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BRIEF REPORT

Musculoskeletal Ultrasound and the Assessment of Disease Activity in Juvenile Idiopathic Arthritis

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Objective. To determine the frequency of subclinical synovitis on musculoskeletal ultrasonography (MSUS) in juvenile idiopathic arthritis (JIA) and correlate patient- and provider-reported outcome measures with MSUS synovitis.

Method. JIA patients with an active joint count (AJC) of >4 underwent a 42-joint MSUS performed at baseline and 3 months. B-mode and power Doppler images were obtained and scored (range 0–3) for each of the 42 joints. Outcomes evaluated included physician global assessment of disease activity (PhGA), patient global assessment of disease activity (PtGA), patient pain, Childhood Health Assessment Questionnaire (C-HAQ), and AJC. Subclinical synovitis was defined as synovitis detected by MSUS only. Generalized estimation equations were used to test the relationship between clinical arthritis (positive/negative) and subclinical synovitis (positive/negative). Spearman's correlation coefficients (r_s) were calculated to determine the association between MSUS synovitis and patient- and physician-reported outcomes.

Results. In 30 patients, subclinical synovitis was detected in 30% of joints. Clinical arthritis of the fingers, wrists, and knee joints was significantly associated with MSUS synovitis in these joints. PtGA and the C-HAQ had a moderate ($r_s = 0.44$, $P = 0.014$) to weak ($r_s = 0.37$, $P = 0.045$) correlation with MSUS synovitis. There was a statistically significant strong correlation between MSUS synovitis and PhGA ($r_s = 0.61$, $P = 0.001$), but a weak correlation with AJC ($r_s = 0.37$, $P = 0.048$) at the follow-up visit.

Conclusion. Subclinical synovitis was commonly observed in this cohort of JIA patients. The fair-to-moderate correlation of MSUS synovitis with patient- and provider-reported outcomes suggests that MSUS assesses a different, possibly more objective, domain not determined by traditional JIA outcome measurements.

INTRODUCTION

In children, arthritis, or a joint with active inflammation, is characterized by the presence of either joint swelling or a joint with limited range of motion (ROM) and pain upon motion or tenderness upon palpation. Clinically determined arthritis serves as the current standard assessment to diagnose juvenile idiopathic arthritis (JIA) and is an important outcome measure (1). JIA, the most common rheumatic disease in children, can result in irreversible joint damage and detrimental outcomes when not treated adequately. Therefore, timely and accurate detection of arthritis is essential to improve the outcome and quality of life in children with JIA. However, the use of the clinician-determined active joint count to inform the decision-making process is potentially problematic for several reasons. First, JIA commonly presents

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SIGNIFICANCE & INNOVATIONS

- Subclinical synovitis in children with juvenile idiopathic arthritis (JIA) is frequently detected using ultrasound (US).
- Clinical arthritis of the finger, wrist, and knee joints is associated with evidence of musculoskeletal ultrasonography (MSUS) synovitis of these joints.
- Subclinical synovitis and tenosynovitis are currently underrepresented in the active joint count total for monitoring JIA disease activity. The addition of MSUS may better reflect disease activity.
- US-determined synovitis has strong-to-weak correlation with patient- and provider-reported outcomes, suggesting that US may provide an important adjunct to the clinical evaluation.

between the ages of 2–6 years. Given patient-reported tenderness is a key component of active arthritis (along with limited ROM), many toddlers and young children are unable to reliably report JIA symptoms, which can contribute to joints being overlooked. Second, the presence of common childhood conditions (e.g., joint hypermobility) complicates the assessment of joint mobility and function. Finally, the clinical assessment of arthritis has poor-to-moderate interrater agreement (2). Thus, clinical assessment of arthritis may not be sufficient to diagnose active arthritis and may potentially lead to adverse outcomes in JIA.

