Inactive disease in polyarticular juvenile idiopathic arthritis: current patterns and associations

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Objectives. To describe the achievement of inactive disease (ID) and remission in polyarticular juvenile idiopathic arthritis (JIA) and to measure the associations among patient characteristics, imaging results and these outcomes.

Methods. We performed a retrospective cohort study of children with polyarticular JIA diagnosed and treated at Seattle Children’s Hospital between 1 January 2000 and 31 December 2006. Each patient’s disease status (active disease vs ID) was determined for every clinic visit. Adjusted relative risk estimates were obtained using Mantel–Haenszel methods.

Results. One hundred and four children were included. Patients were followed up for an average of 30 months. Patients achieved 138 episodes of ID. Fifty-one patients achieved 69 episodes of clinical remission on medication. When duration of active disease was summed over each patient’s follow-up, patients spent a mean of 66.3% of their follow-up with active disease. Patients with evidence of joint damage on imaging studies obtained within 6 months of their first clinic visit spent a mean of 79% of their follow-up with active disease. Patients without these findings spent a mean of 58.5% of their follow-up with active disease ($P < 0.001$). Children who were RF+ and children with early evidence of joint damage tended to have a higher prevalence of active disease during the follow-up period.

Conclusions. In this cohort, children with polyarticular JIA spent the majority of their follow-up with active disease. Because children with early radiographic evidence of joint damage and children who were RF+ tended to have the most active disease, improving outcomes for these subgroups may be an important goal for prospective study.

Key words: Polyarticular juvenile idiopathic arthritis, Outcome measures, Remission.

Introduction

Juvenile idiopathic arthritis (JIA) is the most common of the paediatric rheumatic illnesses, with an estimated annual incidence of 3.2–6.1 in 100000 children [1–3]. Despite improved awareness of the disease and expanded treatment options, several large, prospective, observational studies have reported that nearly one-half of the patients with JIA had recurrent or persistent disease activity on entry into adulthood, with active arthritis, ongoing joint destruction and a decreased quality of life [4–7].

Although the goal of treatment in JIA is inactive disease (ID) and remission, standardized criteria did not exist for these disease states until 2004 when proposed definitions for ID, clinical remission on medication (CRM) and clinical remission off medication (CR) were published by Wallace et al. [8]. A subsequent retrospective study of children with JIA who were diagnosed and treated between 1980 and 1999 reported that children with polyarticular JIA tended to spend the highest proportion of follow-up with active disease as compared with other JIA categories [9]. Although it is anticipated that children diagnosed and treated more recently have improved outcomes due to improved disease recognition and earlier use of DMARDs, these data do not currently exist in the published literature.

Furthermore, while RF status and young age at disease onset previously have been associated with more severe disease [10–12], the association of such factors with ID and remission in current cohorts is not known. The associations between imaging findings and these outcomes also have not been explored in polyarticular JIA.

The primary objectives of this investigation were to provide current descriptive data regarding the achievement of ID and remission in children with polyarticular JIA and to identify associations between specific patient characteristics, in particular RF status and the presence of joint damage on early imaging studies, with these outcomes.

Patients and methods

Patients

Eligible patients were identified through a search of the billing database at Seattle Children’s Hospital (SCH) in Seattle, WA associated with the International Classification of Diseases (ICD)-9 diagnosis codes for polyarticular JIA (acute and chronic) and JRA not otherwise specified, who were diagnosed and treated in the SCH rheumatology clinic between 1 January 2000 and 31 December 2006. Patients were included if they met the 2001 Edmonton ILAR criteria for a diagnosis of polyarticular JIA (RF+ or RF−) [13], and if they had a minimum of 6 months of follow-up care in the clinic, to ensure a minimum of two consecutive visits per patient.

Patients who had >1 visit with a rheumatologist outside of SCH, who had received >6 months of care from an outside rheumatologist during their disease course or who were missing clinician documentation for ≥1 of their clinic visits, were excluded to ensure that data on sequential visits would be available for each patient’s disease course. Approval for this study was obtained from the SCH institutional review board.

Data collection

Data were collected for each patient from each of their SCH rheumatology clinic visits during the study period and from correspondence that occurred between visits. Paper charts and computerized medical records were reviewed. Data collected at the first clinic visit included sex, age, duration of symptoms prior to first SCH visit, imaging results, laboratory test results and medication use. At each subsequent clinic visit, data were collected for each of the ID criterion as published by Wallace et al. [8]. Data were also collected on medication start and stop dates and imaging results. To facilitate comparison with previously published cohorts, patients were dichotomized by...
RF status (one or more positive RF tests vs negative RF titre) for the analyses based on RF status.

