Comparison of Adults With Polyarticular Juvenile Idiopathic Arthritis to Adults With Rheumatoid Arthritis

A Cross-sectional Analysis of Clinical Features and Medication Use

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Background/Objective: Many individuals with juvenile idiopathic arthritis (JIA) have persistent disease into adulthood. Polyarticular JIA (pJIA) is often mislabeled as rheumatoid arthritis (RA) in adult rheumatology clinics, and treatment for adult pJIA patients is not well defined. We aimed to describe clinical features and medication use in the adult pJIA population in relation to an RA control cohort.

Methods: We performed a cross-sectional study of 45 adults with pJIA and 94 with RA seen from 2013 to 2017. Clinical characteristics including time to methotrexate initiation. With 0.70 years in RA patients (\( p < 0.01 \)) and TNFi use, particularly for etanercept, was sustained longer with a median drug survival of 4.41 years compared with 0.70 years in RA patients (\( p < 0.01 \)).

Conclusions: Although often considered together in adult rheumatology practice, adults with pJIA are distinct from patients with RA. Medication use markedly differed between the 2 populations with greater prevalence and duration of TNFi use in pJIA patients. Further study is needed to improve outcomes in this unique population.

Keywords: classification criteria, juvenile idiopathic arthritis, medications, rheumatoid arthritis, transition

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that pJIA patients would have earlier initiation of methotrexate (MTX) after diagnosis and more frequent anti-tumor necrosis factor (TNFi) use than RA patients.

PATIENTS AND METHODS

Study Design and Patient Population
We performed a cross-sectional study of adults with pJIA compared with a control RA cohort. All patients were older than 18 years at enrollment and seen through the Penn State Hershey Medical Center system. Adults with pJIA were seen by an adult rheumatologist from January 1, 2013, to June 1, 2015, and were previously diagnosed with pJIA by a pediatric rheumatologist. Available electronic medical records were reviewed for demographics, disease history including onset within the first 6 months with subsequent course, and detailed medication use. The ILAR JIA classification criteria were used to assign JIA subtype (R.R. J., N.L., D.M.F., and H.D.). A total of 67 JIA subjects were identified, of which 22 were excluded for not having a polyarticular disease course; the 45 remaining subjects with either an RF-positive or RF-negative polyarticular disease course were included for analysis. Polyarticular disease course was defined as arthritis affecting 5 or more joints after the first 6 months of disease. Because pJIA data were obtained through chart review and the disease onset history was often unavailable, we used a definition of polyarticular course for the adult pJIA, which, in addition to RF-positive and RF-negative pJIA subtype, potentially included patients with systemic-onset or extended oligoarticular JIA subjects.

A total of 164 adults with RA from the longitudinal Penn State Investigation of Remission in Rheumatoid Arthritis cohort were included for analysis. All RA patients were seen at the Penn State Hershey Rheumatology clinics for a diagnosis of RA by an adult rheumatologist from June 1, 2015, to June 1, 2017. Enrolled RA patients were diagnosed with RA by their rheumatologist, identified by the study coordinator (D.M.F.), underwent informed consent, and were enrolled in the study. Demographic information, disease history, and medication use were obtained from both electronic medical record review and patient-completed questionnaire. Data from the pJIA and RA cohorts were entered into respective Research Electronic Data Capture databases.16 Both studies were approved by the Pennsylvania State University Institutional Review Board, were conducted under Good Clinical Practice guidelines, and were in compliance with the Helsinki Declaration.

Data Extraction Definitions

Medical Record Extraction
Electronic medical record data from 2003 to present and laboratory and radiographic data from 1996 to present were available for review. Data on demographics, disease history, and medication use were extracted by the study coordinator (D.M.F.) and reviewed by a rheumatologist (R.R.J.) for accuracy. Additional information from RA patients on disease features and comorbidities was obtained through a subject-completed questionnaire.