Ultrasound (US) is a patient-friendly, convenient, and accessible examination. Musculoskeletal ultrasonography (MSUS) is a radiation-free, objective imaging tool that can be used to assess joint inflammation. In adults with rheumatoid arthritis, MSUS has become a valid tool for the assessment of arthritis (3). Previous studies suggest that MSUS is more sensitive than clinical examination in the assessment of synovitis (4). In children, the use of MSUS in JIA is evolving. The definitions of sonographic findings in joints in healthy children as well as in children with JIA have been established (5,6). In addition, the need for standardized and validated MSUS scanning protocols and scoring systems in pediatrics has been addressed, including the recent publication of a detailed joint-specific scanning protocol and scoring system that was found to be highly reliable (7).

We established the Musculoskeletal UltraSound In Childhood Arthritis Limited (MUSICAL) examination, which represents a set of 10 joints that identified 100% of children with synovitis among a more comprehensive US examination (total of 42 joints). The MUSICAL score was developed for quantification of synovitis. Initial construct validation of this score was done through correlation of MSUS findings with validated clinical composite scores. However, the correlation between physical examination, physician, and patient-reported outcomes and pediatric-specific MSUS scoring systems needs to be further investigated.

The aims of this study were to 1) determine the frequency of subclinical synovitis in peripheral joints per MSUS, 2) evaluate the association between clinical findings of arthritis and MSUS findings of synovitis, and 3) examine the relationship between MSUS synovitis and standardized physician- and patient-reported outcomes in children with active JIA.

PATIENTS AND METHODS

Patients. Children diagnosed as having JIA and clinical arthritis of ≥4 joints were recruited from the rheumatology clinic of Children's Healthcare of Atlanta, Cincinnati Children's Hospital Medical Center, and Nationwide Children's Hospital between November 2017 and August 2019 (7). Clinical arthritis was defined as the presence of either joint swelling or the presence of joint tenderness and limited ROM. Patients were excluded if they received an intraarticular glucocorticoid injection within 4 weeks prior to the baseline visit or received oral steroids or a conventional or biologic disease-modifying antirheumatic drugs (DMARDs) in the week prior to the first MSUS examination. The study was approved by the institutional review board at each center, and informed consent was obtained from all patients.

Clinical assessment. Joint examination was undertaken at baseline and 3 months later to assess the active joint count (AJC) or presence of clinical arthritis of the shoulders, elbows, wrists, fingers, hips, knees, ankles, and toe joints and to document presence of tendon involvement or tenosynovitis by a "joint exam–certified" pediatric rheumatologist according to the Pediatric Rheumatology Collaborative Study Group (8). At baseline, disease subtype according to International League of Associations for Rheumatology categories (7) was recorded. Information collected during each visit included general demographic and disease characteristics, current medications, pain visual analog scale (VAS) score (0 [no pain] to 10 [maximum pain]), patient/parent global assessment of disease activity (PtGA) VAS score (0 [very good] to 10 [very poor]), physician global assessment of disease activity (PhGA) VAS score (0 [no activity] to 10 [maximum activity]), and the Childhood Health Assessment Questionnaire (C-HAQ) responses. The C-HAQ is a valid, arthritis-specific measure to evaluate functional disability (8).

US assessment. A complete MSUS examination of 42 joints was completed at both baseline and at 3-month follow-up (bilateral shoulder, elbow, wrist, metacarpophalangeal [MCP] joints 1–5, proximal interphalangeal [PIP] joints1–5, hip, knee, ankle, and metatarsophalangeal [MTP] joints 1–5 at each of the 2 study visits). MSUS examination was performed by an expert American College of Rheumatology Musculoskeletal Ultrasound–certified pediatric rheumatologist (PV-F, EJO, and TVT) who was blinded to physical examination findings and the symptoms of participants. Real-time MSUS examination was performed at all sites using a General Electric US system Logiq S8 XDclear machine equipped with a 6–15 MHz multifrequency linear transducer and a 4–18 MHz frequency

footprint linear transducer. The settings for B-mode and color-coded power Doppler (PD) were standardized among all General Electric US machines (7). However, images of the 3 first subjects enrolled in the study were collected using a MyLab Alpha machine (Esaote) with a multifrequency linear transducer of 6–18 MHz. Still MSUS images were taken at the point of maximum joint findings abnormalities as determined by the sonographer.