Imaging data were obtained from imaging reports and original images were not re-reviewed. Inflammatory markers were recorded as normal or elevated. An abnormal ESR was defined as $>20\text{ mm/h}$.

**ID and remission**

Each patient’s disease status (active disease vs ID) was determined for every clinic visit. All patients were classified as having active disease at their first SCH clinic visit. Patients were classified as having ID if they met the following criteria: physician global assessment of disease activity of 0 on a 10 point visual analogue scale or documented physician assessment of ID; no active arthritis; no active uveitis; no fever; no rash, serositis, splenomegaly or lymphadenopathy attributable to JIA; normal ESR and/or CRP.

Because laboratory testing was not obtained at every clinic visit, a normal ESR and/or CRP were not required for ID classification if the patient otherwise met ID criteria. If disease state could not be classified due to missing data or unclear documentation, the visit was recorded as ‘not classifiable’.

Patients could have multiple episodes of active disease and ID. The start of an episode of active disease was defined as the date of the patient’s first SCH clinic visit and of any subsequent clinic visits where the disease state was classified as active and the disease state at the prior clinic had been categorized as ID. The end of an episode of active disease was defined as the first subsequent visit date when the patient met the criteria for ID. The start of an episode of ID was defined as the date of clinic visits when the patient was determined to have ID and the disease state at the prior clinic had been categorized as active disease. The end of an episode of ID was defined as the first subsequent visit date when the patient had active disease. Each episode of ID was also reviewed to determine if it met the criteria for CRM (6 months of ID while receiving any anti-arthritis or anti-uveitis medications) or CR (1 year of ID while not receiving any anti-arthritis or anti-uveitis medications) [8].

**Statistical analyses**

Chi-squared testing was used for comparison of proportions between groups. Mantel–Haenszel methods were used to calculate unadjusted and adjusted relative risk (RR) estimates. For continuous variables with approximately normal distributions, the unpaired $t$-test was used for comparisons between means. The Wilcoxon rank-sum test was used for comparison of medians. Correlations were measured with Pearson coefficients.

Prevalence curves were generated using the method described by Pepe and colleagues [14, 15] because it incorporates Kaplan–Meier estimates and allows for the description of the prevalence of a transient condition, thereby accounting for the fact that patients in this cohort may have had multiple transitions in and out of active disease along with a variable duration of follow-up. The curves were truncated at 3 years due to the small number of patients followed beyond this time point.

Reported results are based on analyses which excluded ‘unclassifiable’ clinic visits. Supplemental analyses performed categorizing these unclassifiable visits as either all active or all inactive did not yield substantially different results from those reported.

Data analyses were performed using Stata Version 9 statistical software (StataCorp, College Station, TX, USA).

**Results**

**Patient characteristics**

One hundred and forty-five children were initially identified. Sixteen children were excluded due to prior treatment by an outside rheumatologist, 12 patients were excluded because they did not have their follow-up care at SCH and 13 patients were excluded because they had <6 months of care in the clinic. One hundred and four patients were included (Table 1). RFs were not routinely re-checked; however, nine patients had an RF$^+$ on more than one occasion. Fourteen RF$^+$ patients were also tested for the presence of anti-cyclic citrullinated peptide antibodies (anti-CCPs) and nine of these patients were both anti-CCP$^+$ and RF$^+$.

Five HLA-B27$^+$ children were included in this cohort and met the criteria for polyarticular JIA. None of these children were males older than the age of 6 years, and none had axial involvement or enthesitis, which would have excluded them from the cohort. An average of 15 patients per year met inclusion criteria for the study (range 7–23). Median duration of follow-up was 27.4 months (mean 29.9; range 6.1–77.2 months). Forty-eight patients (46%) reported >6 months of symptoms prior to their first SCH clinic visit.

The mean age of RF$^+$ patients at their first visit was 12 years, which was significantly older than patients who were RF$^-$ ($P < 0.001; 95\% \text{ CI} 1.5, 5.4$). There were no additional statistically significant differences between these two groups of patients in the characteristics summarized in Table 1.

