Detection of Active Disease in Juvenile Idiopathic Arthritis: Sensitivity and Specificity of the Physical Examination vs Ultrasound

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ABSTRACT. ***Objective.*** To determine sensitivity and specificity of the physical examination (PE) for identifying synovitis in the knee and ankle joints of children with juvenile idiopathic arthritis (JIA), and to identify cases in which ultrasound (US) screening augments the PE.

Methods. Nineteen patients with JIA were referred for US. Both knees and ankles were examined using US with and without power Doppler. Active arthritis on PE was defined as (1) non-bony swelling or (2) limitation of motion with either pain on motion or tenderness to palpation. Active arthritis on US was defined as synovial hyperplasia, effusion, or increased vascularity on power Doppler scan.

Results. There was agreement between US and PE in 75% of cases. PE was 64% sensitive and 86% specific for identifying active arthritis. PE was 100% specific if (1) the patient was positive for both PE criteria or (2) if arthritis was present on PE in the knees. When the PE was negative and the US was positive, 21.4% developed active disease on PE within 6 months. In cases where the PE was positive and US was negative, the joint involved was most often the ankle and frequently the subtalar joint.

Conclusion. PE is neither highly sensitive nor specific for identifying active synovitis when compared to US, and screening with US can identify subclinical disease. In joints with both non-bony swelling and limitation of motion with pain on motion or tenderness, and in the knee joint, little additional information is gained by US. This has implications for classification and treatment of JIA. (J Rheumatol First Release Sept 15 2011; doi:10.3899/jrheum.110360)

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Juvenile idiopathic arthritis (JIA) is a heterogenous group of chronic arthritides affecting children under the age of 16 years. Despite the heterogeneity, all forms of JIA can result in significant erosive joint disease affecting function and quality of life. Identifying disease early and treating aggressively is believed to result in better longterm outcomes in adult rheumatoid arthritis, and this is likely true of JIA as well[1]. Presently, pediatric rheumatologists rely heavily on physical examination (PE) to determine which joints have active arthritis. However, there is significant variability even among experienced rheumatologists in making these determinations[2]. Conventional radiographs have low sensitivity for the detection of active arthritis and rarely show changes until late in the disease course[3]. Additionally, advances in magnetic resonance imaging (MRI) and musculoskeletal ultrasound (US) allow detection of subclinical disease[4,5,6,7,8,9], resulting in earlier identification and treatment of arthritis.

MRI has been used selectively in the assessment of children with JIA to confirm active disease and detect subclinical disease[10,11,12]. MRI is effective in identifying bone marrow edema, joint effusion, synovial thickening and enhancement, and articular cartilage erosions, and detects disease before it is apparent on PE[13]. While MRI is a useful method for evaluating subclinical disease, it is costly and time-consuming. Additionally, the need for sedation for scanning young children prevents its use as a screening examination. While US lacks the fine detail seen on MRI, it offers information regarding vascularity, cartilage thickness, and pannus formation. The short duration of the test renders sedation unnecessary; coupled with its reduced cost this makes US an excellent method for screening for subclinical disease.

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While previous studies looked at the correlation between PE and US with Doppler, they have not addressed the followup findings on PE. Identification of subclinical disease is also relevant when considering the classification system of JIA. The number of joints affected in the first 6 months determines disease classification and influences treatment decisions[14]. US could be potentially useful in making these determinations.

Our study was performed (1) to determine the sensitivity and specificity of various aspects of the PE for identifying synovitis in knee and ankle joints of children with JIA; and (2) to identify cases in which US screening would provide additional findings not detected on PE.

MATERIALS AND METHODS

Between August 2009 and August 2010, patients with JIA seen in the pediatric rheumatology clinic who were found to have at least 1 active knee or ankle joint on PE were asked to participate in the study. Diagnosis of JIA and subtype was established using the International League of Associations for Rheumatology criteria[14]. PE were performed by an attending pediatric rheumatologist along with either a pediatric rheumatology fellow or a nurse practitioner. Active joints were defined as either (1) non-bony swelling or effusion, or (2) limitation of motion (LOM) with either pain on motion (POM) or tenderness to palpation (TTP). Patients meeting entry criteria who agreed to participate were sent for US of the knees and ankles. Informed consent was obtained and the study was approved by the Institutional Review Board. Followup PE performed in the 3- to 6-month period following the initial US were reviewed.