Interrater reliability among 4 readers (PV-F, EJO, JR, and TVT) was assessed prior to the scoring of the images (7). Once excellent reliability was met for all views collected (intraclass correlation coefficient >0.75) the total number of images was equally distributed among the 4 readers for scoring purposes. Readers were blinded to the clinical data, and a recently published pediatric-specific semiquantitative scoring system ranging from 0 (normal) to 3 (severe) was used (7). Subclinical synovitis was defined as B-mode grade 2 MSUS findings (moderate) and grade 3 (severe) MSUS findings, or power Doppler mode of any grade within an area of B-mode findings grade ≥1 in a joint deemed normal on clinical examination.

Statistical analysis. We used descriptive statistics to characterize the assessments of clinical arthritis and subclinical synovitis using the frequency (percentages) for categorical and dichotomous variables, and the mean ± SD or median (interquartile range [IQR]) for continuous variables depending on the distribution of the data. The MSUS models or joint sets (i.e., 42-joint set, reduced joint set, and MUSICAL examination joint set) in the MUSICAL study were used to evaluate the correlation between MSUS and patient- and physician-reported outcomes (7). Briefly, the 42-joint set included all 42 joints scanned. The reduced joint set identified a combination of 10 joints able to detect 100% of subjects with B-mode synovitis within the 42-joint set. The identification of the key views contributing to the reduced joint set resulted in the MUSICAL examination joint set. Data from baseline as well as follow-up visits were used for analysis.

Generalized estimation equations were used to run a repeated measures logistic regression analysis (controlling for within-subject correlation) to test the relationship between clinical arthritis (positive/negative) and subclinical synovitis (positive/negative). Odds ratios and confidence intervals (CIs) are reported from this analysis. Wilcoxon's signed rank test was used to test whether there were significant changes in the number of joints with subclinical synovitis from baseline to follow-up visit in each individual patient. The strength of the associations between MSUS synovitis, patient-reported outcomes, and physician-reported outcomes were calculated using Spearman's correlation. *P* values less than 0.05 were considered significant (9). All data were analyzed using SAS, version 9.4.

RESULTS

Of the 30 JIA patients enrolled in the study, 70% were female, with a median age of 14 years (IQR 12–16 years) (see Supplementary Table 1, available on the *Arthritis Care & Research* website at http://onlinelibrary.wiley.com/doi/10.1002/acr.25073/abstract). MSUS was used to detect subclinical synovitis in 15% (hip joint) to 40% (MCP joints) of joints (Figure 1). Not only moderate but also severe findings of MSUS synovitis were present in some joints with subclinical synovitis (see Supplementary Figure 1, available at http://onlinelibrary.wiley.com/doi/10.1002/acr.25073/abstract). The presence of joint swelling, rather than joint pain, and limited ROM was the main abnormality documented for the joints with clinical arthritis that were not detected on MSUS. Given that this was a cohort of newly diagnosed patients (median duration of arthritis of 1 month [CI 0–34]), and