**Imaging results**

A total of 86 (82.7%) patients had radiographic imaging prior to their first clinic visit or during their first 6 months of care and 96 (92.3%) had radiographic imaging performed at some point during their follow-up (Table 2). Of the 247 imaging studies there were 177 (71.7%) X-rays, 39 (15.8%) CT scans, 26 (10.5%) MRIs and five bone scans. Twenty-three of the 86 patients (26.7%) who had imaging studies obtained prior to first SCH visit or during their first 6 months of care had radiographic evidence of joint damage, as manifested by the presence of joint space narrowing and/or erosions. Thirty-seven percent of patients...
who had imaging any time during the study period had radiographic evidence of joint damage. When patients were dichotomized into those who had >6 months of reported symptoms prior to their first clinic visit and those who had ≤6 months of symptoms, those who had >6 months of symptoms had an almost 3-fold increased RR of joint damage on imaging studies within their first 6 months of SCH care (RR = 2.97; 95% CI 1.3, 6.8; P < 0.01). There was no significant difference in proportion of children within these two subgroups who had imaging performed.

RF+ status was also significantly associated with the presence of joint space narrowing and/or erosions on imaging within the first 6 months of care (RR = 2.5; 95% CI 1.21, 5.16; P = 0.01). Adjustment for duration of symptoms prior to first visit (>6 or ≤6 months) and highest age quartile (>13.5 years) decreased the RR (adjusted RR = 1.81; 95% CI 0.96, 3.43; P = 0.44).

### Table 2. Patient characteristics and imaging results

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Erosions and/or joint space narrowing within 6 months</th>
<th>Any imaging study with erosions and/or joint space narrowing*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>23 (26.7)</td>
<td>32 (37.2)</td>
</tr>
<tr>
<td>Female</td>
<td>21 (27.6)</td>
<td>30 (35.3)</td>
</tr>
<tr>
<td>ANA+</td>
<td>13 (22.8)</td>
<td>23 (39.7)</td>
</tr>
<tr>
<td>RF+</td>
<td>10 (45.5)*</td>
<td>14 (58.3)*</td>
</tr>
<tr>
<td>Anti-CCP+</td>
<td>2 (20)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>HLA-B27+</td>
<td>2 (66.7)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>C-reactive protein elevated at first visit</td>
<td>11 (33.3)</td>
<td>14 (36.8)</td>
</tr>
<tr>
<td>ESR elevated at first visit</td>
<td>12 (24.5)</td>
<td>17 (30.4)</td>
</tr>
<tr>
<td>More than 6 months between symptom onset and first clinic visit</td>
<td>6 (14)</td>
<td>14 (26.9)</td>
</tr>
<tr>
<td>Less than 6 months between symptom onset and first clinic visit</td>
<td>17 (40.5)*</td>
<td>19 (43.2)*</td>
</tr>
</tbody>
</table>

Values are given as n (%). Percentages are based on the total number of patients who had imaging during the specified time frame. *An imaging study performed at any time during the patient’s time in the cohort.

### Table 3. Medication use by imaging results and RF status

<table>
<thead>
<tr>
<th>Medication</th>
<th>First 6 months</th>
<th>Ever use*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>JSN+</td>
<td>JSN−</td>
</tr>
<tr>
<td>NSAID</td>
<td>21 (91.3)</td>
<td>55 (87.3)</td>
</tr>
<tr>
<td>MTX</td>
<td>22 (95.7)*</td>
<td>48 (76.2)</td>
</tr>
<tr>
<td>Oral corticosteroids</td>
<td>16 (69.6)</td>
<td>38 (60.3)</td>
</tr>
<tr>
<td>Intravenous corticosteroids</td>
<td>1 (4.4)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>IA corticosteroid injection</td>
<td>8 (34.8)</td>
<td>24 (38.1)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>5 (21.7)*</td>
<td>4 (6.4)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Any TNF− inhibitor</td>
<td>5 (21.7)*</td>
<td>4 (6.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RF+</th>
<th>RF−</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID</td>
<td>23</td>
<td>59</td>
</tr>
<tr>
<td>MTX</td>
<td>22</td>
<td>53</td>
</tr>
<tr>
<td>Oral corticosteroids</td>
<td>20 (76.9)</td>
<td>37 (54.4)</td>
</tr>
<tr>
<td>Intravenous corticosteroids</td>
<td>1 (3.9)</td>
<td>2 (2.9)</td>
</tr>
<tr>
<td>IA corticosteroid injection</td>
<td>6 (23.1)</td>
<td>30 (44.1)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>5 (19.2)</td>
<td>6 (8.8)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>1 (1.5)</td>
<td>3 (11.5)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>1 (3.9)</td>
<td>1 (1.5)</td>
</tr>
<tr>
<td>Any TNF− inhibitor</td>
<td>5 (19.2)</td>
<td>7 (10.3)</td>
</tr>
</tbody>
</table>

