Ultrasonography *vs.* clinical examination in children with suspected arthritis. Does it make sense to use poliarticular ultrasonographic screening?

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Abstract

Background

Juvenile idiopathic arthritis (JIA) is a term that encompasses all forms of arthritis that begin before the age of 16 years old, persist for more than 6 weeks and are of unknown cause. The ILAR criteria for JIA classification are based on the number of joints involved. The aim of our study was to compare clinical evaluation and ultrasonography (US) in the assessment of joint synovitis in children with suspected JIA.

Patients and methods

We enrolled in our study all children who presented at our outpatient clinic of Paediatric Rheumatology with suspected JIA. All the children underwent a clinical examination for joint swelling (40 joints), a tender joint count (42 joints) and US examination (42 joints) on the same day. They all returned to the clinic after approximately 2 weeks with the results of the tests prescribed at the first visit and a diagnosis was formulated.

Results

Thirty-one children were enrolled. More synovitis was identified by US than by than clinical examination (42 joints vs. 27). Clinical examination classified as swollen 13 joints that did not result affected at US. Of the 94 painful joints, 24 were affected by synovitis at US. The final diagnoses were: 9 children with JIA (any form), 9 were classified as healthy and 13 with other diseases. One child was reclassified and 2 were diagnosed with JIA thanks to US.

Conclusions

US detected more synovitis than clinical examination in children with suspected JIA, therefore, US should be included in the screening procedure of children with suspected JIA.

Key words

ultrasound, JIA, children, clinical examination

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Introduction

Juvenile idiopathic arthritis (JIA) is a term that encompasses all forms of arthritis that begin before the age of 16 years, persist for more than 6 weeks and are of unknown cause. JIA is the most common chronic rheumatic disease in children, with a prevalence that varies between 16 and 150 per 100,000 in developed countries (1). The most widely used classification for JIA is that of the International League of Associations for Rheumatology (ILAR) (2). This classification recognizes seven disease categories, principally based on clinical findings such as the number of joints involved and enthesis involvement.

Recently Magni-Manzoni *et al*. (3) and Haslam KE *et al*. (4) have demonstrated that subclinical synovitis is common in children and may therefore lead to erroneous classification of the disease, with important clinical and therapeutic implications.

The aim of our study was to compare clinical evaluation and ultrasonography in the assessment of joint synovitis in children with suspected JIA, who presented at our Paediatric Rheumatology outpatient clinic due to pain in one or more joints for more than 2 weeks.

Patients and methods

We evaluated for possible enrollment in our study all consecutive children who presented at our Paediatric Rheumatology outpatient clinic between June and December 2009, who had been referred by their family paediatrician due to suspected JIA. The criteria for enrollment were the presence of pain in one or more joints, with or without swelling, persisting for more than 2 weeks, as evaluated by the rheumatologist at the time of the initial visit. Informed consent was obtained from all the patients' parents or guardians, as appropriate.

At the time of the initial visit all the patients' personal details, the duration of symptoms and a brief family history were recorded. Clinical evaluation was performed by a rheumatologist with 7 years' experience in clinical rheumatology. A total of 40 joints were assessed for swelling and 42 for tenderness/pain on motion (10 metacarpophalangeal (MCP), 10 proximal interphalangeal joints of the hands (PIP), 2 wrists, 2 elbows, 2 shoulders, 2 hips – pain only assessment – 2 knees, 2 ankles, 10 metatarsophalangeal (MTP) joints). To define swelling and pain in the children's joints we used a standard technique as described previously (5), but with a dichotomous score (grades 1-2-3 of swelling/pain were classified as present, grade 0 as absent) in order to facilitate joint classification and reduce the total examination time and children's discomfort. We included shoulders and hips in the clinical examination in order to provide an idea of effective sensitivity and specificity of the clinical examination of these joints in children with recent onset of symptoms.