Sonography was performed by a single sonographer and images were reviewed by a pediatric radiologist and a musculoskeletal radiologist in consensus. Both radiologists were blinded to the results of the PE. Images of both knees and ankles were obtained with a 12 MHz linear transducer with and without power Doppler. They included a longitudinal midline image of the distal femur over the suprapatella bursa, a coronal image of the medial and lateral femorotibial joints, and a longitudinal midline image of the tibiotalar joint. Sonographically active arthritis was defined as either mild or moderate hyperemia, synovial thickening, or the presence of a joint effusion. Hyperemia on power Doppler images was quantified as none (0 color pixels), mild (1 or 2 color pixels), or moderate (> 2 color pixels), and synovial thickening was present if there was measurable thickening of the wall of the suprapatella bursa.

RESULTS

The knees and ankles of 19 patients with JIA were evaluated. Patient characteristics are described in Table 1.

Clinical findings. On PE, 46 (60.5%) joints were inactive and 30 (39.5%) were active. Of the clinically active joints, 6 (20%) had non-bony swelling alone, 4 (13%) had limitation with either POM or tenderness alone, and 20 (66.6%) met both criteria.

Ultrasound findings. On sonography, 37 (48.7%) joints were inactive and 39 (51.3%) were active. Fourteen (35.9%) of the sonographically active joints had synovial thickening, 21 (53.8%) had joint fluid, and 27 (69.2%) had hyperemia.

Concordance of PE and US findings. Concordance was calculated to be 0.5 using a kappa statistic, indicating moderate strength of agreement. Clinicians and radiologists agreed in 75% of cases (see Table 2 for joint-specific data).

Table 1. Patient characteristics (n=19).

Characteristic	
Sex (%)	
Male	8 (42)
Female	11 (58)
Mean age, yrs (range)	9.5 (1–17)
Type of arthritis	
Oligoarticular JIA	6
Polyarticular JIA	4 (RF-negative)
Extended oligo-JIA	5
Enthesitis-related JIA	1
Systemic JIA	3
Medications	
NSAID	10
DMARD	6
Anti-tumor necrosis factor	3

JIA: juvenile idiopathic arthritis; NSAID: nonsteroidal antiinflammatory drugs; DMARD: disease-modifying antirheumatic drugs; RF: rheumatoid factor.

Table 2. Activity status on physical examination (PE) and ultrasound (US) by joint type.

Status	Knee	Ankle	Total
Total evaluated	38	38	76
Active on PE	20	10	30
Active on US	29	10	39
Active on PE and US	20	5	25
Inactive on PE and US	9	23	32
Active on PE, inactive on US	0	5	5
Inactive on PE, active on US	9	23	24

Sensitivity and specificity analysis. A summary of the sensitivity and specificity analysis can be found in Table 3. Overall sensitivity and specificity of the PE for detecting synovitis were 64% and 86%, respectively. When the definition of clinically active arthritis was restricted to include only joints with both (1) non-bony swelling and (2) LOM with either POM or TTP, specificity reached 100%, with a drop in sensitivity to 46%. Sensitivity was the highest (64%) when the definition of clinically active disease was broadened to include either (1) non-bony swelling or (2) LOM with either POM or TTP.

DISCUSSION

While our study confirms previous reports demonstrating a moderate to high degree of concordance between the PE and US[6], we found that the sensitivity of the PE alone was poor. When the standard definition of clinically active arthritis was used, the PE was only 64% sensitive compared to US, yielding a high rate of false negatives. This was similar to previous findings[4]. However, when the various combinations of PE findings were evaluated, specificity of the PE improved significantly. In joints with both non-bony swelling and LOM with POM or TTP, the PE was 100% specific for identifying arthritis. Similarly, if either non-

Table 3. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of various aspects of the PE for detecting arthritis as compared to US.