Values are given as n (%). *Medication was prescribed at any time during the patient’s time in the cohort. Any corticosteroid: oral corticosteroid, intravenous corticosteroids, IA corticosteroid injection or any combination. *Any TNF− inhibitor: etanercept, infliximab, adalimumab or any combination of these medications. *P < 0.05 for comparison of medication use between patients with and without the characteristic. JSN+: joint space narrowing/erosions present on imaging obtained within 6 months of first rheumatology clinic visit; JSN−: joint space narrowing/erosions not present on imaging obtained within 6 months of first rheumatology clinic visit. Defined as positive if titres were elevated on one or more occasions.

Patients who were older than 13.5 years at their first clinic visit were approximately 2-fold more likely to have evidence of joint damage on imaging obtained within their first 6 months of care (RR = 2.67; 95% CI 1.38, 5.16; P = 0.004). This RR remained elevated after adjustment for time between symptom onset and first clinic visit (≥6 months vs <6 months) and for RF status (RR = 2.21; 95% CI 1.14, 4.27; P = 0.55).

### Medication use

The majority of children in this cohort received one or more DMARDs during their first 6 months of care (Table 3). Twelve patients (11.5%) received a TNF-α inhibitor during their first 6 months of care. Additional medications that were used by small percentages of patients during the follow-up period included anakinra, aza (n = 1), ssz (n = 9), HCQ (n = 13) and rituximab.

There was an overall trend towards RF+ patients receiving more medications during their first 6 months of care (Table 3). When compared with patients who were RF−, RF+ patients were somewhat more likely to receive oral corticosteroids during their first 6 months of care (P = 0.05). Patients who had early radiographic evidence of joint damage also tended to receive more medications and were significantly more likely to receive MTX and etanercept (P = 0.04 for each) during their first 6 months of care (Table 3).

### Proportion of disease course with active disease

When each patient’s total duration of active disease was summed over their entire disease course patients spent a mean of 66.3% of their disease course with active disease (median 63%; range 7.3–100%) (Fig. 1). There was a weak, but statistically significant, negative correlation between proportion of disease course spent with active disease and duration of follow-up (r = −0.23; 95% CI −0.4, 0.04; P = 0.02).

RF+ patients spent an average of 73.8% of their course with active disease (median 73.9%; range 30.9–100%), while RF− patients who were older than 13.5 years at their first clinic visit were approximately 2-fold more likely to have evidence of joint damage on imaging obtained within their first 6 months of care (RR = 2.67; 95% CI 1.38, 5.16; P = 0.004). This RR remained elevated after adjustment for time between symptom onset and first clinic visit (≥6 months vs <6 months) and for RF status (RR = 2.21; 95% CI 1.14, 4.27; P = 0.55).
patients spent an average of 64.2% of their follow-up with active disease (median 58%; range 7.3–100%; P = 0.07).

Patients who had erosions or joint space narrowing on imaging within 6 months of their first clinic visit spent an average of 79% of their disease course with active disease (median 83.7%; range 27.4–100%). Those who did not spend an average of 58.5% with active disease (median 53.9%; range 7.3–100%; P < 0.001). Patients who had erosions or joint space narrowing on imaging at any time during their follow-up spent an average of 74.3% of their follow-up with active disease, whereas those who did not spent 60% with active disease (P = 0.01).

ID

A total of 1118 visits were analysed. Disease activity status was not classifiable for 89 of these visits (8%) and ESR and/or CRP data were available for 72% of the visits. Over the follow-up period, 83 patients achieved a total of 138 episodes of ID. The average episode length was 8 months (median 6 months; range 1–31.7 months). Approximately 50% of the patients in the cohort were in ID at their last clinic visit of the follow-up period.

Twenty-five patients (30.1%) achieved a minimum of one visit that met criteria for ID during their first 6 months of care. The majority of patients (78.3%) who achieved ID at some point during their follow-up achieved it during their first year of follow-up. Among children who achieved ID during their time in the cohort, the median duration of active disease from their first clinic visit to the first clinic visit with ID was 7.6 months (range 1–40.5 months). The median duration for RF+ patients was 8.5 months (range 3.3–42.7 months) and for RF− patients it was 7.6 months (range 1–40.5 months; P = 0.09). The median duration for patients who had evidence of joint damage on imaging studies obtained within their first 6 months of care was 7.9 months vs 7.3 months for children without evidence of joint damage (P = 0.8).