Ultrasonographic examination was performed immediately after the clinical examination, on the same day as the first visit, by a rheumatologist with 8 years' experience in musculoskeletal US. The same 42 joints were assessed for the presence of synovitis, effusion and power Doppler (PD) signal. US examination was performed using an Esaote Technos MP and Esaote Mylab 70XVG ultrasound systems (Esaote SpA, Genoa, Italy) equipped with multi-frequency probes from 8 to 18Mhz. Synovitis was defined as hypoechoic or hyperechoic tissue in the joint cavity that was not compressible with the probe. Joint effusion was defined as hypo/anechoic material in the joint space that was easily compressible with the probe. The PD signal was considered positive in the presence of spots within the joint space. Effusion and synovitis were graded using a semi-quantitative score: grade 0=absent, grade 1=mild, grade 2=moderate, grade 3=severe. Grading was performed following global evaluation of the joint with longitudinal, coronal and transverse scans rather than a single standard scan. In a recent paper Collado *et al*. (6) suggest that a small amount of liquid could be found in the palmar aspect of MCP and in the knee joints in healthy children; for this reason we decided to evaluate only the dorsal aspect of the MCPs and to consider as not pathological a minimal amount of liquid in the knees.

The clinician and ultrasonographer

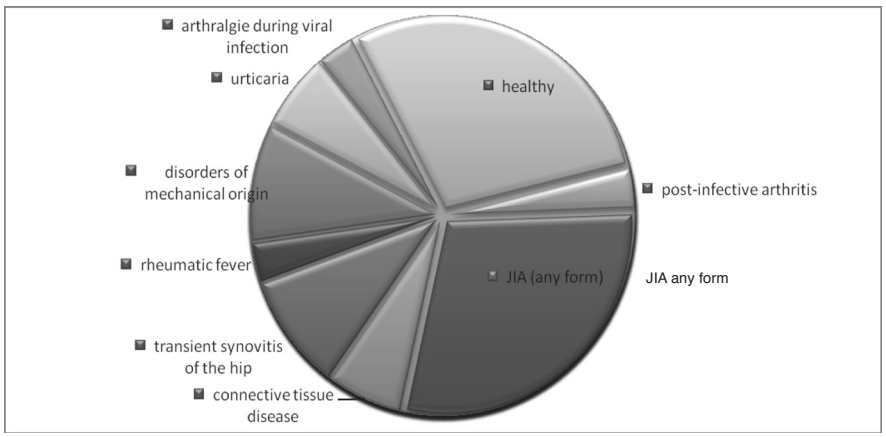

Fig. 1. Diagnoses made at t2.

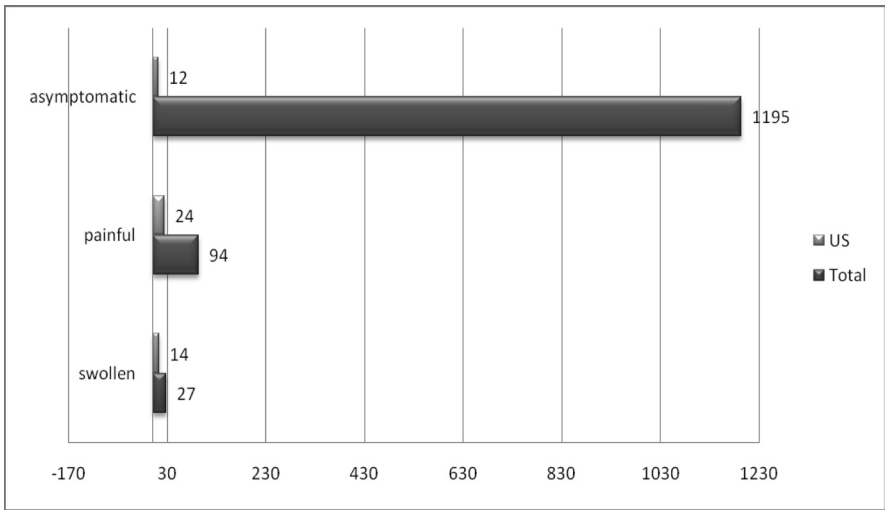

Fig. 2. Prevalence of US joint involvement in asymptomatic joints, painful joints and swollen joints according to clinical examination.