Date of Study Enrollment
For RA patients, date of study enrollment was considered to be the day the patient completed informed consent. For adult JIA patients, date of study enrollment was considered to be the day of the most recent outpatient rheumatology visit in the aforementioned study period.

RESULTS

Demographics
Table 1 shows the demographic characteristics of adult pJIA and RA patients. Adult pJIA patients were unexpectedly younger than RA patients (27.4 vs. 56.1 years, \( p < 0.01 \)), and a higher proportion were female (88.9% JIA vs. 73.4% RA, \( p = 0.04 \)). The majority of patients were white (95.6% pJIA vs. 92.6% RA, \( p = 0.72 \)), and no patients were Hispanic. Patients with pJIA had a longer history of disease (20.6 vs. 11.1 years, \( p < 0.01 \)) compared with a control RA cohort. All patients were older than 18 years at enrollment and seen through the Penn State Hershey Medical Center system. Adults with pJIA were seen by an adult rheumatologist from January 1, 2013, to June 1, 2015, and were previously diagnosed with pJIA by a pediatric rheumatologist. Available electronic medical records were reviewed for demographics, disease history including onset within the first 6 months with subsequent course, and detailed medication use. The ILAR JIA classification criteria were used to assign JIA subtype (R.R. J., N.L., D.M.F., and H.D.). A total of 67 JIA subjects were identified, of which 22 were excluded for not having a polyarticular disease course; the 45 remaining subjects with either an RF-positive or RF-negative polyarticular disease course were included for analysis. Polyarticular disease course was defined as arthritis affecting 5 or more joints after the first 6 months of disease. Because pJIA data were obtained through chart review and the disease onset history was often unavailable, we used a definition of polyarticular course for the adult pJIA, which, in addition to RF-positive and RF-negative pJIA subtype, potentially included patients with systemic-onset or extended oligoarticular JIA subjects.

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Classification Criteria Methods
Both the 1987 and 2010 Criteria were used in this study for RA classification of both study populations.11,12 Scores were cumulative and not limited to those that were present on the date of study enrollment; if a patient met 1 specific component of classification criteria at any time, then he/she obtained the appropriate number of points toward his/her final score.

Medication Use
Medication use was classified as current, former, or never. Medications were considered to be currently used if the medication was actively listed in the patient's chart on the day of study enrollment. Medications were considered to be formerly used if they had been prescribed in the past but were not actively listed on the day of study enrollment. If chart review could not identify documentation of a specific medication, then that medication was considered never used. For each drug, start date, end date, and dose were extracted from each patient's medical record.

Time to Initiate MTX
The time to initiate MTX was defined as the time from the date of diagnosis to the time of MTX prescription. In some instances, the exact date was not known; in these cases, the best approximation was used.

Medication Survival
Medication survival was defined as the elapsed time from medication start date to medication end date. If the medication was continued through study enrollment, then date of enrollment was used as medication end date.

Statistical Analysis
All analyses were performed using SAS version 9.4 (Cary, NC), and figures were created using Python version 3.5. \( \chi^2 \) Tests for homogeneity or Fisher exact test and Student \( t \) test or Welch \( t \) test, where necessary, were used to test for differences in demographics, clinical features, and classification criteria between pJIA and RA patients. McNemar test was used to compare the proportion of RA patients who met the 1987 Revised ACR criteria versus the 2010 RA Criteria, as well as to compare the proportion of adult JIA patients who met these 2 sets of criteria.

Cross-sectional comparison of medication use at time of study enrollment was performed using \( \chi^2 \) tests for homogeneity with Fisher exact test where appropriate. The Wilcoxon rank-sum test was used to evaluate median drug survival time for TNFi after adjusting for overall disease length. To compare time to MTX initiation between pJIA and RA patients, Kaplan-Meier survival curves were constructed for initial analysis and a Weibull accelerated failure-time model was developed to adjust for overall disease length and sex. \( p < 0.05 \) was considered statistically significant, and adjustment for multiple comparisons was performed where necessary, using Bonferroni method.