Children who received MTX and/or oral steroids within their first 6 months of clinic follow-up tended to be more likely to achieve ID during their first year of follow-up. RR was 1.77 (95% CI 1.01; 3.11; P = 0.01) for MTX and 1.41 (95% CI 0.97, 2.03; P = 0.05) for oral steroids. After adjustment for RF status and elevation of CRP or ESR at first clinic visit, the RRs were 2.03 (95% CI 0.84, 4.95; P = 0.01) and 1.37 (95% CI 0.95, 1.99; P = 0.74), respectively.

RF+ children were less likely to achieve ID during their first 6 months of follow-up (RR = 0.26; 95% CI 0.07, 1.03; P = 0.02) and somewhat less likely to achieve ID during their first year of follow-up (RR = 0.74; 95% CI 0.46, 1.18; P = 0.15). After adjustment for oral corticosteroid use during the first 6 months of care, the RRs were 0.23 (95% CI 0.06, 0.97; P = 0.97) and 0.69 (95% CI 0.43, 1.1; P = 0.77), respectively. None of the nine children who had > 1 RF+ titre achieved ID within their first 6 months of care. Patients aged 5.3–10 years were approximately 2-fold more likely to achieve ID during their first 6 months of care than children in the other age quartiles (RR = 2.23; 95% CI 1.11, 4.84; P = 0.02).

The proportion of children who had evidence of joint damage on imaging obtained within 6 months of their first clinic visit did not significantly differ from the rest of the cohort in the proportion who achieved ID within 6 months and 1 year.

Twenty-one patients did not achieve ID during their time in the cohort. These patients had significantly shorter duration of follow-up (20.5 vs 31.7 months; P = 0.002). These patients were also significantly less likely to have an imaging study obtained during their first 6 months of care than those who did achieve ID during their time in the cohort (RR = 0.34; 95% CI 0.17, 0.7; P = 0.005). There were no significant differences in medication use between patients who did and did not achieve ID during their time in the cohort.

The prevalence of active disease in this cohort and selected subgroups over time is summarized in Fig. 2. While there was an apparent decrease in the prevalence of active disease over the first year of follow-up, this decrease was not sustained after the first year of follow-up (Fig. 2A). RF+ patients tended to have a less rapid decrease in the prevalence of active disease over the first year of care than the RF− patients (Fig. 2B). Patients with early imaging evidence of joint damage tended to have a higher prevalence of active disease throughout the first three years of follow-up than did patients without these findings (Fig. 2C).

Remission

Fifty-one patients achieved 69 episodes of CRM. Sixty-nine of the 138 episodes of ID (50%) resulted in CRM. There were no episodes of CR Twenty-five patients were in CRM at their last clinic visit of the follow-up period. Median time to first episode of CRM was 16.2 months (mean 18.2; range 7.9–48.7 months). Patients who achieved CRM during their time in the cohort had significantly longer mean follow-up than those who did not (37.4 vs 21.7 months; P < 0.001). Patients who were followed up for ≥ 3 years were more likely to achieve CRM than patients who were followed up for < 3 years (RR = 1.52; 95% CI 1.07, 2.16; P = 0.02).

Forty-two percent (n = 11) of RF+ patients and 50% of RF− patients (n = 34) achieved CRM (P = 0.5).

Patients who had erosions or joint space narrowing on imaging obtained within their first 6 months of follow-up were significantly less likely to achieve CRM than those patients who did not (RR = 0.34; 95% CI 0.15, 0.76; P < 0.001), even though the mean duration of follow-up for this group (26.5 months) was not significantly different from patients who did not have these findings (30 months; P = 0.4).

Discussion

In this cohort, children with polyarticular JIA spent an average of 66.3% of their disease course with active disease, despite expected improvements in disease activity due to earlier prescription of
DMARDs and improved disease recognition. Children with early radiographic evidence of joint damage and children who had one or more positive RF titres tended to be less likely to achieve ID during their first 6 months of care, even though they also tended to receive more medications during their first 6 months of SCH care. Patients with early radiographic evidence of joint damage spent a significantly larger proportion of their disease course with active disease, and were less likely to achieve ID and CRM during their time in the cohort. RF$^+$ patients were less likely to achieve ID within their first 6 months of care and tended to spend a larger proportion of their disease course with active disease than the RF$^{-}$/C0 patients.