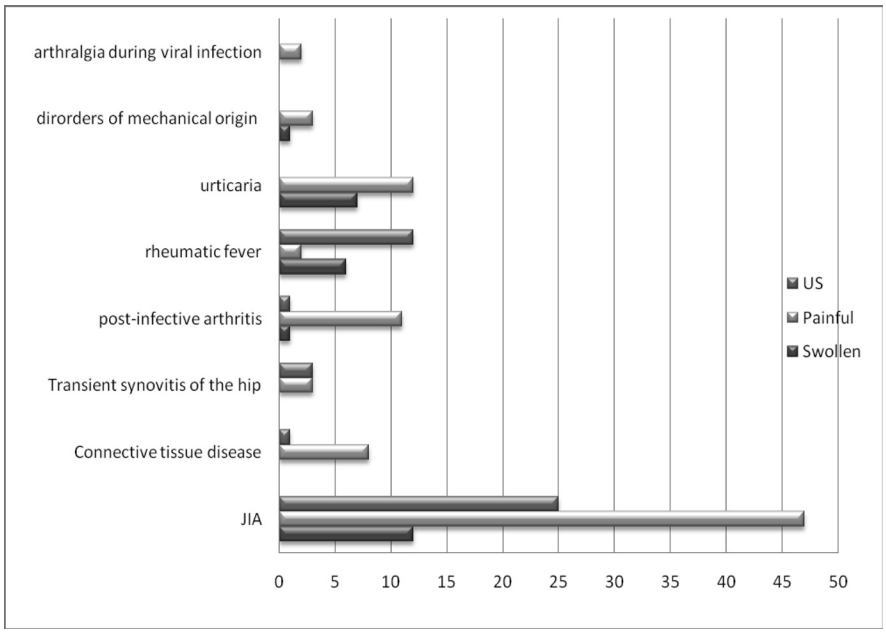

Fig. 3. Prevalence of swollen, painful and US involved joints according to final diagnosis.

were blinded to each others' findings at the time of the evaluations. After the first visit, the children returned after 2–4 weeks (time 2, t2) with the results of all tests prescribed by the pediatric rheumatologist at the time of the first visit. On this occasion, the clinician retrieved the ultrasonographic findings and formulated the diagnosis.

Results

We enrolled in our study 31 children (16 boys and 15 girls) with mean age of 8 years (standard deviation, SD±3.7). The final diagnoses at t2 were 6 children with extended oligoarthritis, 1 child with rheumatoid factor negative polyarthritis, 1 child with psoriatic arthritis, 2 with connective tissue disease, 3 with transient synovitis of the hip, 1 with post-infectious arthritis, 1 with rheumatic fever, 1 with Osgood-Schlatter disease, 1 with post-traumatic patellar bursitis, 1 with patellar instability, 1 with diffuse articular pain in the course of a viral infection, 2 with urticaria, 1 with enthesitis related arthritis, and 9 children were classified as healthy (Fig. 1).

At clinical examination, of the total of 1240 joints assessed for effusion/synovitis and 1302 for pain, 27 (2.2%) and 94 (7.2%) were found positive, respectively. At US examination 42 joints out of 1302 (3.22%) were found positive for synovitis and/or effusion. Of the 27 joints clinically assessed as swollen only 14 (51.8%) had synovitis at US, and of the 94 joints classified as painful 24 (25%) had synovitis at US. Finally of the 1195 joints that were negative at clinical examination, 12 revealed synovitis on US (Fig. 2).

Considering the final diagnosis, clinical examination demonstrated a higher sensitivity in children with transient synovitis of the hip, where all hips classified as affected presented effusion on US examination. On the other hand, in the nine cases in which no pathology was found, clinical examination revealed 19 tender joints (5% of the total) and 4 swollen joints (1.5% of the total), whereas US examination revealed no effusion or synovitis in any joint. In the 9 cases of JIA (any form) clinical examination revealed 12 swollen joints (3.7% of the total) and 47 tender joints

(12% of the total), while US examination revealed 25 affected joints in these children (7% of the total). Of these 25 joints identified as affected at US, 12 were classified as swollen at clinical examination (48%) and 18 were classified as tender (72%). In the two cases of children with urticaria we found a high degree of false positive joints (7 swollen and 12 tender joints) at clinical examination, due to the presence of skin oedema (Fig. 3).

If we divide the children into three groups by age (0–5, 6–10, 11 or more years old) we find that clinical examination demonstrated similar sensitivity in identifying swollen joints in all groups (31%, 28% and 36% respectively). Furthermore, the tender joint count identified active joints in 54%, 19% and 28% of the three groups. Even if we eliminate from this analysis the cases in which pain was justified by disorders of mechanical origin (patellar instability, Osgood-Schlatter and prepatellar bursitis), there is no significant change in the final results (54%, 20% and 29%).