	Sensitivity, %	Specificity, %	PPV, %	NPV, %
Non-bony swelling (NBS)	45	89	85	66
Limitation of motion (LOM) WITH pain on motion (POM) or tenderness to palpation (TTP)	54	92	88	65
Either (1) NBS or (2) LOM with POM or TTP	64	86	83	70
Both (1) NBS and (2) LOM with POM or TTP	46	100	100	64
Knees active by either criteria	69	100	100	50
Ankles active by either criteria	50	82	50	82

bony swelling and LOM with POM or TTP were present at the knee alone, specificity for active arthritis was 100%. In these clinical settings, additional screening with US did not augment the PE. Of note, only patients with the PE finding of at least 1 clinically active joint were referred for US; therefore, it is likely that there was a higher pretest probability of having other active joints in these patients. Therefore, in patients with at least 1 clinically active joint, it may be useful to screen clinically inactive joints, as the overall sensitivity of the PE was low.

Our followup data support previous studies that indicate that US is able to detect subclinical disease[4,5,6]. Fourteen joints exhibited sonographic findings of active disease but were inactive on PE (9 knees, 5 ankles). On followup PE, 5 of the 14 joints (35.7%) developed signs of active arthritis, suggesting that there was likely subclinical disease at the time of the initial PE. All 5 of these joints had either diffusion or synovial thickening with or without increased vascularity on US. Of the 14 joints, 1 was lost to followup. In the remaining 8 of the 14 joints, mild hyperemia was the only indicator of disease activity on US. While color Doppler evaluation improves detection of hyperemia and may predict radiographic progression of disease, mild hyperemia alone without other sonographic indicators of disease may not be an independent determinant of active disease and may lead to sonographic false positives. Thus, given our data, we suggest that mild hyperemia alone is not sufficient to diagnose active arthritis.

Of the 5 joints active on PE and inactive on US, all were ankle joints, and further review of the charts revealed that 4 had subtalar disease. The discordant result likely reflects the technical difficulties associated with sonographic evaluation of the subtalar joint. Previous reports have also attributed false-negative US findings in the ankle joint to subtalar disease[15]. Tenosynovitis may also result in a false-negative US finding of disease activity[15], and was not assessed in our patient population.

Limitations of our study are that neither the sonographer nor the interpreting radiologists were blinded to the patient's diagnosis. Additionally, only patients with a known diagnosis of JIA and at least 1 active joint were included in the study, increasing the pretest probability and making the results less applicable to patients with disease in remission, or to patients without a diagnosis of JIA. Active synovitis was not confirmed by another imaging technique and no US was performed at the time of the followup PE. Some patients were started on systemic medications during the followup period, potentially altering their PE. However, one would assume that this would skew the data toward overall improvement on PE. Therefore, the finding that 5 of the 14 joints inactive on PE and active on US developed signs of active arthritis on followup PE is still an important observation. Scanning planes were limited and surrounding structures such as tendons were not imaged. Lastly, PE was performed by more than 1 clinician and interobserver disagreement may have been present.

Our data suggest that US is not necessary in all patients with JIA but may augment the PE in patients with at least 1 active joint. In patients with both non-bony swelling and LOM with either POM or TTP, or in patients with either of the aforementioned criteria, PE is highly sensitive and US findings do not contribute to clinical management. Subtalar disease and mild hyperemia may lead to false-negative and false-positive findings on US, respectively. However, overall, the sensitivity of the PE was lacking, calling attention to the need for better screening tests for subclinical disease. US is cost-effective, painless, and does not require sedation. Detection of subclinical disease by US may lead to more aggressive treatment, better treatment outcomes, and decreased longterm disability. Future studies looking at additional joints as well as other serologic markers will help clarify situations where US might be most useful.

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