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Treatment of Patients with Juvenile Idiopathic Arthritis (JIA) in a Population-Based Cohort

Jorge A. Zamora-Legoff, **Megan L. Krause**, **Cynthia S. Crowson**, **Theresa Wampler Muskardin**, **Thomas Mason**, and **Eric L. Matteson**

Division of Rheumatology; Division of Biomedical Statistics and Informatics, Department of Health Sciences Research; Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, MN, USA

Abstract

Objective—A population-based cohort was utilized to evaluate medication and intraarticular injections utilization for patients with juvenile idiopathic arthritis (JIA).

Methods—In a geographically defined population, all incident cases of JIA cases were identified between January 1, 1994 and December 31, 2013 based first on diagnosis code followed by medical chart confirmation. Medications and intraarticular glucocorticoid injections were abstracted. Predictors of first disease modifying antirheumatic drug (DMARD)/biologic and injections were reported as a hazard ratio (HR) with 95% confidence intervals (CI) adjusted for age and sex. Kaplan-Meier methods evaluated therapy at 6 months and 1 year. Injections were reported per 100 person-years (py) with 95% CI using Poisson methods.

Results—Seventy-one incident cases were identified. Forty-two (59%) were female with mean age (standard deviation) at diagnosis of 8.2 (5.3) years. Twenty-six (37%) utilized at least 1 DMARD or biologic, which in 77% of these was prescribed in the first 6 months. Subtype of JIA was significantly associated with DMARDs/biologics ($p<0.001$). Intraarticular injections were performed in 48%. The rate of intraarticular injections was 20.7 per 100 py (95% CI 16.5, 25.6). The rate of joint injections was higher in the first year after diagnosis ($p<0.001$) and more common in recent years ($p<0.001$).

Conclusion—The majority of patients with JIA in a modern population-based cohort do not require DMARDs or biologics. In those who do, the majority receive these within the first 6 months. Intraarticular injections were utilized in almost half of patients with JIA and were increasingly used.

Increasing options are fortunately available for treatment for juvenile idiopathic arthritis (JIA) including biologic therapies (1). However, more recently available medications are not without potential side effects in addition to cost (2). The need for medication management and escalation of therapy is impacted by multiple factors including JIA subtype and the number of joints involved (1). The most recent American College of Rheumatology (ACR)

Corresponding Author/Request for Reprints: Eric L. Matteson, 200 First Street SW, Rochester, MN 55905, Phone: 507-284-8450, Fax: 507-284-0564, Matteson.eric@mayo.edu.

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guidelines utilize the number of joints to help guide management of these children with early adoption of methotrexate in situations of high disease activity and poor prognostic factors followed by tumor necrosis factor (TNF) inhibitors if disease activity is unable to be controlled promptly (1).

The distribution of subtype and severity of JIA is likely different when evaluated in referral center populations as compared to a population-based cohort (3, 4). Therefore, the utilization of medications likely varies in part due to the studied population. Further, ultrasound technology is increasingly available which may make intraarticular injections more appealing as an option in therapy (5).

This study sought to evaluate trends in medication use and intraarticular glucocorticoid injections in a modern population-based cohort of patients with JIA. This cohort represents the spectrum of severity of JIA to evaluate routine management of patients with JIA. Further, this cohort spans the timeframe of approval of biologics to evaluate their adoption.

Methods

Patient Cohort

Incident cases of JIA who met ILAR criteria between January 1, 1994 and December 31, 2013 were identified in Olmsted County, Minnesota utilizing the Rochester Epidemiology Project (6, 7). Initially, diagnosis codes were utilized followed by medical record review to confirm. Further details regarding the search are available in previously published work (8). Patients were followed retrospectively through their medical records until death, migration from Olmsted County or December 31, 2014.

Information regarding medications and intraarticular glucocorticoid injections was obtained via review of the complete medical record. If the patient received an injection or medication by an institution outside of Olmsted County, Minnesota and this was referenced in the medical record, it was also recorded.

Additional demographic information including age and sex as well as JIA features including subtype, joint involvement at diagnosis, time from symptom onset to diagnosis, laboratory studies at diagnosis (hemoglobin, leukocytes erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]) and serologic data (anti-nuclear antibody [ANA], anti-cyclic citrullinated peptide [ACPA], rheumatoid factor [RF], and HLA-B27) were obtained.

