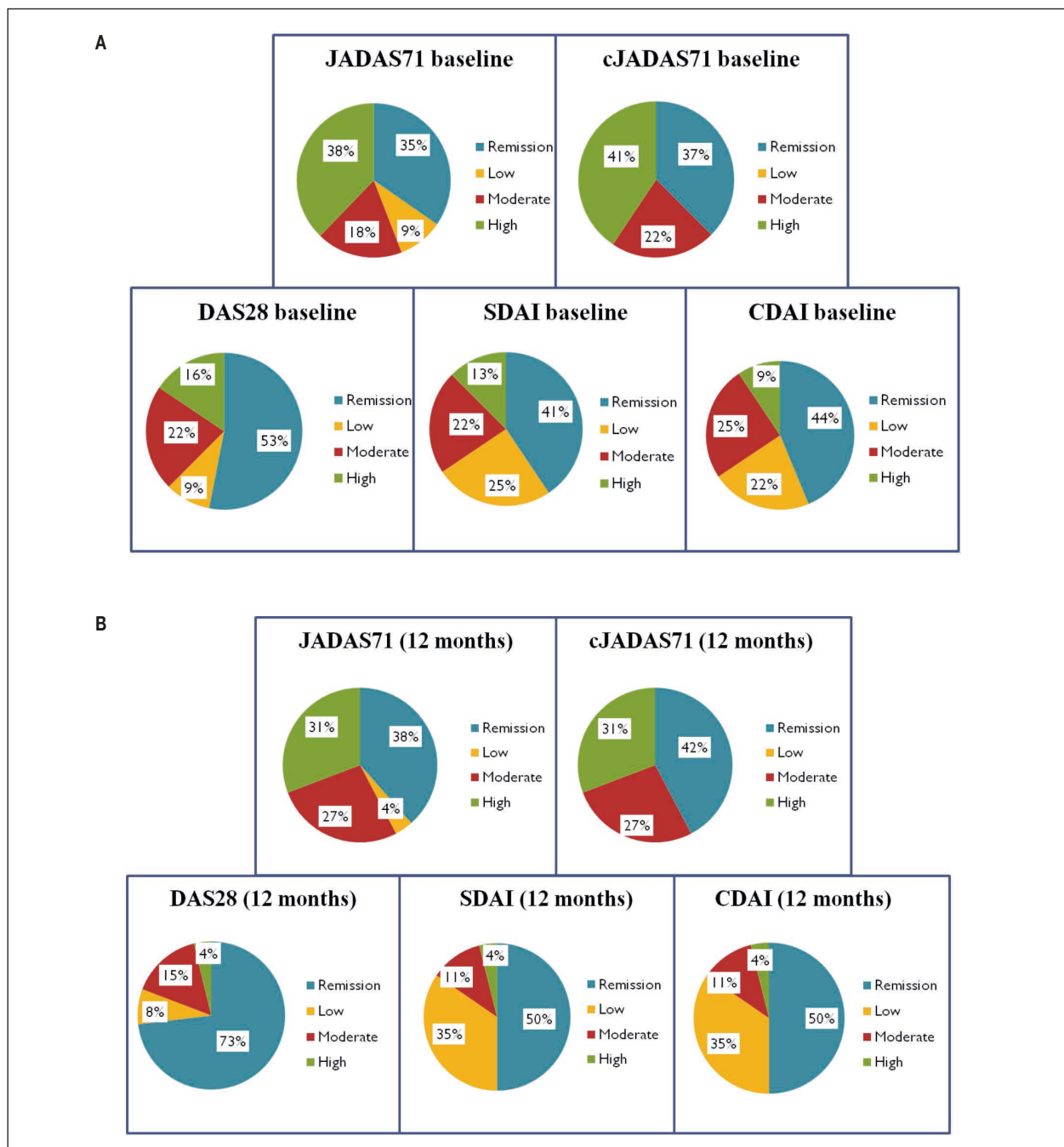
In clinical practice, a patient with JIA who transfers to adult rheumatologist care is evaluated with the disease activity scores validated for RA (DAS28, SDAI, and CDAI) and not for JIA. Given the differences between the "scores" used in adulthood and pediatric age, our study aimed to assess the level of agreement between JADAS and DAS28, SDAI, or CDAI during transitional care. Since JADAS10 and JADAS27 may have a joint count lower than the active joints in a subject with polyarticular JIA, we choose the JADAS71 as the single score for comparison with the adult one. The JADAS71-DAS28 correlation was good, but dispersion of some points from the regression line was seen mainly in patients with polyarticular JIA.

Most patients with oligoarticular JIA are located in a part of the graph corresponding to the "non high disease activity" for DAS28 and JADAS71. However, two oligoarthritis patients were on "high disease activity" for the JADAS71 and "non high disease activity" for the DAS28 index. Patients with polyarthritis showed even greater dispersion from the regression line. Furthermore, for low and high DAS28 values, the dispersion from the regression line was more pronounced. This indicates that, although the correlation between DAS28 and JADAS71 can be defined as globally good,