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and were less likely to be current smokers (6.8% vs. 19.2%, \( p = 0.06 \)). A higher proportion of RA than adult pJIA patients tested positive for RF (78.3% vs. 29.0%, \( p < 0.01 \)) and anti–cyclic citrullinated peptide (CCP) (74.4% vs. 28.6%, \( p = 0.02 \)).

### Classification Criteria

The proportion of patients who met the 1987 Criteria and 2010 RA Criteria was determined for each group (Table 2). More RA patients met the 1987 Criteria (88.3%) compared with the 2010 Criteria (71.1%, \( p = 0.04 \)). Conversely, more pJIA patients met the 1987 RA Criteria (71.1%) compared with the 2010 Criteria (46.7%, \( p < 0.01 \)). Although there was no difference in the odds of pJIA or RA patients meeting the 1987 Revised ACR Criteria (odds ratio [OR], 0.67; 95% confidence interval [CI], 0.30–1.50; \( p = 0.32 \)), pJIA patients had lower odds than RA patients of meeting the 2010 Criteria (OR, 0.12; 95% CI, 0.05–0.27; \( p < 0.01 \)). Adult pJIA patients also were less likely to meet either classification criteria compared with RA patients (OR, 0.19; 95% CI, 0.07–0.54; \( p < 0.01 \)).

### Medication Use

Medication use in pJIA and RA patients was determined at the time of study enrollment (Table 3). More JIA patients (66.7%) had a history of previously using MTX compared with RA patients (39.4%, \( p = 0.01 \)). However, there was no statistically significant difference between current MTX use (24.4% of JIA vs. 41.5% of RA, \( p = 0.15 \)) or never use (8.9% of JIA vs. 19.2% of RA, \( p = 0.36 \)). More adult RA patients were currently using hydroxychloroquine (HCQ) (35.1%) compared with adult pJIA patients (6.7%, \( p < 0.01 \)). Similarly, previous HCQ use was more common in RA patients (31.9%) compared with adult pJIA patients (13.3%, \( p = 0.06 \)); pJIA patients were more likely to have never used HCQ (80.0%) compared with RA patients (33.0%, \( p < 0.01 \)). Leflunomide was rarely used in either group, and no differences were observed between pJIA and RA patients. While sulfasalazine was also used infrequently, RA patients were less likely to have used it in the past compared with pJIA patients (25.5% vs. 46.7%, \( p = 0.04 \)).

Adult pJIA patients were more likely to be currently using etanercept (33.3%) compared with RA patients (8.5%, \( p < 0.01 \); Table 4); conversely, RA patients were more likely to have never used etanercept (60.6%) compared with JIA patients (31.1%, \( p < 0.01 \)). Previous use of etanercept was not different between pJIA (35.6%) and RA patients (30.9%, \( p = 1.00 \)). Adult pJIA patients were more likely to be currently using any TNFi compared with RA patients (48.9% JIA vs. 18.1% RA, \( p < 0.01 \)), although previous use of TNFi was similar between groups (31.1% JIA vs. 30.9% RA, \( p = 1.00 \)). Rheumatoid arthritis patients were more likely to have never used any TNFi (51.1%) compared with adult JIA patients (20.0%, \( p < 0.01 \)). Abatacept and rituximab were rarely used in either population, and there was no significant difference in their use between pJIA and RA patients.

### Time to Initiate MTX

Given that MTX is the criterion-standard first-line drug in both cohorts, the time from disease diagnosis to MTX initiation was compared between groups. This analysis was carried out for patients with both disease diagnosis and MTX start date information available, which was 31 adult pJIA and 90 RA patients. Among these, 4 adult JIA and 23 RA patients had a known diagnosis date and had never used MTX; these patients were right censored.