Finally, in the joint-based analysis we found that clinical examination was more accurate in identifying joint effusion in knees (7/10, 70%) and less sensitive in the small joints of the feet and hands (2/10, 20%) and elbows (1/6, 16%) (Fig. 4). Moreover, the swollen joints were frequently not painful and/or did not present reduction of the range of motion (43%).

In almost all cases in which clinical examination failed to reveal joint effusion (Fig. 5), US examination revealed grade 1 effusion and/or synovitis. In one case there was grade 2 effusion of the elbow and grade 2 synovitis of a wrist but with grade 1 effusion. US determined a reclassification of arthritis in one case and was the determining factor for the diagnosis of two cases of JIA.

The average time for the execution of US was about 1 hour for younger and restless children and about 30–40 minutes for older and collaborating ones.

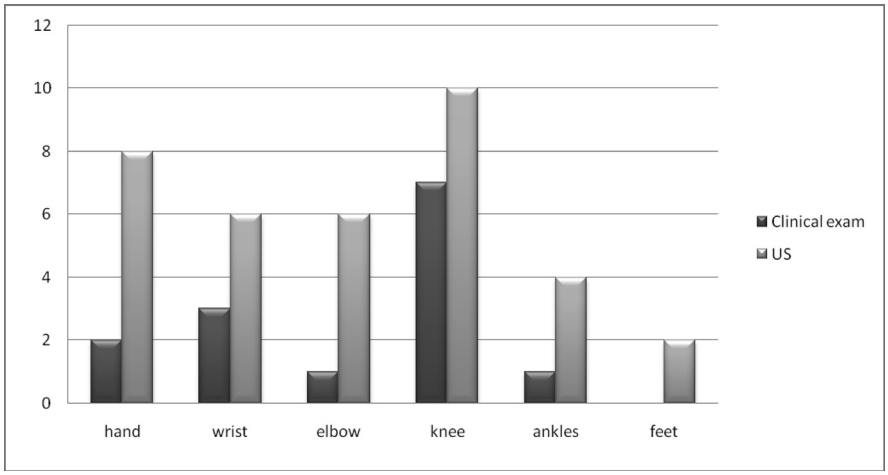

Fig. 4. Prevalence of joint effusion according to clinical examination and US at various sites. Shoulders were negative either at clinical exam or US and have been omitted. Hips were evaluated only for tenderness at clinical exam.

Discussion

US has gained an important position in rheumatologists' clinical practice. This is due to its intrinsic characteristics, such as low costs, rapidity, lack of radiation. It has also been demonstrated that US can easily identify a large series of joint and peri-articular disorders of inflammatory or mechanical origin (7). In adult patients, US can identify joint synovitis with a sensitivity similar to that of MRI (8-10) and is superior to clinical examination as it can detect subclinical synovitis in patients with rheumatoid and early arthritis (11, 12). For these reasons, US could be a valuable tool in the assessment of JIA, as it is the only examination that can offer a significant amount of information on a large number of joints in a relatively short time and with minimal discomfort of the patient. In fact, the first studies on the utility of US in the assessment of joint involvement in JIA have recently been published (3, 4). In these studies US has demonstrated a greater sensitivity in identifying joint synovitis than clinical examination alone. This is of major importance, as clinical classification and therapeutic strategy in JIA are guided by the number of joints involved (1). In both studies, US examination was carried out in children with a clinically established diagnosis of JIA.