Statistical Analysis

Descriptive statistics (means, percentages, etc.) were used to summarize the characteristics of the study population. Cox models adjusted for age and sex were used to examine potential predictors of use of the first DMARD/biologic and intraarticular glucocorticoid injection. Results were reported with hazard ratios (HR) with 95% confidence intervals (CI). Kaplan-Meier methods were utilized to estimate the percentage of the cohort with medication use and occurrence of intraarticular glucocorticoid injections at 6 months and 1 year after diagnosis of JIA. Intraarticular glucocorticoid injection rates were also reported as rate per 100 person-years with corresponding 95% CI using Poisson methods, since each patient

could have multiple injections. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and R 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient Cohort

There were 71 incident cases of JIA identified. The mean age of diagnosis was 8.2 (5.3) years with 42 (59%) females (Table 1). The mean length of follow-up after diagnosis was 8.5 (5.8) years. The most common JIA subtype was oligoarticular disease occurring in 45 (63%). Polyarthritis occurred in 9 (12%). Unclassified based on the JIA criteria (either not meeting criteria for any subtype or meeting categorization for 2 subtypes) occurred in 12 (17%). Systemic (2, 3%), psoriatic arthritis (2, 3%), and enthesitis related arthritis (1, 1%) all occurred uncommonly.

Medications

All patients were treated with at least 1 NSAID over the course of their follow-up. Twenty-six (37%) patients were treated with a DMARD over the course of their follow-up. The most common DMARD was methotrexate, utilized in 25 (35%). This was followed in terms of frequency by hydroxychloroquine in 7 (10%) and sulfasalazine in 6 (8%). No other oral immunosuppressant was used in this cohort.

Biologic therapy was used in a minority (9, 13%). All patients who were treated with a biologic had received at least 1 DMARD prior to initiation of the biologic. Nine (13%) patients were treated with TNF inhibitors. One (1%) patient was treated with an IL-1 inhibitor.

Systemic glucocorticoids were used in 19 (27%) over the course of their follow-up. When combining DMARDs, biologics, and systemic glucocorticoids, 32 (45%) received at least 1 of these during their follow-up.

JIA subtype was significantly associated with utilization of a DMARD or biologic ($p<0.001$; Table 2). Patients with polyarthritis were more likely to require medications than those with oligoarthritis (HR 13.2; 95% CI 4.9, 35.3). Joint involvement at diagnosis specifically elbow ($p=0.001$), wrist ($p<0.001$), metacarpophalangeal joint (MCP) ($p<0.001$), and proximal interphalangeal (PIP) joint ($p<0.001$) were associated with use of DMARDs or biologics. The presence of tenosynovitis at diagnosis was also associated with use of first DMARD or biologic (HR 4.2, 95% CI 1.2, 15.2). Age, sex, calendar year of diagnosis, and time from symptom onset to diagnosis were not associated with the use of DMARDs or biologics.

An abnormal ESR (≥25 mm/1 hour) at diagnosis was marginally associated with use of a first DMARD/biologic (HR 2.4; 95% CI 1.0, 5.6). In contrast, hemoglobin at diagnosis, leukocytes at diagnosis, CRP, ANA, RF, ACPA, and HLA-B27 were all not associated with risk of DMARD or biologic use.

Overall, 28% of patients had received a DMARD or biologic within the first 6 months after diagnosis, which is the majority of the 37% who would receive it at some time during follow-up. By 1 year after diagnosis, this had increased slightly to 31% and to 34% by 2 years. When comparing by JIA subtype at 6 months after diagnosis, 13% of those with oligoarthritis were receiving DMARD or biologic as compared to polyarthritis 89%.

Joint Injections

In total, 34 (48%) patients had at least 1 joint injection. Most commonly patients received a single injection (15, 21%). Of those who received an injection, the occurrences of injections was 1-13 with the number of joints injected at a single occurrence ranging from 1-7.

In terms of site, the knee was the most commonly injected joint and accounted for 49% of the injections. Ankles (13%), hips (10%), and wrists (9%) were the next most commonly injected joints. The remaining 19% included shoulders, elbows, metacarpophalangeal joints, proximal interphalangeal joints, carpal tunnel, and metatarsophalangeal joints.

The overall rate of injections was 20.7 (95% CI 16.5, 25.6) per 100 person-years. JIA subtype was not associated with joint injections (p=0.98, Table 3). For oligoarthritis, the rates were 19.4 (95% CI 14.5, 25.6) per 100 person-years, for polyarthritis 30.5 (95% CI 16.7, 51.2) per 100 person-years, and for undifferentiated arthritis 22.5 (95% CI 12.9, 36.6) per 100 person-years.