Overall, the unadjusted median time to MTX initiation in months for JIA patients was 114.0 and for RA patients was 16.8 (\( p = 0.02 \); Fig. A). A significant association of time to MTX initiation with disease length was also observed (\( p < 0.01 \)); for both pJIA and RA patients with a disease length of 10 years or less, the

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**TABLE 1.** Demographics of Adult pJIA and RA Patients

| Variable | JIA (n = 45), Mean (SD) or n (%) | RA (n = 94), Mean (SD) or n (%) | \( p \) value |
|----------|---------------------------------|---------------------------------|-------------|
| Age, y   | 27.4 (9.3)                      | 56.1 (13.2)                     | <0.01       |
| Sex, % female | 40 (88.9%)                     | 69 (73.4%)                      | 0.04        |
| Body mass index, kg/m\(^2\) | 28.64 (8.84)               | 29.68 (7.16)                     | 0.46        |
| White\(^a\) | 43 (95.6%)                      | 87 (92.6%)                      | 0.72        |
| Hispanic | 0                               | 0                               | —           |
| Current smoker | 3 (6.8%)\(^b\)            | 18 (19.2%)                      | 0.06        |
| Disease length, y | 20.6 (10.6)               | 11.1 (10.1)                      | <0.01       |
| RF\(^+\) | 9/31 (29.0%)                    | 65/83 (78.3%)                   | <0.01       |
| CCP\(^a\) | 1/7 (28.6%)                     | 58/78 (74.4%)                   | 0.02        |

\(^a\)Fisher exact test was used.  
\(^b\)One pJIA subject had unknown smoking status.

**TABLE 2.** Proportion of Patients Meeting 1987 Revised ACR and 2010 ACR/EULAR Classification Criteria for RA

| Criteria          | JIA | RA | OR\(^a\) | 95% CI | \( p \) value |
|-------------------|-----|----|----------|-------|-------------|
| Met 1987 RA Criteria | 71.1% | 78.7% | 0.67 | (0.30–1.50) | 0.32 |
| Met 2010 RA Criteria | 46.7% | 88.3% | 0.12 | (0.05–0.27) | <0.01 |
| Met either 1987 or 2010 RA Criteria | 73.3% | 93.6% | 0.19 | (0.07–0.54) | <0.01 |

\(^a\)Odds ratio of meeting classification criteria for pJIA patients compared with RA patients. Of the 6 RA patients not meeting either criteria, 3 patients had spontaneous drug-free remission, and 3 patients had long RA disease duration in remission on combination DMARDs, but presenting history was unavailable.
median number of months from diagnosis to MTX initiation was 3.0. For pJIA and RA patients with a disease length of more than 10 years, the median time from diagnosis to MTX initiation was 108.7 months (p < 0.01). After adjustment for disease length, there was no significant difference in time to MTX initiation between pJIA and RA patients (hazard ratio [HR], 1.34; 95% CI, 0.81–2.22; p = 0.25; Fig. B). However, disease length remained a significant predictor of time to MTX initiation; for each additional year of disease length, the average time to MTX increased by 14% (HR, 1.14; 95% CI, 1.11–1.17; p < 0.01; Fig. B).

Medication Survival

Median survival time for use of etanercept, infliximab, and adalimumab was compared in pJIA and RA patients (Table 5). Among patients who ever used etanercept, the median survival time was longer in pJIA patients (4.4 years) compared with RA patients (0.7 years, p < 0.01). Median survival time of infliximab in pJIA patients (0.5 years) was not significantly different from RA patients (3.2 years, p = 1.00); nor was there a difference in median survival time of adalimumab between pJIA (2.0 years) and RA (0.8 years, p = 1.00). However, overall TNFi survival was longer in pJIA patients compared with RA patients (6.6 vs. 2.3 years, p < 0.01).