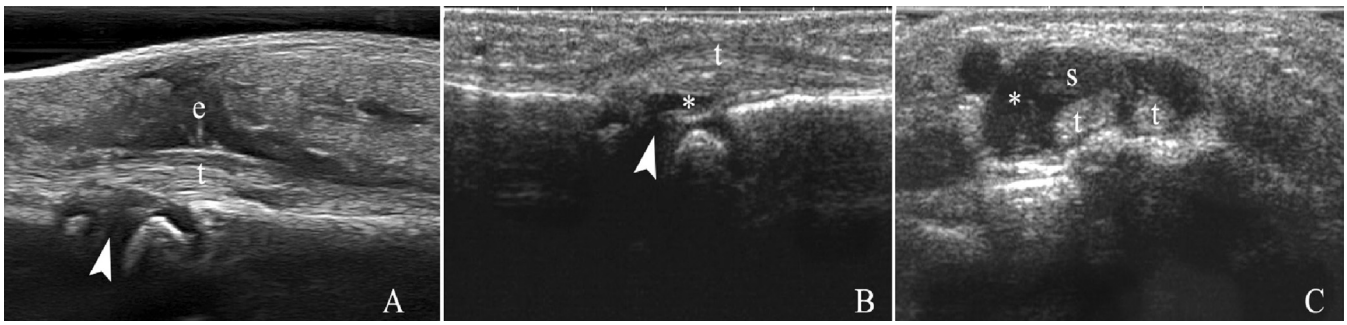

Fig. 5. The most common pitfalls of clinical examination found in our series of patients. Panel **A**: severe subcutaneous oedema of the hand in a child with urticaria, Panel **B**: a grade 1 effusion in a metacarpal-phalangeal joint Panel **C**: tenosynovitis of the extensor rdialis tendons at the wrist. Arrowhead: MCP joint, **t**: tendons, asterisk: effusion, **e**: subcutaneous oedema, **s**: synovial proliferation in the tendon's sheath during tenosynovitis.

To our knowledge, this study is the first in which US was performed in children with suspected JIA, in a context similar to an "early arthritis clinic" for adults. Our aim was to investigate the utility of US in such a context by comparing US findings and clinical examination in the classification of children with suspected JIA.

In this study, US detected more affected joints than clinical examination (42 *vs*. 27 joints). This result is similar to that reported by other authors (3, 4). Of the 31 children enrolled, only 9 received a final diagnosis of any form of JIA (29%). US was valuable in distinguishing false positive joints, as verified in the cases of urticaria or prepatellar bursitis, thus permitting a correct diagnosis. This is in accordance with the results of Magni-Manzoni *et al*. and Haslam *et al*., in whose studies 23 and 6 joints, respectively, were classified as affected by clinical examination but were normal at US. In our study, 2 more children could have been classified as affected by arthritis in the absence of US. On the other hand, in some cases of our cohort of children, US revealed synovitis in joints that resulted unaffected at clinical examination. By US two children were diagnosed as affected by arthritis and 1 child was reclassified as having the polyarticular form.

If we consider the age of the children, we found no significant differences of the capacity of clinical examination to detect joint synovitis. To our knowledge, this is the first controlled US analysis. Magni-Manzoni *et al*. report that age did not affect the correlation between their clinical and US findings, but do not show this data in the paper. It would be reasonable to assume that clinical examination of small children may be more challenging because of the dimensions of the joints and the patients' willingness to collaborate. Nonetheless, clinical examination demonstrated similar sensitivity to US in evaluating joint swelling in all age groups (0–5, 6–10, above 11 yrs). Considering tender joints, clinical examination was more accurate in younger children (<5 yrs), in whom 54% of the joints classified as active by palpation and range of motion were actually affected by synovitis at US. This percentage decreased in older children (19% and 28%). The absolute number of tender joints could be the reason for this discrepancy, as we found only 11 tender joints in younger children (<5 yrs), *versus* 21 joints in the 6–10 group and 50 joints in the older group (excluding the 2 children with urticaria and oedema of the hands that was referred as pain in the underlying joints).