The use of injections became more common over the duration of the study. Calendar year of diagnosis was associated with utilizing an injection in management with a 12% increase in injections per year during the study period (HR 1.12, 95% CI 1.05, 1.20). The rate of injections in 1994-2003 was 11.1 (95% CI 6.0, 18.6) per 100 person-years compared to 24.9 (95% CI 19.5, 31.5) in 2004-2014. Age, sex, and time from symptom onset to diagnosis were not associated with the use of joint injections.

Disease duration also appeared to influence the rates of joint injections. Within the first year of diagnosis, the rate was highest at 54.6 (95% CI 38.6, 75.0) per 100 py. Rates were lower subsequently (year 1-4 following diagnosis: 11.7, 95% CI 7.4, 17.6); year 5-9: 18.4, 95% CI 11.1, 28.7; and 10+ years: 11.7, 95% CI 3.8, 27.3 per 100 py).

A positive ANA was also associated with first joint injection (HR 2.58; 95% CI 1.16, 5.74). Other laboratory tests including hemoglobin at diagnosis, leukocytes at diagnosis, ESR at diagnosis, CRP at diagnosis, ACPA, and HLA-B27 were not associated with the use of injections. The first intraarticular injection of glucocorticoid was administered within the first 6 months of disease in 30% of patients. This rate increased to 35% by 1 year, which is the majority of the 48% that would ultimately receive these injections at some time during followup. In patients with oligoarthritis, 36% had the first injection by 6 months and 38% by 1 year. For patients with polyarthritis, 22% had within the first 6 months and 33% within the first year.

Medication and Intraarticular Injection Combination Regimens

At 6 months, 38 (54%) of patients were treated with NSAIDs only, which decreased to 34 (48%) by 1 year. A further12 (17%) were treated with only DMARDs, biologics, or systemic glucocorticoids at 6 months and 1 year. Eleven (15%) of patients were treated with joint injections without any additional DMARD, biologic, or systemic glucocorticoids at 6 months and 12 (17%) at 1 year. Those who were treated with both injections and DMARDs/biologics/systemic glucocorticoids accounted for 10 (14%) at 6 months and 13 (18%) at 1 year.

Discontinuation Rates

Of the 26 patients who received DMARDs or biologics, only 7 (27%) were able to discontinue medications for at least 1 year. Discontinuation rate at 1 year was 4% ± 4%, 2 years 20% ± 8%, 5 years 30% ± 10%, and at 10 years 61% ± 18%.

Follow-up

At the time of last follow-up, 35 (49%) were on some medication including NSAIDs, DMARD, biologic, or systemic glucocorticoids. Of the 38 who had available follow-up information past the age of 18 years, 18 (47%) were on some medication for JIA beyond the age of 18 years.

Discussion

In this population-based cohort in which oligoarthritis was the most common subtype, less than half of individuals used DMARDs, biologics, or systemic glucocorticoids. The need for DMARDs, biologics, or systemic glucocorticoids was significantly associated with the JIA subtype. Injections became increasingly more common over the course of the years in this study and were a commonly used modality; almost half the patients had at least 1 injection. In those patients who required medical treatment beyond NSAIDs, most required ongoing DMARD therapy with a minimum being able to stop for more than 1 year.

There are a number of factors which influence analysis of medication use in patients with JIA, including method of case ascertainment (referral based versus population based), distribution of JIA subtype, and timeframe of study. Referral center based studies demonstrate higher use of DMARDs and biologics potentially reflective of JIA subtype distribution and increased disease severity of patients (3, 4, 9). A study of 149 patients with median follow-up of 33 months from referral centers in Amsterdam, reported DMARD use in 95% of patients and biologic use in 20%. In that cohort, polyarticular disease accounted for 56% of patients and only 22% had oligoarthritis, in contrast to our study with 63% with oligoarthritis and 12% with polyarthritis (10). Further, a cross-sectional study of patients with JIA done as part of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry from 2010-2011 identified 2748 children with median duration of 3.9 years (11). Up to 74% had received a DMARD at one point in their disease course and 45% a biologic. Systemic corticosteroids were received in 38%. JIA subtype and number of active joints were associated with nonbiologic DMARD and biologic DMARDs. Oligoarthritis only accounted for 34% of this cohort, again a rate much lower than that of our cohort.