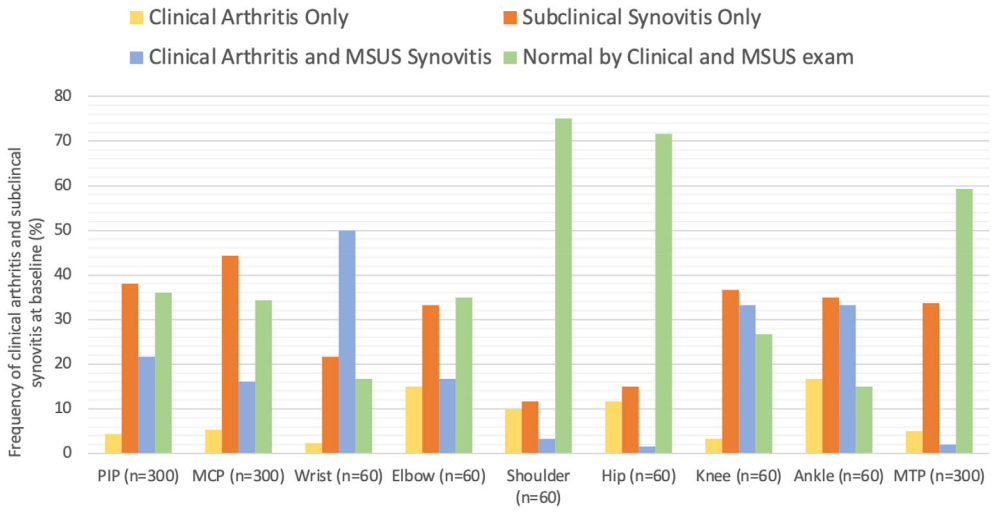

Figure 1. Frequency of clinical and subclinical synovitis at baseline in proximal interphalangeal (PIP), metacarpophalangeal (MCP), wrist, elbow, shoulder, hip, knee, ankle, and metatarsophalangeal (MTP) joints upon clinical examination and/or musculoskeletal ultrasound (MSUS).

Table 1. Frequency of clinical and subclinical synovitis in peripheral joints*

	Clinical arthritis only	Subclinical synovitis only	Clinical arthritis and MSUS synovitis
Baseline visit†			
PIP (n = 300)	13 (4.3)	114 (38.0)	65 (21.7)
MCP (n = 300)	16 (5.3)	133 (44.3)	48 (16.0)
Wrist (n = 60)	7 (11.7)	13 (21.7)	30 (50.0)
Elbow (n = 60)	9 (15.0)	20 (33.3)	10 (16.7)
Shoulder (n = 60)	6 (10.0)	7 (11.7)	2 (3.3)
Hip (n = 60)	7 (11.7)	9 (15.0)	1 (1.6)
Knee (n = 60)	2 (3.3)	22 (36.7)	20 (33.3)
Ankle (n = 60)	10 (16.7)	21 (35.0)	20 (33.3)
MTP (n = 300)	15 (5.0)	101 (33.7)	6 (2.0)
Follow-up visit‡			
PIP (n = 290)	15 (5.2)	90 (31.0)	46 (15.9)
MCP (n = 290)	21 (7.2)	94 (32.4)	33 (11.4)
Wrist (n = 58)	7 (12.1)	13 (22.4)	22 (37.9)
Elbow (n = 58)	5 (8.6)	20 (34.5)	10 (17.2)
Shoulder (n = 58)	3 (5.2)	7 (12.0)	2 (3.4)
Hip (n = 58)	4 (6.9)	4 (6.9)	NA
Knee (n = 58)	1 (1.7)	17 (29.3)	12 (20.7)
Ankle (n = 58)	8 (13.8)	15 (25.9)	15 (25.9)
MTP (n = 290)	16 (5.5)	82 (28.3)	6 (2.1)

* Values are the number (%) of joints. MCP = metacarpophalangeal; MSUS = musculoskeletal ultrasound; MTP = metatarsophalangeal; NA = not applicable; PIP = proximal interphalangeal.
† A total of 30 participants attended the baseline visit.
‡ A total of 29 participants attended the follow-up visit.

most began treatment, the frequency of joints with clinical arthritis and subclinical synovitis detected at the follow-up visit was lower than at baseline (see Table 1 and Supplementary Figure 2, at http://onlinelibrary.wiley.com/doi/10.1002/acr.25073/abstract). Most strikingly, only 30% of ankle joints reported to be normal upon clinical assessment were found to be normal on MSUS examination. A higher but still fairly low percentage of 40–50% of PIP, MCP, wrist, elbow, and knee joints that were normal upon clinical examination were also found to be normal on MSUS.