Regarding individual joints, clinical examination demonstrated poor sensitivity in assessing the small joints of the hands and feet (20%) and elbows. It has already been shown that the small joints of the hands are those in which there are more clinical discrepancies between observers (13). Magni-Manzoni *et al*. (3) also reported that subclinical synovitis was more common in hands and wrists in their cohort of patients. Similar results were also reported by Haslam *et al*. (4). In another study (14), where US and clinical examination were performed only at MCP joints of children with established JIA, the authors report a significant association between the grade of clinical severity and the presence of abnormalities on US. However, in this study the authors evaluated five US parameters (erosions, cartilage thinning, joint synovitis and effusion, tenosynovitis) and four clinical parameters (tenderness, pain on motion, swelling and limitation of motion) performing a global statistical analysis among all these parameters. Nevertheless, they also report a high prevalence of abnormalities in US in clinically normal joints (22/89) and a low Kappa agreement (0,1) between the two methods if we consider a dichotomous score at clinical examination (normal/abnormal). The knee was the joint with the highest clinical examination sensitivity in our patients (70%). This percentage is similar to those of the other 2 studies mentioned above, but it is still lower than sensitivity of clinical examination of the knee in adult patients with rheumatoid arthritis (93%) as demonstrated in a recent study by Riente *et al*. (15). In a study performed by Kakaty *et al*. (16) comparing clinical examination and US assessment of the knee in children with juvenile rheumatoid arthritis, the authors found a low sensitivity and a high specificity of clinical examination (42% and 86% respectively, calculated from the data reported in the paper) but they used a composite index to define "active joint". This index included the presence of pain (score 0.1), swelling (score 0.4) and functional impairment (score 0–4). Patients with mean score >1 were classified as active knee involvement. That means that patients with only slight effusion (score 1) were classified as inactive and this could explain the high specificity and the discrepancy with our data. Hip joint tenderness demonstrated a high correlation with US joint effusion, particularly in the cases of mono-articular involvement, such as transient hip synovitis (3/3). Considering the hip globally, in

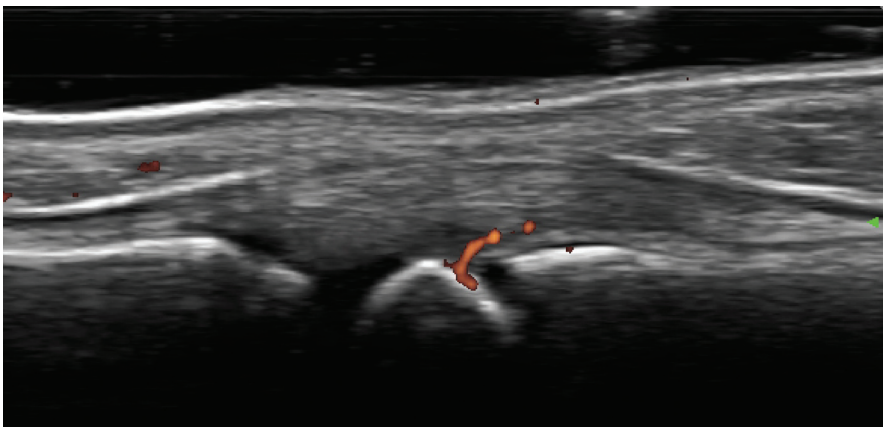

Fig. 6. Power Doppler positive signal in a MCP joint of a healthy child. This finding is relatively frequent in MCPs of healthy younger children, adjacent to the growth plate, probably due to the presence of nutrition vessels.

all forms of arthritis, we found that clinical examination (intended as tenderness/pain on motion) had a sensitivity of 83% and a specificity of 100% in detecting hip involvement.

In our study we preferred not to report PD findings as it is not yet clear the vascular pattern of the joints in children. Based on personal experience, in unpublished data of other experienced ultrasonographers, and in the data reported by Karmazyn *et al*. (14), PD signal could be found in joints of healthy children, especially the younger ones, due to the presence of nutrition vessels (Fig. 5). It has also been demonstrated that PD signal could be found in wrists and MCPs of healthy adults (17). On the other hand, Collado *et al*. (6) report that no abnormal PD signal was found in joints of healthy children. In the study of Magni-Manzoni (3), PD signal is considered as one of the three features used to classify a joint as active so no separate data are provided in the paper for the presence of PD alone and the interpretation of the sonographer in that case. Haslam *et al*. (4) did not evaluate this aspect in their work.

In fact a large control group could be useful to address this and other issues, but healthy volunteers of this age are really difficult to recruit. Another limitation of our study is the lack of validation of the US findings with other techniques such as MRI, which would be very hard to achieve as MRI cannot acquire images of such a large number of joints in a reasonable time. Furthermore, general anesthesia is necessary to perform MRI on younger patients.

In summary, US demonstrated a higher sensitivity than clinical examination in identifying joint synovitis in children. This was particularly true for the small joints of the hands and feet. Furthermore, in our series of children, US was a determining factor for the correct diagnosis and classification of 3 children with JIA and was useful in identifying extra-articular causes of tissue swelling that mimicked joint effusion. We believe that US should be performed in all children with suspected JIA, as the number of joints involved is crucial for correct classification and an appropriate treatment strategy.