An evaluation of adult patients with JIA from the British Society for Rheumatology Biologics Register (BSRBR-RA) identified 225 subjects with disease duration of median 21 years (12). Half had taken only one biologic, and half of these patients discontinued their first biologic with equal rates of inefficacy and adverse events (12).

Our study is more reflective of medication use patterns of other population-based studies. In the prospective Canadian cohort, (Research in Arthritis in Canadian Children emphasizing Outcomes study [ReACCh-Out]) that identified 1104 children with JIA, the majority received NSAIDs (88%), similar to our study. The use of DMARDs was lower in our cohort, 37%, compared to this cohort of 55%. The use of biologics was quite similar, 13% in our cohort versus 12%. The difference in DMARDs may reflect the different distribution of subtypes of JIA with oligoarthritis representing 38% in the Canadian cohort but 63% in our cohort (13). Similarly in 440 patients from regions of Scandinavian counties with long-term follow-up, NSAIDs were prescribed in 97% while 32% received systemic glucocorticoids (3). Slightly over half (58%) received other medications including DMARDs and biologics. Similar to our study, beyond NSAIDs, methotrexate was the most commonly used drug (48%). Biologics, specifically TNF inhibitors, were utilized in 17.5% of patients (3). A number of recent studies have noted that biologics are being used earlier in the disease course (13, 14). While our study did not demonstrate this trend, this is likely reflective of the overall low rates of biologics in this cohort.

Intraarticular injections are frequently utilized in management of JIA. Long-term follow-up of a Scandinavian population revealed that 75% of patients had received an injection (3). In the CARRA registry, nearly half had received an intraarticular injection, similar to our study (4). Another study evaluating intraarticular injections as monotherapy reported that repeated injections were associated with reduced rates of remission (15). It is unclear what the influence of ultrasound guided procedures is on utilization of injection as a treatment modality or its impact on likelihood of remission.

JIA affects the well-being of patients into adulthood. Characterization of remission and disease inactivity vary by study methodology and patient population. In the ReACCh-Out cohort, inactive disease was seen in 45% within 1 year in the overall cohort increasing to 95.2% at 5 years (13). Remission rates were as high as 57% at 5 years for those with oligoarthritis but 0% in those with RF-positive polyarthritis (13). Medications were discontinued in 67% within 5 years at least once (13). Similarly, a long-term follow-up of a population-based cohort in Scandinavian countries revealed that at last follow-up, less than half were in remission off medication (3). Medication discontinuation was utilized as a surrogate for remission in our study; patients were further followed through study end date. Treatments were not prescribed according to a standardized treatment protocol, but rather an individualized approach and reflective of routine clinical practice. Medication abstraction was not performed via prescription analysis, and thus it cannot be confirmed that the patients actually took medications as prescribed.

A strength of this study is its population-based design and complete medical record review. It should represent the wide spectrum of clinical severity of JIA in the community. Significant episodes of care provided outside the Rochester Epidemiology Project catchment

generally are recorded in the medical records and would be accessible and available for review during this study. The follow-up was long and extended into adulthood for many patients.

This study evaluated medication and intraarticular glucocorticoid injection use in a modern population-based cohort of patients with JIA. The majority of patients had oligoarticular disease, with a subset having more severe disease requiring definitive therapy with disease modifying agents into adulthood. This emphasizes the wide spectrum of disease severity with a majority not requiring escalation of therapy beyond NSAIDs.

