Impact of musculoskeletal ultrasound on clinical practice in paediatric rheumatology

J.C. Nieto-González[1], I. Monteagudo[1], L. Vargas-Henny[2], I. Janta[1], E. Naredo[1], L. Carreño[1]

[1]Rheumatology Department and Paediatric Rheumatology Unit;
[2]Immunology Department, Hospital General Universitario Gregorio Marañón, Madrid, Spain.

Abstract

Objective

Musculoskeletal ultrasound (MSUS) is an imaging technique increasingly used in paediatric rheumatology. The aim of our study was to evaluate the extent to which MSUS may influence the diagnosis and management decisions in daily clinical practice in paediatric rheumatology.

Methods

All child patients attending our PR unit over a 3-month period were included. A consultant rheumatologist assessed juvenile patients and weighted the need for MSUS assessment under a Likert scale from 0 (not necessary) to 5 (very necessary) with scanning performed when the Likert score was greater than 0. The rheumatologist completed a questionnaire used to report previous and current diagnosis, therapeutic decisions and disease activity. An assistant rheumatologist who was blinded to the questionnaire carried out the MSUS scanning of selected joints. After MSUS examination, a second questionnaire was completed by the consultant rheumatologist reporting changes in diagnosis and systemic and local treatment, if applicable.

Results

We included 111 patients [73 (65.8%) female]. Fifteen (13.5%) were new patients and 96 (86.5%) follow-up patients. Fifty-one (45.9%) patients were diagnosed with JIA. 65 (58.6%) patients qualified for MSUS. A total of 108 joints from 65 patients were clinically assessed with 93 (86.1%) joints deemed to require complementary MSUS assessment (mean assessed joints 1.4 per patient). Of the 65 patients undergoing MSUS, 38 (58.5%) patients there was a change in diagnosis, therapeutic decisions or both following the MSUS information.

Conclusion

MSUS may play a significant role in local diagnosis and therapeutic decisions among follow-up JIA patients and could help in the management of rheumatic diseases in children. Further longitudinal studies are needed to confirm the impact of MSUS in paediatric rheumatology.

Key words
musculoskeletal ultrasound, paediatric rheumatology, impact

Juan Carlos Nieto-González, MD
Indalecio Monteagudo, PhD
Loreto Vargas-Henny, MD
Iustina Janta, MD
Esperanza Naredo, PhD
Luis Carreño, PhD

Please address correspondence to:
Juan Carlos Nieto-González,
C/ María Moliner 9, portal 12, 2º B,
28523 Rivas Vaciamadrid,
Madrid, Spain.
E-mail: juancarlos.nietog@gmail.com

Received on November 12, 2014; accepted in revised form on March 26, 2015.

Funding: J.C. Nieto-González has received speaker fees from Abbvie, Roche Farma, Pfizer, MSD; I. Monteagudo has received speaker fees from Abbvie, Roche Farma, Bristol-Myers Squibb, Pfizer, UCB; E. Naredo has received speaker fees from Abbvie, Roche Farma, Bristol-Myers Squibb, Pfizer, UCB, General Electric Healthcare, and Esaote, and has also received research funding from UCB and MSD.

Competing interests: none declared.

Introduction

Paediatric rheumatologists see a wide variety of patients. The diseases traditionally considered as rheumatic include rheumatic fever, juvenile idiopathic arthritis (JIA), juvenile systemic lupus, juvenile dermatomyositis, juvenile scleroderma, vasculitic syndromes, autoinflammatory diseases and a number of rare conditions. Prominent involvement of the musculoskeletal system and chronic or recurrent inflammation of connective tissues characterise almost all of these conditions. Clinical examination is still the standard method for detecting synovitis and assessing disease activity in JIA and other chronic arthritic conditions despite MSUS being more sensitive than clinical assessment in detecting synovitis (1). Musculoskeletal ultrasound (MSUS) is an imaging technique increasingly used in rheumatology, both in adults and children (2), and has shown added value in the diagnosis and management of these diseases in children (3, 4). MSUS is non-ionising, quick, safe, and friendly, making this imaging modality especially appropriate for children.

There are a number of studies that have shown the impact of MSUS in adult rheumatology (5-12); however, to the best of our knowledge there are no studies on the impact of MSUS in children. The aim of our study was to evaluate the extent to which MSUS could affect standard procedures for diagnosis, evaluation of disease activity as well as treatment decisions.

Patients and methods

All juvenile patients attending our paediatric rheumatology (PR) clinic at the Gregorio Marañón University Hospital over a three month period were included in the study. A consultant rheumatologist with 25 years' experience in PR assessed clinically the patients and graded the need for MSUS under a Likert scale from 0 (not necessary) to 5 (very necessary), selecting the joint or joints to be scanned. MSUS was performed on all patients where the Likert score was greater than 0. Factors influencing the Likert score included clinical assessment of current or historically symptomatic joints, disease activity and laboratory data.

A questionnaire was created for the study to be completed for all patients. Patient demographics, disease history, inflammatory activity status, diagnosis and current treatment were all recorded by the attending rheumatologist. Following the visit, the rheumatologist recorded the global patient disease diagnosis, local diagnosis, *i.e.* pathological findings at joint level, or both. Any therapeutic decisions were also recorded.