MSUS detection of synovitis in clinically active joints varied. For instance, upon clinical examination, 90% of active knee joints were found to have MSUS findings of synovitis; however, only 12.5% of hip joints and 25% of shoulder joints with clinical arthritis were abnormal on MSUS (Table 1). The odds of having MSUS examination findings consistent with synovitis when physical examination was positive for arthritis is shown in Supplementary Table 2 (available at http://onlinelibrary.wiley.com/doi/10.1002/acr.25073/abstract). As expected, at follow-up, a significant decrease in subclinical synovitis was found especially at the PIP, MCP, knee, and ankle joints, as well as the total joint count per participant (see Supplementary Table 3, available at http://onlinelibrary.wiley.com/doi/10.1002/acr.25073/abstract).

Clinically, tenosynovitis was found in the ankle, wrist, and finger tendon group(s). In addition to these tendon groups, MSUS revealed the presence of tenosynovitis in the biceps tendon in the absence of shoulder arthritis. Overall, tenosynovitis was more

Table 2. Correlation between MSUS synovitis and patient- and physician-reported measures of disease activity and damage

	Baseline MSUS synovitis		Follow-up MSUS synovitis	
	42-joint set†	MUSICAL joint set‡	42-joint set†	MUSICAL joint set‡
Pain VAS	0.27 (0.158)	0.28 (0.145)	0.02 (0.928)	0.11 (0.563)
PtGA	0.37 (0.047)§	0.44 (0.014)§	0.22 (0.248)	0.30 (0.084)
C-HAQ	0.27 (0.153)	0.37 (0.045)§	0.04 (0.844)	0.10 (0.590)
AJC	0.12 (0.528)	0.24 (0.209)	0.37 (0.048)§	0.25 (0.184)
PhGA	0.30 (0.112)	0.22 (0.254)	0.61 (<0.001)§	0.49 (0.017)§

* Values are the correlation (*P* value), by Spearman's correlation (very weak = 0.0–0.19, weak = 0.2–0.39, moderate = 0.4–0.59, strong = 0.6–0.79, very strong = 0.8–1.0). Musculoskeletal ultrasound (MSUS) synovitis was defined as B-mode grade 2 and grade 3 MSUS findings with any power Doppler–mode grade 0, 1, 2, and 3 MSUS findings. AJC = active joint count; C-HAQ = Childhood Health Assessment Questionnaire; PhGA = physician global assessment of disease activity; PtGA = patient/parent global assessment of disease activity; VAS = visual analog scale.
† The 42-joint set included a total of 42 joints examined using MSUS.
‡ The Musculoskeletal UltraSound In Childhood Arthritis Limited (MUSICAL) joint set included a total of 10 joints examined using MSUS.
§ *P* values less than 0.05 were considered significant.

often detected on MSUS than on physical examination (see Supplementary Table 4, available at http://onlinelibrary.wiley.com/doi/10.1002/acr.25073/abstract).

The correlations between MSUS synovitis, patient-reported outcomes, and physician-reported outcomes are shown in Table 2. At baseline, there was a statistically significant moderate correlation between PtGA and MSUS synovitis, particularly in the MUSICAL joint set ($r_s = 0.44$, $P = 0.014$), and a weak agreement between C-HAQ and MSUS synovitis in the MUSICAL joint set ($r_s = 0.37$, $P = 0.045$). At the follow-up visit, AJC was found to have a weak correlation in the 42-joint MSUS joint set. PhGA rather than PtGA was found to have a moderate correlation with MSUS synovitis as defined in both the 42-joint set and the MUSICAL joint set.