**DISCUSSION**

Adult rheumatologists face challenges caring for and managing pJIA patients.15 Regardless of whether pJIA patients progress smoothly through a well-designed transition from pediatric to adult rheumatology or present after years of lack of care from loss of health insurance, the ideal management of these patients with established disease and multiple comorbidities has not been studied in randomized controlled trials.8,10,18 This gap in clinical knowledge is highlighted by data showing that adult rheumatologists assign a diagnosis of RA to 45% of JIA patients immediately after transition from pediatric care.8 In the present single-center cross-sectional study, we assessed clinical features, RA classification according to the 1987 and 2010 Criteria, and medication use in 45 pJIA patients, compared with 94 RA patients. Our study provides a pragmatic look at the pJIA adult population and shows it to be a population unique from RA.

Individuals with pJIA were, as expected, younger, but also almost 90% were female, and disease duration was longer compared with RA subjects, which were not expected findings. Rheumatoid factor–negative polyarthritis was the predominant subtype of JIA in our cohort, consistent with what is known about this disease. Fewer than 50% of pJIA subjects met the 2010 Criteria, whereas more than 70% met the 1987 RA classification criteria; pJIA subjects had 88% lower odds of meeting the 2010 Criteria compared with RA patients. Our findings build on the study by Oliveira-Ramos et al.,19 in which 36 (57.1%) of 65 RF-negative pJIA patients met the 2010 Criteria, whereas 65 (95.6%) of 68 RF-positive pJIA subjects met the 2010 Criteria.

A closer look at the 1987 and 2010 RA Criteria explains the difference. The 2010 Criteria were optimized for early RA diagnosis, placing emphasis on acute inflammatory markers, high-titer RF or CCP antibodies, and high numbers of inflamed joints.20 Conversely, the 1987 Revised ACR RA classification criteria consider presence of joint damage and rheumatoid nodules, features of long-standing disease. Differences in the weighting of RF and CCP antibodies in these 2 classification criteria may explain why pJIA patients were less likely to meet the 2010 Criteria. For example, a patient with high-titer RF and/or CCP antibodies is given 3 (50%) of the 6 points needed for an RA diagnosis, regardless of the pattern or extent of joint involvement. In the 1987 Criteria, CCP was not included, and the presence of RF assigns

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**TABLE 3. DMARD Medication Use in Adult pJIA and RA Patients**

| Drug          | JIA (n = 45) | RA (n = 94) | p value |
|---------------|-------------|-------------|---------|
| Methotrexate  |             |             |         |
| Current       | 11 (24.4%)  | 39 (41.5%)  | 0.15    |
| Past          | 30 (66.7%)  | 37 (39.4%)  | 0.01    |
| Never         | 4 (8.9%)    | 18 (19.2%)  | 0.36    |
| HCQ           |             |             |         |
| Current       | 3 (6.7%)    | 33 (35.1%)  | <0.01   |
| Past          | 6 (13.3%)   | 30 (31.9%)  | 0.06    |
| Never         | 36 (80.0%)  | 31 (33.0%)  | <0.01   |
| Leflunomide   |             |             |         |
| Current       | 3 (6.7%)    | 1 (1.1%)    | 0.19    |
| Past          | 3 (6.7%)    | 18 (19.2%)  | 0.16    |
| Never         | 39 (86.7%)  | 75 (79.8%)  | 0.97    |
| Sulfasalazine |             |             |         |
| Current       | 1 (2.2%)    | 8 (8.5%)    | 0.48    |
| Past          | 21 (46.7%)  | 24 (25.5%)  | 0.04    |
| Never         | 23 (51.1%)  | 62 (66.0%)  | 0.28    |

All p values are adjusted for multiple comparisons using Bonferroni method.

*a-Fisher exact test used.

