Developing a Predictive Score for Chronic Arthritis among a Cohort of Children with Musculoskeletal Complaints—The Chronic Arthritis Score Study

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Objective To explore if features obtained from a carefully taken medical history can be predictors of the final diagnosis in children with musculoskeletal complaints.

Study design We collected detailed clinical information on 178 children referred to our Pediatric Immunology and Rheumatology Unit by their primary care pediatrician for musculoskeletal complaints; a univariate logistic analysis was performed to identify variables correlated with the diagnosis of chronic arthritis. The variables identified were combined in a linear score that indicates the probability for a patient with musculoskeletal pain to receive the diagnosis of chronic arthritis.

Results The joint swelling pattern ($P < .0001$), the precipitating factors of pain ($P = .001$), the duration of morning stiffness ($P < .0001$) and the frequency of pain ($P < .0001$), were found to be independently correlated with the diagnosis of chronic arthritis and were used to develop a diagnostic score. This score had a sensitivity of 90.9% and specificity of 95.3%.

Conclusions We developed a score that could be useful in the daily clinical routine to correctly direct the differential diagnosis in a child with musculoskeletal complaints, rationalizing time and resources necessary to reach a definitive diagnosis. *(J Pediatr 2016;169:188-93)*.

Musculoskeletal pain is one of the most common complaints in the pediatric population and affects between 10% and 20% of children.[1,2] It is one of the leading causes of office visits among pediatricians and one of the most common reasons why these children are referred to a rheumatologist.[3-5]

The differential diagnosis of children with musculoskeletal symptoms may cover a wide range of diseases,[6-10] with a variable spectrum of severity, from benign conditions, such as "growing pains," to potentially fatal disorders, such as leukemia.[11-13] Musculoskeletal pain may contribute to the clinical presentation of various rheumatic diseases, such as juvenile idiopathic arthritis (JIA), systemic lupus erythematosus, and Henoch-Schönlein purpura.[8,9] However, isolated pain is, in most cases, secondary to a noninflammatory condition, including orthopedic diseases (trauma, Osgood-Schlatter disease, Legg-Calvé-Perthes disease), hypermobility, "growing pains," and postural disorders.[1,12,14]

In this context, a careful review of the clinical history, together with a detailed physical evaluation, are helpful tools when approaching children with musculoskeletal pain, enabling the diagnosis of majority of cases.[7,15]

In this study, we analyzed the clinical presentation of children referred for musculoskeletal complaints by their primary care pediatrician to our Pediatric Immunology and Rheumatology Unit. Our aims were to explore if features obtained by a careful medical history can predict the final diagnosis and to identify which features would be more predictive of chronic arthritis.

Methods

We enrolled all patients who were referred to our Immunology and Rheumatology Unit for musculoskeletal complaints between June 2012 and December 2013. Only children referred by their primary care pediatrician were enrolled, and children referred from other specialists or facilities (ie, adult rheumatologists, other pediatric subspecialists, emergency department, and other pediatric clinics) were excluded. At the time of the first evaluation, we obtained the patient and family medical history, focusing on the pain frequency and pattern, precipitating factors of pain, joint swelling pattern, stiffness, and constitutional symptoms. All data were

ANA	Antinuclear antibodies
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
JIA	Juvenile idiopathic arthritis
RF	Rheumatoid factor

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The authors declare no conflicts of interest.

http://dx.doi.org/10.1016/j.jpeds.2015.10.081

entered into a database, together with demographic information and, when available, specific laboratory tests performed before our evaluation, such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), antinuclear antibodies (ANA), and rheumatoid factor (RF).

Once recruited, all patients were followed until a final diagnosis was confirmed. According to the final diagnosis, we categorized each patient to 3 groups: chronic arthritis, infectious-related arthritis (including acute rheumatic fever and reactive arthritis), and noninflammatory disorders (ie, orthopedic disorders, benign hypermobility syndrome, and postural defects). All the data recorded were taken during routine visits, and patients were followed as per normal clinical practice. No study-specific procedures were undertaken. Consent was obtained from all parents/guardians of the children to record the data.