The questionnaire also included 4 MSUS assessment justifications:

1. Assessment of disease activity based on inflammatory findings at joint level.
2. Diagnosis at joint level for reasons other than assessment of joint inflammatory activity, *e.g.* mechanical pain.
3. Evaluation of response to treatment started or intraarticular injections done in previous visits.
4. Other reasons, *e.g.* evaluation of salivary glands.

An assistant rheumatologist, with 2 years' MSUS experience in PR and blinded to the questionnaire, scanned the selected joints immediately following clinical evaluation. A complete US examination was performed for each scanned joint in strict adherence to the EULAR Guidelines for musculoskeletal ultrasound in rheumatology (1, 13). The MSUS assessment consisted of dynamic examination on B-Mode and power Doppler, with a Logic E BT12 (General Electric Healthcare, Wuxy, China), using a linear probe (5-13 MHz) or a stick probe (6.5-18 MHz) depending on the depth and site of the joint.

On scanning completion, MSUS findings were passed to the consultant rheumatologist. A second questionnaire was then completed by the consultant rheumatologist which included the results from scanning. The two questionnaires were then compared with any changes in disease activity evaluation, global and local diagnosis, or therapeutic decisions noted.

MSUS is a safe, non-invasive imaging technique used extensively in general clinical practice, therefore it is appropriate for the assessment of children.

The study was approved by the ethics committee of the H.G.U. Gregorio Marañón.

Table I. Demographics and previous diagnosis in the total population and patients who underwent MSUS.

	Total	Patients with MSUS
Number of patients	111	65 (58.6%)
Sex (F/M) (69.2/30.8%)	73/38 (34.2/65.8%)	45/20
Age; mean (SD)	6.9 (5)	6.4 (5.2)
Diagnosis	n (%)	n (%)
Juvenile idiopathic arthritis	51 (45.9)	42 (64.6)
Conective tissue disease	13 (11.7)	2 (3.1)
Hip transient synovitis	5 (4.5)	3 (4.6)
Unspecific arthralgia/arthritis	17 (15.3)	10 (15.4)
Reactive arthritis	2 (1.8)	2 (3.1)
Mechanical back pain	3 (2.9)	0
Other diseases	9 (8.1)	0
Osteoporosis	1 (0.9)	0
No diagnosis (new patients)	10 (9)	6 (13.8)

MSUS: musculoskeletal ultrasound; SD: standard deviation.

Table II. Joints assessed, clinically and with MSUS.

	Number of assessed joints with MSUS		
	Total patients (n=65)	JIA (n=42)	No JIA (n=23)
Knee	42	30	12
Ankle	17	11	6
Wrist	11	5	6
Hand	8	7	1
Hip	7	2	5
Elbow	6	3	3
Foot	2	1	1
Total	93	59	34

MSUS: musculoskeletal ultrasound; JIA: juvenile idiopathic arthritis.

Statistical analysis

Quantitative measures were summarised in mean, range and standard deviation (SD). Qualitative measures were summarised by percentages.

Results

The study included 111 patients [73 (65.8%) female]. Fifteen (13.5%) were new patients and 96 (86.5%) follow-up patients. Fifty-one (45.9%) patients were previously diagnosed with JIA, subcategory breakdown being: persistent oligoarthritis, 30 patients (58.8%); extended oligoarthritis, 3 patients (5.8%); polyarticular arthritis rheumatoid factor negative, 9 patients (17.6%); enthesitis-related arthritis, 6 patients (11.8%); and psoriatic arthritis, 3 patients (5.8%). Sixty (54.1%) patients were non-JIA patients.

Table I shows demographic data and all previous diagnosis. Of 13 (11.7%) patients who had connective tissue disease, 6 had juvenile dermatomyositis, 3 juvenile systemic lupuserythematosus, 2 juvenile scleroderma, 1 primary juvenile Sjögren's syndrome and 1 Behçet's disease. Of 9 patients (8.1%) with other diseases, 2 had uveitis; 2, recurrent idiopathic pericarditis; 1, epiescleritis; 1, aphthas appellants; 1, isolated nettle-rash; 1, chronic recurrent ostemielitis; and 1 had factor 5 Leiden deficiency.

The consultant rheumatologist judged the need for MSUS greater than 0 on the Likert scale in 65 (58.6%) patients (mean score 3.46, range 1–5). A score greater than 3 was accorded in 61 of the 65 (93.8%). A total of 108 joints from 65 patients were clinically assessed and of these, 93 joints (86.1%) underwent MSUS assessment. The mean number of assessed joints in each MSUS examination was 1.4, both in JIA and no-JIA patients. In the majority of patients just one or two joints were assessed. Table II shows the assessed joints with MSUS in JIA patients and non-JIA patients (Fig. 1).

Table III shows the reasons for MSUS, which were mainly diagnostic at the joint level in non-JIA patients and for joint inflammatory activity assessment in JIA patients.