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**TABLE 4. Biologic Medication Use in Adult pJIA and RA Patients**

| Drug          | JIA (n = 45) | RA (n = 94) | p value |
|---------------|-------------|-------------|---------|
| Etanercept    |             |             |         |
| Current       | 15 (33.3%)  | 8 (8.5%)    | <0.01   |
| Past          | 16 (35.6%)  | 29 (30.9%)  | 1.00    |
| Never         | 14 (31.1%)  | 57 (60.6%)  | <0.01   |
| Infliximab    |             |             |         |
| Current       | 1 (2.2%)    | 4 (4.3%)    | 1.00    |
| Past          | 5 (11.1%)   | 11 (11.7%)  | 1.00    |
| Never         | 39 (86.7%)  | 79 (84.0%)  | 1.00    |
| Adalimumab    |             |             |         |
| Current       | 6 (13.3%)   | 5 (5.3%)    | 0.30    |
| Past          | 7 (15.6%)   | 18 (19.2%)  | 1.00    |
| Never         | 32 (71.1%)  | 71 (75.5%)  | 1.00    |
| All a-TNF     |             |             |         |
| Current       | 22 (48.9%)  | 17 (18.1%)  | <0.01   |
| Past          | 14 (31.1%)  | 29 (30.9%)  | 1.00    |
| Never         | 9 (20.0%)   | 48 (51.1%)  | <0.01   |
| Abatacept     |             |             |         |
| Current       | 2 (4.4%)    | 7 (7.5%)    | 1.00    |
| Past          | 3 (6.7%)    | 9 (9.6%)    | 1.00    |
| Never         | 40 (88.9%)  | 78 (83.0%)  | 1.00    |
| Rituximab     |             |             |         |
| Current       | 3 (6.7%)    | 1 (1.1%)    | 0.19    |
| Past          | 4 (8.9%)    | 7 (7.5%)    | 1.00    |
| Never         | 38 (84.4%)  | 86 (91.5%)  | 0.63    |

All p values are adjusted for multiple comparisons using Bonferroni method.

*a-Fisher exact test used.

a-TNF indicates TNF inhibitors.
FIGURE. Time to MTX initiation. A, Median time to MTX for JIA patients = 114.0 months, RA patients = 16.8 months ($\chi^2 = 5.41$, $p = 0.02$).

B, Disease length (>10 vs. $\leq$10 years), HR, 1.14 (95% CI, 1.11–1.17; $p < 0.01$); diagnosis (JIA vs. RA), HR, 1.34 (95% CI, 0.81–2.22; $p = 0.25$).

After adjustment for disease length, no significant association between time to MTX and diagnosis type was observed. Color online-figure is available at http://www.jclinrheum.com.

TABLE 5. TNFi Medication Survival (Years)

| Drug          | JIA, n | JIA, Median$^a$ (IQR) | RA, n | RA, Median$^a$ (IQR) | $p$ value |
|---------------|--------|-----------------------|-------|----------------------|-----------|
| Etanercept    | 30     | 4.41 (2.50–8.93)      | 30    | 0.70 (1.42–2.32)     | $<0.01^b$ |
| Infliximab    | 5      | 0.53 (0.17–5.21)      | 8     | 3.16 (2.58–5.50)     | 1.00$^b$  |
| Adalimumab    | 12     | 2.03 (1.00–6.78)      | 19    | 0.75 (0.46–1.53)     | 1.00$^b$  |
| Total TNF     | 35     | 6.61 (2.96–10.24)     | 38    | 2.25 (0.98–5.63)     | $<0.01$   |

Some subjects used more than 1 TNFi over the time course of their disease.

$^a$Time in years.

$^b$Adjusted for multiple comparisons using Bonferroni method.

IQR indicates interquartile range.
only 1 point (25%) out of 4 needed for RA classification. With the advent of CCP testing and increased emphasis on early diagnosis in adult RA, understanding and classification of these 2 diseases, pJIA and RA, have diverged. Whereas RF-positive pJIA is often thought to have similar underlying pathophysiology to adult RA, RF-negative pJIA has more varied clinical features compared with RA.1-21 To our knowledge, this study is the first to compare the 1987 and 2010 RA Criteria in adult pJIA and emphasizes that these former pediatric patients, particularly the RF-negative subset, are a distinct clinical entity for whom further study is needed to determine optimal management. Adult rheumatologists would benefit from increased familiarity with the ILAR JIA classification criteria to optimally care for the pJIA population.2