DISCUSSION

In a cohort of recently diagnosed polyarticular-course JIA patients, pathologic sonographic findings consistent with inflammatory arthritis were found in ~50% of imaged joints. MSUS detected synovitis in ~66% of joints determined to have arthritis according to clinical examination. Subclinical synovitis, defined as the presence of moderate-to-severe B-mode MSUS synovitis findings, was not clinically detected by an experienced rheumatology provider in ~33% of joints examined. Moreover, ~50% of joints with subclinical synovitis had severe, rather than moderate, findings of sonographic synovitis. Pediatric rheumatology providers could therefore be missing marked joint abnormalities in ≥15% of joints. This is especially true for the ankle region, which is relatively complex. The frequency of subclinical synovitis observed in our study is in line with previously reported abnormal MSUS findings in 30% of joints assessed and determined to be normal on physical examination (4). However, unlike previous studies and to minimize bias in the interpretation of MSUS findings, we used stringent and standardized interpretation criteria (7).

Previous studies aiming to determine the significance of subclinical synovitis in JIA (10,11) were limited due to the lack of validated and standardized pediatric-specific sonographic assessment and scoring systems. They often included heterogeneous study cohorts with a wide range of disease and remission duration. Imaging findings in a patient who entered remission 3 months prior may be different than after 2 years in remission. In the current study, the use of pediatric-specific sonographic definitions of synovitis (5), standardized scanning protocols, reliable scoring systems (12), and a longitudinal assessment in a homogenous cohort of newly diagnosed JIA patients with polyarticular onset provides a strong framework to support further studies examining therapeutic and prognostic implications of subclinical synovitis.

Growing evidence suggest that timely management of JIA is related to better disease outcomes (13), since imprecise detection of joint involvement and the degree of inflammation in children with JIA may increase the risk of irreversible joint damage, poor disease prognosis, and impaired quality of life. The high frequency of subclinical synovitis in our cohort raises concerns of missed opportunities to implement treatment plans that appropriately addressed the needs of patients and that ultimately may result in improved outcomes. The statistically significant decrease in the frequency of MSUS synovitis from baseline to follow-up suggest that it is a sensitive measurement responsive to therapeutic interventions.

Our study underlines the lack of sensitivity of physical examination in detecting tendon involvement. Subclinical tenosynovitis was found in 20% of potential sites. In addition, none of the findings of MSUS tenosynovitis were detected on physical examination—neither as clinical arthritis nor clinical tenosynovitis. Precise establishment of the location of joint and tendon inflammation may have significant treatment implications (14).

Our prior work demonstrated that the MUSICAL joint set had a statistically significant moderate correlation with clinical Juvenile Arthritis Disease Activity Score in 10 joints, a validated disease activity measurement in JIA (7). The discordance found in this study between patient- and physician-reported measures of disease activity and MSUS, also differing between baseline and follow-up for correlations with the same measure, may be related to poor agreement in PhGA among providers (15). It may also be due to inherent limitations of these measures to reliably assess disease activity in individual patients as opposed to entire cohorts and highlights the role of MSUS complementing clinical assessment of any peripheral joint in JIA. Future longitudinal cohort studies are needed to elucidate the correlation between radiologic findings of synovitis, patient/parent- and provider- determined measurements of disease activity, and chronicity at different disease stages. Magni-Mazoni et al (4) reported low and even negative correlation between MSUS features of synovitis and PtGA, pain assessment, and PhGA. Similarly, in our study, pain assessment was found not to correlate with MSUS synovitis at either study visit. Cognitive, emotional, and situational factors may exaggerate or minimize self-reported ratings of pain and well-being (16). MSUS could serve as a more objective outcome measure.

The relatively small sample size without full representation of JIA subtypes in the present analysis is a limitation of this study. However, our analysis included 1,260 and 1,218 joints examined using MSUS at enrollment and follow-up visits, respectively. If taken by anatomical site, there were data regarding 300 MCP, PIP, and MTP joints as well as 60 wrist, elbow, shoulder, knee, and ankle joints at 2 time points, which to our knowledge is one of the largest pediatric cohorts reported. In an effort to avoid overestimation of the joint disease burden in MSUS, we chose stringent cutoff values to delineate the presence of sonographic synovitis following previously established definitions of sonographic features of synovitis in children (5,6). Our present study

suggests that the information provided by standardized MSUS assessment could complement the available instruments for measuring JIA disease activity and therefore strengthen the medical decision-making process to improve outcomes in children with JIA.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Vega-Fernandez had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Analysis and interpretation of data. Vega-Fernandez, Oberle, Cassedy, Roth, Ting.