Statistical Analyses

We used Fisher exact test to analyze the distribution of the variables recorded in the database within the three groups. We considered a P value of <.05 as statistically significant. We used a leave-one-out cross-validation to select the variables associated with the diagnosis of chronic arthritis; we then performed a logistic regression, using these features as independent variables and the probability of having chronic arthritis as the dependent variable, in order to build a model that could indicate the probability for a patient with musculoskeletal pain to receive the diagnosis of chronic arthritis.

Results

A total of 178 patients were recruited, 95 (53%) females and 83 (47%) males. Mean age was 8.5 ± 3.6 years. The 3 subpopulations did not differ in age at onset, and in children with chronic arthritis, there was a higher percentage of females (72%), compared with the other subpopulations ($P = .0145$).

Thirty-six patients had chronic arthritis (20% of the population), of whom 26 were females and 10 males, with a mean age at onset of 8.2 ± 4.1 years. All patients had JIA according to the International League of Associations for Rheumatology criteria[16-18]; 28 patients had infection-related arthritis (16% of the population) of whom 10 were females and 18 males, with a mean age at onset of 8 ± 3.8 years. Furthermore, 114 patients had noninflammatory disorders (64% of the population) of whom 59 were females and 55 males (48%), mean age at onset was 8.7 ± 3.5 years. Further information on the initial and final diagnosis is provided in Table I. We performed a Fisher exact test, in order to describe the distribution of the recorded variables within the three groups (Table II).

Joint pain was recorded in 163 out of the 178 (92%) patients. The group of patients with chronic arthritis showed a dichotomic pain distribution (persistent pain vs absence of pain), and the 2 other groups showed a more heterogeneous distribution of pain characteristics. By the Fisher exact text both the constant presence (56%) and absence of pain (36%) were associated with the diagnosis of chronic arthritis ($P < .0001$ and $P < .0001$, respectively). The presence of recurrent pain with more than 1 episode per month was significantly associated ($P < .0001$) with noninflammatory disorders.

Evening/night pain was more frequently reported by the patients with noninflammatory disorders (48% of these patients) ($P < .0001$). This characteristic was not found in any of the patients who received a diagnosis of chronic arthritis or infections-related arthritis. The presence of morning pain was observed in a higher percentage (26%) of patients with chronic arthritis compared with the 2 other groups (4% and 7% of children, respectively; $P < .009$).

The analysis of precipitating factors of pain identified features associated with each of the categories: rest in 68% of patients with chronic arthritis ($P = .001$), a prior infection in 79% of children with infection-related arthritis ($P < .0001$), and activity in 46% of patients with noninflammatory disorders ($P < .0001$). None of the patients who experienced pain only after activity received a diagnosis of chronic arthritis.

Eighty-three percent of children with chronic arthritis had daily persistent joint swelling in 1 or more joints ($P < .0001$).

Table I. Initial diagnostic suspicion by the referring physician and final diagnosis

	Chronic arthritis 36 patients (20%)		Infection-related arthritis 28 patients (16%)		Noninflammatory disorders 114 patients (64%)	
Diagnostic suspicion	Arthritis	27	Arthritis	12	Arthritis	11
	Joint pain	5	Joint pain	8	Joint pain	93
	Joint swelling	4	Joint swelling	3	Joint swelling	3
			Limp	1	Limp	7
			Acute rheumatic fever	4		
Final diagnosis	Systemic arthritis	1	Acute rheumatic fever	7	Postural abnormalities†	53
	Oligoarthritis	22	Poststreptococcal reactive arthritis	5	Benign joint hypermobility syndrome	9
	Polyarthritis	7	Parvovirus B19 infection	1	Orthopedic disorders‡	13
	Psoriatic arthritis	2	Posttubercolosis infection	1	Growing pains	39
	Enthesitis-related arthritis	4	Post upper respiratory or gastrointestinal tract infection*	14		

*Including transient synovitis of the hip.
†At least one of the following: cervical kyphosis (1), thoracic kyphosis (9), hyper-lordosis (10); nonstructural scoliosis (12); increased femoral anteversion (9); genu-varus (5), genu-valgus (8), patella femoral malalignment (2); flat feet (6), planovalgus feet (8); generalized joint hypermobility (Beighton score >4 with negative Brighton criteria: 14).
‡Structural scoliosis (3); Osgood-Schlatter disease (4); Hoffa syndrome (2); Sever disease; Perthes' disease (1); posttraumatic injury (3).