Regarding medications used in the pJIA population, we started with investigating MTX as it is the current cornerstone DMARD in both pJIA and RA treatment recommendations.13-14,17 Methotrexate has been shown to be effective in both JIA and in moderate to severe RA.22,23 Current MTX use did not differ between groups, but adult pJIA subjects had increased prevalence of previous use of MTX (p = 0.01, Table 3). Theoretical explanations for the increased former (but not current) MTX use in pJIA include lack of efficacy, desire to drink alcohol, and/or concerns regarding potential pregnancy and fetal toxicity in young adults. Traditionally, pJIA treatment response to MTX has been observed as MTX nonresponders versus responders, and this is emphasized in the 2011 ACR treatment recommendation for JIA.13 After MTX failure in pJIA, rather than subsequently adding other nonbiological therapy to MTX as is done in RA such as triple therapy of MTX, sulfasalazine, and HCQ,15,24 biological therapy with TNFi as monotherapy is often the next step in pJIA, rather than combination nonbiological therapy. Our findings of increased former MTX use in the adult pJIA population suggest that future studies are needed to evaluate if combination nonbiologic therapy would be effective in this adult pJIA population. Preliminary studies in pediatric pJIA show promise with this approach.13,25,26

Hydroxychloroquine utilization was significantly lower in adult pJIA than in RA (Table 3). This finding correlates with longstanding level A treatment recommendations against the use of HCQ in pJIA.13 However, these recommendations are based on a single 1986 study of penicillamine and HCQ in severe juvenile RA (JRA).27 Juvenile RA was the terminology used prior to the ILAR classification; negative results of this 30-year-old study in JRA patients may not apply to the JIA patient population. In adult RA, HCQ is often used for mild disease or in combination with other traditional or biologic DMARDs.28,29 Potentially, HCQ could be utilized by adult rheumatologists for adult pJIA patients, although ideally the effectiveness of HCQ in combination with other DMARDs would need to be studied in this population.

Early DMARD initiation improves long-term outcome in RA patients.30 The 1990s witnessed an explosion of evidence in both JIA and RA supporting early MTX initiation. In 1992, MTX was shown to be effective in JRA, with a preponderance of evidence that earlier initiation of MTX led to improved outcomes.22,23,31,32 Although adult pJIA patients in our study appeared to initiate MTX later after disease diagnosis compared with RA patients, this is explained, at least in part, by the difference in disease length between these 2 cohorts (Figure, B). Median time to MTX for pJIA and RA patients diagnosed within the past 10 years was 3.0 months, compared with 108.7 months in pJIA and RA patients diagnosed more than 10 years prior to enrollment. The primary reason for this vast difference in time to MTX initiation is unclear but may be multifactorial. One possible explanation is delay to specialized care; some patients were not seen by a pediatric rheumatologist until years after pJIA onset. Another possible factor may be recall bias, which is inherent to all retrospective studies; this may be especially problematic in pJIA subjects with longer disease duration and onset during childhood years when parents were mainly responsible for medical care. However, recall bias alone is unlikely to explain the observed difference. With the development of new therapeutics and evidence-based medicine,33 we suspect that the earlier use of MTX over the past decade in both RA and pJIA reflects overall improvement in awareness of how to more optimally care for this population.