REFERENCES

1. Palman J, Shoop-Worrall S, Hyrich K, et al. Update on the epidemiology, risk factors and disease outcomes of Juvenile idiopathic arthritis. Best Pract Res Clin Rheumatol 2018;32:206–22.
2. Scott IC, Scott DL. Joint counts in inflammatory arthritis. Clin Exp Rheumatol 2014;32 Suppl 85:S–7–12.
3. Naredo E, Collado P, Cruz A, et al. Longitudinal power Doppler ultrasonographic assessment of joint inflammatory activity in early rheumatoid arthritis: predictive value in disease activity and radiologic progression. Arthritis Rheum 2007;57:116–24.
4. Magni-Manzoni S, Epis O, Ravelli A, et al. Comparison of clinical versus ultrasound-determined synovitis in juvenile idiopathic arthritis. Arthritis Rheum 2009;61:1497–504.
5. Roth J, Ravagnani V, Backhaus M, et al. Preliminary definitions for the sonographic features of synovitis in children. Arthritis Care Res (Hoboken) 2017;69:1217–23.
6. Collado P, Windschall D, Vojinovic J, et al. Amendment of the OMERACT ultrasound definitions of joints' features in healthy children when using the DOPPLER technique. Pediatr Rheumatol Online J 2018;16:23.
7. Vega-Fernandez P, Ting TV, Oberle EJ, et al. Musculoskeletal ultrasound in childhood arthritis limited examination: a comprehensive, reliable, time-efficient assessment of synovitis. Arthritis Care Res (Hoboken) 2023;75:401–9.
8. Consolaro A, Giancane G, Schiappapietra B, et al. Clinical outcome measures in juvenile idiopathic arthritis. Pediatr Rheumatol Online J 2016;14:23.
9. Mukaka MM. Statistics corner: a guide to appropriate use of correlation coefficient in medical research. Malawi Med J 2012;24:69–71.
10. De Lucia O, Ravagnani V, Pregnolato F, et al. Baseline ultrasound examination as possible predictor of relapse in patients affected by juvenile idiopathic arthritis (JIA). Ann Rheum Dis 2018;77:1426–31.
11. Lanni S, van Dijkhuizen EH, Vanoni F, et al. Ultrasound changes in synovial abnormalities induced by treatment in juvenile idiopathic arthritis. Clin Exp Rheumatol 2018;36:329–34.
12. Vega-Fernandez P, Ting T, Oberle E, et al. Musculoskeletal ultrasound study in childhood arthritis: a limited examination [abstract]. Arthritis Rheumatol 2020;72 Suppl 4. URL: https://acrabstracts.org/abstract/musculoskeletal-ultrasound-study-in-childhood-arthritis-a-limited-examination/.
13. Ong MS, Ringold S, Kimura Y, et al. Improved disease course associated with early initiation of biologics in polyarticular juvenile idiopathic arthritis: trajectory analysis of a Childhood Arthritis and Rheumatology Research Alliance consensus treatment plans study. Arthritis Rheumatol 2021;73:1910–20.
14. Lanni S, Marafon DP, Civino A, et al. Comparison between clinical and ultrasound assessment of the ankle region in children with juvenile idiopathic arthritis. Arthritis Care Res (Hoboken) 2021;73:1180–6.
15. Taylor J, Giannini EH, Lovell DJ, et al. Lack of concordance in interrater scoring of the Provider's Global Assessment of children with juvenile idiopathic arthritis with low disease activity. Arthritis Care Res (Hoboken) 2018;70:162–6.
16. Stinson JN, Kavanaugh T, Yamada J, et al. Systematic review of the psychometric properties, interpretability and feasibility of self-report pain intensity measures for use in clinical trials in children and adolescents. Pain 2006;125:143–57.