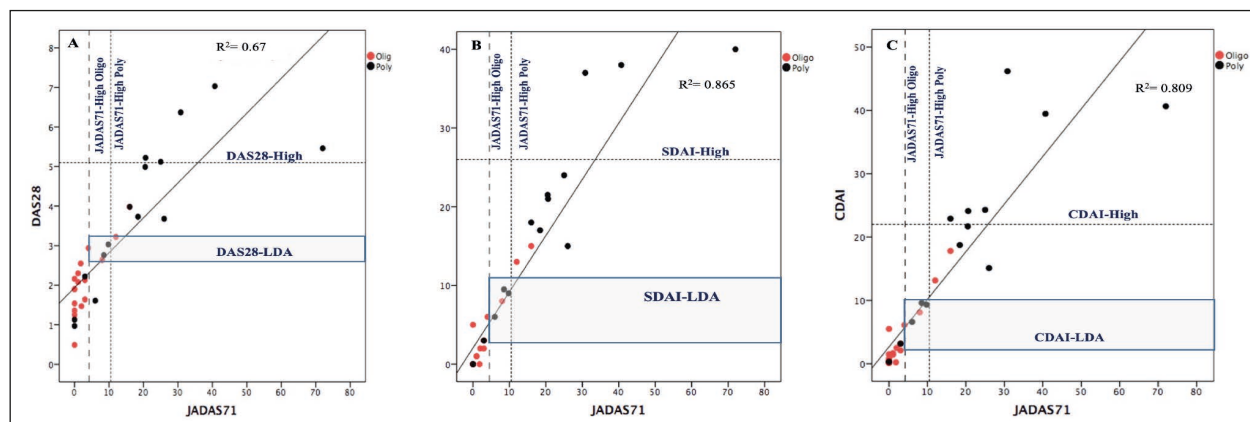
the concordance between the two indices is poor in polyarthritis patients and in those with high or low DAS28 scores.

Like our work, an English study analyzed the correlation between DAS28 and JADAS

in a cohort of 49 patients with polyarticular JIA (14). A good correlation was seen between the disease activity scores (Spearman's  $r=0.69$ ,  $p<0.0001$ ) and the authors showed a discrepancy in thresholds for



**Figure 1** - The distribution of different disease activities for each single score at baseline (A) and at 12 months (B) is shown. JADAS71, Juvenile Arthritis Disease Activity Score 71 joints; cJADSA71, clinical JADAS71; DAS28, Disease Activity Score 28 joints; SDAI, Simplified Disease Activity Index; CDAI, Clinical Disease Activity Index.



**Figure 2** - The graphic of linear regression of the correlation between the continuous variables is shown: between Juvenile Arthritis Disease Activity Score 71 joints (JADAS71) (oligoarticular red dots and polyarticular blue dots) and Disease Activity Score 28 joints (DAS28) (A), JADAS71 and Simplified Disease Activity Index (SDAI) (B) and between JADAS71 and Clinical Disease Activity Index (CDAI) (C). On the abscissae axis, JADAS71 has been reported. The high disease activity [cutoff of 10.5 for polyarticular juvenile idiopathic arthritis (JIA) and 4.2 for oligoarticular JIA] is represented by lines with a parallel pattern to the ordinate axis. In the same way, on the axis of the ordinates DAS28, SDAI, or CDAI with the respective high disease activity cutoffs have been reported. As above, from these cutoff values, a line parallel to the abscissa axis was drawn. The lines drawn from the cutoffs allowed us to define sections of the graph in which the scores relating to the disease activity were located. Despite the strength of the correlation, some patients, mainly oligoarticular JIA, are estimated to low disease activity when ranked with DAS28, SDAI, and CDAI, but on high or moderate disease activity if scored with JADAS71.

high-disease activity between the scores. In fact, when looking at the cut-offs, 13 patients had high disease activity with JADAS-10 > 10.5, but only 1 had DAS28 > 5.1. The authors suggest that a discrepancy in the proportion of patients with active disease is predominantly due to differences in the number and distribution of joints surveyed. In our study, the joints considered are 28 for all of the three adult scores, but while the correlation with DAS28 was fair with R-square and good with Kendal test, the JADAS71-SDAI correlation was excellent, and the graphical representation of linear regression showed a lower dispersion around the line. This result demonstrates that the concordance is not influenced by the number of joints for DAS28 but by the method of structuring the score. The JADAS is a clinical disease activity score and it correlates better with the SDAI.

Nonetheless, some JIA, estimated at low disease activity by SDAI, were at high disease activity if scored with JADAS71, and this implies some concerns about the decision-making turning point. Also in this case, for patients with polyarticular JIA (more deviation from the regression line), the

correlation between indices was less good than for those with the oligoarticular subset. Likewise, the JADAS71-CDAI correlation was excellent, but again, we found patients with “high disease activity” according to the JADAS71 and with “non high disease activity” for the CDAI. The limitations of our study are related to the small number of patients enrolled. Moreover, a possible bias in recruitment may be present: in fact, all the patients enrolled were on biological treatment, and many of them had high disease activity at baseline. Furthermore, this was a retrospective data analysis from a registry assessing all the JIA enrolled in an adult outpatient clinic, and therefore a sample size was not calculated. Since in our clinic the JADAS (especially JADAS71) is performed routinely at each evaluation in patients with JIA in transitional care, it was possible to carry out a correlation study between the clinimetric indices and the longitudinally collected data. Our study suggests that SDAI is the adult score that better correlates with JADAS71. Nevertheless, the fact that some patients are ranked into different classes of disease activities raises some questions on how to pursue a

treat-to-target strategy in these cases. The right clinimetric evaluation for JIA patients to adopt during transition care is still an unmet need. Appropriate prospective studies need to be devised to improve the outcomes of JIA patients in transition care.

### Contributions

FLT, CC, FI, conceptualization, methodology, formal analysis and data curation; MGA, FC, GL, FC, investigation and resources; FLT, FI, writing - original draft preparation; CC, MGA, FC, GL, FC, writing - review and editing. All authors read and approved the final manuscript.

### Conflict of interest

The authors declare no conflict of interest.

### Ethics approval and consent to participate

The study was conducted following the Declaration of Helsinki, and approved by the Institutional Review Board of Bari, Italy (protocol code 5277; date 09 August 2017).

### Informed consent

Informed consent was obtained from parents or legal guardians of all subjects involved in the study.

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None.

### Availability of data and materials

Data and materials are available from the corresponding author upon request.

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