Our study adds to previous reports of effectiveness of TNFi in the adult pJIA population.34,35 Etanercept and adalimumab are both approved for use in JIA,36,37 and infliximab may be prescribed in the United States off-label.36 Although standard disease outcome data are unavailable in this study, the high prevalence of current TNFi use (48.9% pJIA vs. 18.1% RA) and long survivability of TNFi overall (6.6 vs. 2.3 years) attest to the effectiveness of TNFi medications in the adult pJIA population. To our knowledge, this may be the first US adult pJIA cohort to confirm these findings. Although these results may not be surprising to pediatric rheumatologists, the increased medication survivability is striking compared with the RA population and was an unexpected result. Etanercept, since US Food and Drug Administration approval in 1998 for RA and in 1999 for pJIA, has been associated with improvement of not only short-term JIA outcomes but also long-term quality of life and functional outcomes in the pJIA population.37,38 These results mirror the TNFi use by pediatric rheumatology in which 44% of JIA patients used TNFi similar to the 49% of pJIA subjects in our study who were treated with TNFi.39 The medication survivability data support the overall effectiveness of etanercept in this cohort and confirm results of other studies indicating that TNFis are an important treatment option for the adult pJIA population.40 When pJIA subjects are transitioned to adult rheumatology, negative serology should not counter understanding of disease responsiveness and continued use of TNFi medications.

This cross-sectional investigation categorizes unique clinical features and medication use patterns in adults with pJIA. Long-term outcome studies in pJIA are rare in the United States, and our study makes use of a cohort of 45 pJIA subjects with a long mean disease duration of 20.6 years. The electronic medical record available at our institution and continuity of provider care enabled detailed medication and laboratory review with laboratory data available since 1996 and electronic notes since 2003. We confirm that the adult pJIA population is more likely to be seronegative, female, and less likely to meet the 2010 RA Criteria. The medication use investigation is highlighted by the increased prevalence and survivability of TNFi use in the pJIA population.

The study does have limitations. Classification criteria were determined based on chart review; because some patients had disease onset before the electronic medical record became available, early joint count documentation and RF and CCP serology may be unavailable or subject to recall bias. We used a polyarticular disease course to capture the RF-positive and RF-negative pJIA, but this definition may also include extended oligoarticular and systemic-onset subjects in which onset records were not available. Differences in time of diagnosis and disease duration between the pJIA and RA patients may affect the results. Both cohorts had long-standing disease (20 years for pJIA and 11 years for RA) and differences in medication use may reflect treatment advances over the previous 2 decades, particularly the increased availability of biologics over this time period. The time to MTX initiation analysis controlled for differences in disease duration between pJIA and RA patients. Differences in disease duration between the pJIA and RA patients may have affected the other medication use findings, but low sample size limited the ability to adjust for this effect. Additional limitations in the findings are that the data were collected from different time points for both cohorts.
(2013–2015 for pJIA and 2015–2017 for RA). The reason for this variability was that some pJIA patients had transitioned out of our health system by 2015 when the RA cohort was initiated. However, reassuringly, available traditional and biologic DMARDs did not change substantially during this period, and treatment differences are unlikely to be affected by the difference in data collection times. Other limitations include that the majority of pJIA patients were referred from a single pediatric rheumatologist and may not reflect care of pJIA by the larger community of pediatric or adult rheumatology. Conversely, the medication use pattern by adult rheumatology at our institution is supported by similar medication use frequencies by the pediatric rheumatology community at large.\textsuperscript{39} Given the historic nature of this study, clinical features, particularly serologies, were not available on all patients, which also somewhat limit the impact of the findings. However, despite these limitations, the study provides a practical assessment from the adult rheumatologist’s perspective that directly compares the pJIA patients to RA counterparts and highlights differences in clinical features and medication uses. The data confirm other reports of effectiveness of TNFi in this population suggesting that it reflects current practice. Future studies are needed to investigate and improve treatment outcomes in this unique adult population.

KEY POINTS

1. Adult patients with pJIA are a distinct clinical population from RA, as shown by lack of concordance with the 2010 ACR/EULAR RA Classification Criteria.
2. Medication use in adults with pJIA is unique and notable for increased overall frequency of TNFi use and strikingly increased medication survival of etanercept compared with patients with RA.
3. Negative RF and CCP antibodies should not discourage continued use of TNFi in pJIA patients who transfer to adult care.
4. Further study to characterize the long-term outcomes of pJIA is needed to improve the use of targeted therapies to improve outcomes.

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