The retrospective cohort study by Wallace and colleagues [8, 9] described in the introduction was the first study to utilize the proposed definitions of ID and remission, and is the largest to describe the continuous disease course of each patient. The study included 437 patients from SCH and Italy, who had a minimum of 4 years of follow-up between the years 1980–99. Although the majority of children with oligoarticular JIA spent nearly 60% of their disease course with ID, 64% of the patients with RF$^{-}$ polyarticular JIA and 84% of the children with RF$^+$ polyarticular JIA spent $\geq$60% of their disease course with active disease. RF$^+$ patients spent a median of 16% of their follow-up with ID. Median duration of disease until first clinic visit with ID was 29 months for children with RF$^+$ polyarticular JIA and 23 months for children with RF$^{-}$ polyarticular JIA. These findings were confirmed in a small, retrospective, single-centre report from Brazil, in which children with polyarticular JIA were less likely to achieve and maintain ID when compared with the other JIA categories; however, the cohort included only 13 children with polyarticular JIA [16].

The data in this report provide a more current description of ID in polyarticular JIA and generate hypotheses requiring further study in prospective cohorts. Although many of our outcomes cannot be directly compared with these prior studies due to differences in cohort composition and duration of follow-up, it is of note that, similar to these prior reports, RF$^+$ children in this cohort tended to have more active disease and tended to achieve ID later than those who were RF$^{-}$. Although this association may be mitigated by early corticosteroid and/or MTX use, this assessment was limited by sample size. It is also important that the median time to first visit with ID in our cohort was 7.6 months, approximately half the duration reported by Wallace et al. [9]. We hypothesize that this improvement may be due to earlier disease recognition and earlier DMARD prescription. Children aged 5–10 years were more likely to achieve ID within 6 months in this cohort. The significance of this finding is unclear and, similar to the findings reported by Wallace, we did not observe any additional age effects. Although our sample size was too small to assess medication effects, there was a small
but statistically significant association between the use of oral corticosteroids and/or MTX within the first 6 months and the achievement of ID at 1 year.

Importantly, this is the first study to report the continuous disease course of children who had early radiographic evidence of joint damage. Prior studies have reported radiographic evidence of joint damage on studies obtained at diagnosis or within the first year of disease in ~30% of the children with JIA [17, 18]. Our data indicate a similar prevalence of early radiographic evidence of joint damage. In addition, in this cohort, patients with joint space narrowing and/or erosions on imaging studies obtained prior to or within the first 6 months of care were significantly less likely to achieve ID and CRM during their time in the cohort and had a higher prevalence of active disease throughout their first 3 years of follow-up. While this finding requires additional exploration in prospective cohorts, these data indicate that this subgroup may have particularly aggressive disease, even after adjustment for RF status and age at disease onset. Because imaging was not consistently obtained in this cohort, we do not have data regarding progression of these imaging findings. Furthermore, because the imaging data were obtained from reports only, we were unable to report these findings using standardized measures or to assess the severity of the damage.

This report is limited by its observational, single-centre design, short follow-up duration and reliance on retrospective chart review. We cannot account for missing and incorrect data or for changes in disease status between clinic visits. Importantly, we are unable to measure medication effects due to the small sample size and are unable to adjust for confounding by indication, as these data do not include accepted measures of baseline disease severity (active joint count and physician global assessment of disease activity). Patients received a large number of different medication combinations and we do not have medication dosages, route of administration or a measure of medication compliance, which further limited our ability to test for treatment effects.

Although these patients spent the majority of their disease course with active disease, and the prevalence of active disease plateaued at ~50%, we cannot determine whether the absolute levels of disease activity in this cohort were actually lower than those in previously published cohorts, as disease activity in this cohort was dichotomized into active vs inactive. Also, the reliance on observational data likely over-represents patients with the most severe disease as children with less severe disease would be more likely to be lost from the cohort. It is likely that we did not identify any episodes of CR for this same reason, along with the relatively short duration of follow-up and limitations of our data regarding medication use.

Despite these limitations, it is an important observation that these patients with polyarticular JIA spent an average of two-thirds of their follow-up with active disease. It will be important to determine the optimal timing and combination of therapies to achieve and maintain ID, and to attain CRM and CR. Patients with early radiographic evidence of joint damage and patients who are RF+ may be particularly likely to benefit from these interventions.

References