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References

1. Beukelman T, Patkar NM, Saag KG, Tolleson-Rinehart S, Cron RQ, DeWitt EM, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res (Hoboken). 2011; 63(4):465–82. [PubMed: 21452260]
2. Tarkiainen M, Tynjala P, Vahasalo P, Lahdenne P. Occurrence of adverse events in patients with JIA receiving biologic agents: long-term follow-up in a real-life setting. Rheumatology (Oxford). 2014
3. Nordal E, Zak M, Aalto K, Berntson L, Fasth A, Herlin T, et al. Ongoing disease activity and changing categories in a long-term nordic cohort study of juvenile idiopathic arthritis. Arthritis Rheum. 2011; 63(9):2809–18. [PubMed: 21560116]
4. Beukelman T, Ringold S, Davis TE, DeWitt EM, Pelajo CF, Weiss PF, et al. Disease-modifying antirheumatic drug use in the treatment of juvenile idiopathic arthritis: a cross-sectional analysis of the CARRA Registry. J Rheumatol. 2012; 39(9):1867–74. [PubMed: 22859354]
5. Colebatch-Bourn AN, Edwards CJ, Collado P, D'Agostino MA, Hemke R, Jousse-Joulin S, et al. EULAR-PReS points to consider for the use of imaging in the diagnosis and management of juvenile idiopathic arthritis in clinical practice. Ann Rheum Dis. 2015
6. 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(2):390–2. [PubMed: 14760812]
7. Kremers HM, Myasoedova E, Crowson CS, Savova G, Gabriel SE, Matteson EL. The Rochester Epidemiology Project: exploiting the capabilities for population-based research in rheumatic diseases. Rheumatology (Oxford). 2011; 50(1):6–15. [PubMed: 20627969]
8. Krause ML, Crowson CS, Michet CJ, Mason T, Wampler Muskardin T, Matteson EL. Juvenile Idiopathic Arthritis in Olmsted County 1960-2013. Arthritis Rheumatol. 2015 In Press.
9. Manners PJ, Bower C. Worldwide prevalence of juvenile arthritis why does it vary so much? J Rheumatol. 2002; 29(7):1520–30. [PubMed: 12136914]
10. Anink J, Dolman KM, Merlijn van den Berg, van Veenendaal M, Kuijpers TW, van Rossum MA. Two-year outcome of juvenile idiopathic arthritis in current daily practice: what can we tell our patients? J. Clin Exp Rheumatol. 2012; 30(6):972–8.
11. Beukelman T, Haynes K, Curtis JR, Xie F, Chen L, Bemrich-Stolz CJ, et al. Rates of malignancy associated with juvenile idiopathic arthritis and its treatment. Arthritis Rheum. 2012; 64(4):1263–71. [PubMed: 22328538]

12. McErlane F, Foster HE, Davies R, Lunt M, Watson KD, Symmons DP, et al. Biologic treatment response among adults with juvenile idiopathic arthritis: results from the British Society for Rheumatology Biologics Register. Rheumatology (Oxford). 2013; 52(10):1905–13. [PubMed: 23873820]

13. Guzman J, Oen K, Tucker LB, Huber AM, Shiff N, Boire G, et al. The outcomes of juvenile idiopathic arthritis in children managed with contemporary treatments: results from the ReACCh-Out cohort. Ann Rheum Dis. 2014

14. Otten MH, Anink J, Prince FH, Twilt M, Vastert SJ, Ten Cate R, et al. Trends in prescription of biological agents and outcomes of juvenile idiopathic arthritis: results of the Dutch national Arthritis and Biologics in Children Register. Ann Rheum Dis. 2015; 74(7):1379–86. [PubMed: 24641940]

15. de Oliveira Sato J, Albuquerque Pedrosa Fernandes T, Bicalho do Nascimento C, Corrente JE, Saad-Magalhaes C. Probability of remission of juvenile idiopathic arthritis following treatment with steroid joint injection. Clin Exp Rheumatol. 2014; 32(2):291–6. [PubMed: 24238066]

Table 1

Demographics and Medication Use among 71 Patients with Juvenile Idiopathic Arthritis

Characteristic	Value
Female sex	42 (49%)
Age at diagnosis in years, mean (±SD)	8.2 (±5.3)
Length of follow-up in years, mean (±SD)	8.5 (±5.8)
JIA Subtype	
Oligoarticular	45 (63%)
Polyarthritis	9 (12%)
Systemic	2 (3%)
Psoriatic arthritis	2 (3%)
Enthesitis related arthritis	1 (1%)
Unclassified	12 (17%)
Medications	
NSAID	71 (100%)
Methotrexate	25 (35%)
Sulfasalazine	6 (8%)
Hydroxychloroquine	7 (10%)
Any DMARD	26 (37%)
TNF inhibitor	9 (13%)
IL-1 inhibitor	1 (1%)
Any Biologic	9 (13%)
Systemic Corticosteroids	19 (27%)
Any DMARD or Biologic	26 (37%)
Any DMARD, Biologic, or Systemic Corticosteroids	32 (45%)
Intraarticular Corticosteroid Injection	34 (48%)

Values in table are n (%) unless otherwise specified.