References

1. RAVELLI A, MARTINI A: Juvenile idiopathic arthritis. *Lancet* 2007; 369: 767-78.
2. PETTY RE, SOUTHWOOD TR, MANNERS P *et al*.: International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton 2001. *J Rheumatol* 2004; 31: 390-2.
3. 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.
4. HASLAM KE, McCANN LJ, WYATT S, WAKEFIELD RJ: The detection of subclinical synovitis by ultrasound in oligoarticular juvenile idiopathic arthritis: a pilot study. *Rheumatology* 2010; 49: 123-7.
5. RAVELLI A, VIOLA S, RUPERTO N *et al*.: Correlation between conventional disease activity measures in juvenile chronic arthritis. *Ann Rheum Dis* 1997; 56: 197-200.
6. COLLADO P, NAREDO E, CALVO C, CRESPO M: Assessment of the joint recesses and tendon sheaths in healthy children by high-resolution B-mode and power Doppler sonography. *Clin Exp Rheumatol* 2007; 25: 915-21.
7. DELLE SEDIE A, RIENTE L, BOMBARDIERI S: Limits and perspectives of ultrasound in the diagnosis and management of rheumatic diseases. *Mod Rheumatol* 2008; 18: 125-31.
8. SZKUDLAREK M, COURT-PAYEN M, STRANDBERG C, KLARLUND M, KLAUSEN T, ØSTERGAARD M: Power Doppler ultrasonography for assessment of synovitis in the metacarpophalangeal joints of patients with rheumatoid arthritis. A comparison with magnetic resonance imaging. *Arthritis Rheum* 2001; 9: 2018-23.
9. TERSLEV L, TORP-PEDERSEN S, SAVNIK A *et al*.: Doppler ultrasonography and magnetic resonance imaging of synovial inflammation of the hand in rheumatoid arthritis. A comparative study. *Arthritis Rheum* 2003; 9: 2434-41.
10. SZKUDLAREK M, KLARLUND M, NARVESTAD E *et al*.: Ultrasonography of metacarpophalangeal and proximal interphalangeal joints in rheumatoid arthritis. A comparison with magnetic resonance imaging, conventional radiography and clinical examination. *Arthritis Res Ther* 2006; 8: R52.
11. WAKEFIELD RJ, GREEN MJ, MARZO-ORTEGA H *et al*.: Should oligoarthritis be reclassified? Ultrasound reveals a high prevalence of subclinical disease. *Ann Rheum Dis* 2004; 63: 382-5.
12. NAREDO, BONILLA G, GAMERO F, USON J, CARMONA L, LAFFON A: Assessment of inflammation activity in rheumatoid arthritis: a comparative study of clinical evaluation with grey-scale and power Doppler. *Ann Rheum Dis* 2005; 64: 375-81.
13. GUZMAN J, BURGOS-VARGAS R, DUARTE-SALAZAR C, GOMEZ-MORA P: Reliability of the articular examination in children with juvenile rheumatoid arthritis: interobserver agreement and sources of disagreement. *J Rheumatol* 1995; 22: 2331-6.
14. KARAMZYN B, BOWYER SL, SCHMIDT KM *et al*.: US findings of metacarpophalangeal joints in children with idiopathic juvenile arthritis. *Pediatr Radiol* 2007; 37: 475-82.
15. RIENTE L, DELLE SEDIE A, FILIPPUCCI E *et al*.: Ultrasound Imaging for the Rheumatologist. XXVII. Sonographic assessment of the knee in patients with rheumatoid arthritis. *Clin Exp Rheumatol* 2010; 28: 300-3.
16. KAKATY P, SODHI KS, SANDHU MS *et al*.: Clinical and ultrasound assessment of the knee in children with juvenile rheumatoid arthritis. *Indian J Pediatr* 2007; 74: 831-6.
17. TERSLEV L, TORP-PEDERSEN S, QVISTGAARD E *et al*.: Doppler ultrasound findings in healthy wrists and finger joints. *Ann Rheum Dis* 2004; 63: 644-8.