DMARD=Disease Modifying Antirheumatic Drug, JIA=Juvenile idiopathic arthritis, NSAID=Nonsteroidal anti-inflammatory drug

Table 2

Predictors of first DMARD or biologic use in patients with Juvenile Idiopathic Arthritis

	Hazard ratio* (95 % CI)	p-value
Age, years	1.05 (0.98, 1.13)	0.18
Male sex	0.91 (0.41, 2.03)	0.82
Calendar year of diagnosis	1.02 (0.96, 1.09)	0.52
JIA subtype – Polyarthritis (vs Oligoarthritis)	13.17 (4.91, 35.30)	
JIA subtype – Undifferentiated (vs Oligoarthritis)	1.72 (0.52, 5.69)	<0.001
JIA subtype – Other (vs Oligoarthritis)	3.80 (1.03, 13.97)	
Time from symptom onset to diagnosis, months	0.97 (0.91, 1.03)	0.30
Joint involvement at diagnosis - shoulder	1.59 (0.20, 12.87)	0.67
Joint involvement at diagnosis - elbow	4.89 (1.89, 12.61)	0.001
Joint involvement at diagnosis - wrist	7.19 (3.04, 16.99)	<0.001
Joint involvement at diagnosis - MCP	7.31 (3.02, 17.68)	<0.001
Joint involvement at diagnosis - PIP	4.48 (1.98, 10.16)	<0.001
Joint involvement at diagnosis - hip	2.56 (0.54, 12.09)	0.24
Joint involvement at diagnosis - knee	1.07 (0.46, 2.49)	0.87
Joint involvement at diagnosis - ankle	2.33 (0.99, 5.43)	0.052
Joint involvement at diagnosis - MTP	1.83 (0.61, 5.46)	0.30
Joint involvement at diagnosis - toe PIP	0.87 (0.26, 2.95)	0.82
Presence at diagnosis - tenosynovitis	4.18 (1.15, 15.17)	0.030
Hemoglobin at diagnosis	0.94 (0.60, 1.49)	0.80
Leukocytes at diagnosis	1.00 (1.00, 1.00)	0.82
CRP at diagnosis (mg/L)	1.02 (0.99, 1.04)	0.25
ANA	1.53 (0.67, 3.50)	0.31
RF	1.54 (0.51, 4.62)	0.44
ACPA	1.73 (0.36, 8.37)	0.49
HLA B27	0.48 (0.08, 2.80)	0.41
Abnormal ESR (≥ 25 mm/hr)	2.37 (1.00, 5.64)	0.051

RF=rheumatoid factor.

*Adjusted for age and sex. ACPA=anti-citrullinated peptide antibody. ANA=antinuclear antibody. CRP=C-reactive protein. ESR=Erythrocyte sedimentation rate. JIA=juvenile idiopathic arthritis. MCP= metacarpophalangeal joint. MTP=metatarsophalangeal joint. PIP=proximal interphalangeal joint.

Table 3

Predictors of first joint injection in patients with Juvenile Idiopathic Arthritis

	Hazard ratio* (95 % CI)	p-value
Age, years	1.06 (0.99, 1.13)	0.11
Male sex	1.44 (0.72, 2.87)	0.30
Calendar year of diagnosis	1.12 (1.05, 1.20)	<0.001
JIA subtype – Polyarthritis (vs Oligoarthritis)	0.98 (0.36, 2.64)	
JIA subtype – Undifferentiated (vs Oligoarthritis)	0.98 (0.40, 2.41)	0.98
JIA subtype – Other (vs Oligoarthritis)	0.75 (0.17, 3.24)	
Time from symptom onset to diagnosis, months	1.02 (0.98, 1.07)	0.35
Presence at diagnosis - tenosynovitis	2.54 (0.75, 8.545	0.13
Hemoglobin at diagnosis	0.96 (0.67, 1.37)	0.82
Leukocytes at diagnosis	1.00 (1.00, 1.00)	0.067
ESR at diagnosis	1.00 (0.98, 1.02)	0.66
CRP at diagnosis (mg/L)	1.01 (0.99, 1.03)	0.42
ANA	2.58 (1.16, 5.74)	0.020
RF	1.18 (0.43, 3.25)	0.75
ACPA	1.03 (0.16, 6.84)	0.97
HLA B27	3.15 (0.28, 35.22)	0.35

*Adjusted for age and sex. ACPA=anti-citrullinated peptide antibody. ANA=antinuclear antibody. CRP=C-reactive protein. ESR=Erythrocyte sedimentation rate. JIA=juvenile idiopathic arthritis. RF=rheumatoid factor.