In 38 (57.4%) patients there was a change in diagnosis, therapeutic decisions, or both following the MSUS information. Table IV shows changes in diagnosis at the joint level and changes in treatment decisions following MSUS data. Twenty patients (30.3%) underwent changes in both local diagnosis and treatment decisions. In 1 patient with clinical monoarthritis in the right wrist, a global diagnosis of oligoarticular JIA was made and a methotrexate course of therapy prescribed follow-

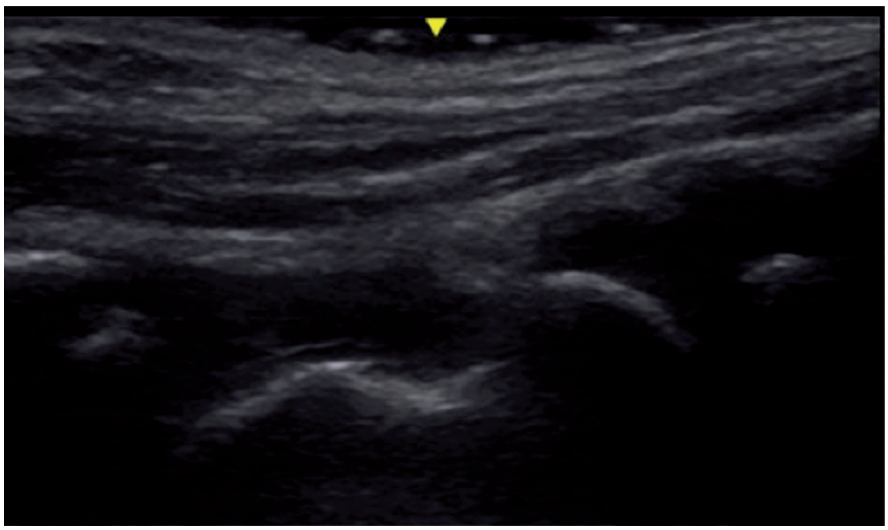

Fig. 1. Muskuloskeletal ultrasound image of an ankle of 4 years-old girl. Longitudinal scan of the anterior recess, showing tibio-talar synovitis.

ing MSUS results. MSUS of wrist and metacarpophalangeal joints billaterally was performed due to occasional arthralgia in both wrists and persistent right wrist monoarthritis with poor response to non-steroid anti-inflammatory drugs. MSUS elucidated synovitis in both wrists and in right 4th compartment tenosynovitis. Sixteen patients (24.2%) saw changes in local diagnosis, mainly mild degrees of synovitis, without changes in therapeutic decisions. Although these joints were either symptomatic or asymptomatic they had a history of inflammation. The consultant rheumatologist, however, did not consider these MSUS findings relevant in light of the clinical examination.

Of the 15 new patients, local inflammation was suspected in twelve (80%). MSUS was performed in 9 (75%) to confirm or rule out clinically suspected synovitis or tenosynovitis. Of the 9 patients who underwent MSUS, four had been previously diagnosed (2 had JIA, 1 hip transient synovitis and 1 reactive arthritis). Mean MSUS assessed joints was 1.5 in new patients, slightly greater than in follow-up patients (mean 1.3). In 3 previously undiagnosed new patients, diagnosis at joint level was changed following MSUS (*i.e.* synovitis) and in 2, local therapeutic decisions were also changed.

Finally, Table V shows therapeutic decision changes in JIA patients following MSUS. Four patients increased or started either synthetic (sDMARD) or biological (bDMARD) disease modifying antirheumatic drugs. Four patients either decreased or stopped DMARD. Therapeutic intra-articular corticosteroid injection was prescribed to 6 patients (9.1%) following MSUS, [5 JIA and 1 with undifferentiated arthritis]. All These injections were guided by US.

Table III. Reasons to ask for MSUS.

Reason	Total (n=65)	JIA (n=42)	No JIA (n=23)
Joint activity assessment	40 (61.5%)	33 (78.6%)	7 (30.4%)
Diagnostic (local)	17 (26.2%)	2 (4.8%)	15 (65.2%)
Assessment of treatment response	8 (12.3%)	7 (16.7%)	1 (4.4%)

MSUS: musculoskeletal ultrasound; JIA: juvenile idiopathic arthritis.

Table IV. Changes in local diagnosis and therapeutic decision.

Changes in local diagnosis/treatment	Total (n=65)	JIA (n=42)	No JIA (n=23)
No changes	28 (42.4%)	16 (38.1%)	12 (52.2%)
Changes in both diagnosis and therapeutic decision in joint activity assessment	15 (23.1%)	13 (31%)	2 (8.7%)
Changes only in diagnosis in joint activity assessment	9 (13.8%)	9 (21.4%)	0
Changes in both diagnosis and therapeutic decision in local diagnostic MSUS	4 (6.2%)	0	4 (17.4%)
Changes only in diagnosis in local diagnostic MSUS	4 (6.2%)	0	4 (17.4%)
Changes in both diagnosis and therapeutic decision in assessment of treatment response	2 (3.1%)	1 (2.4%)	1 (4.3%)
Changes only in diagnosis in assessment of treatment response	3 (4.6%)	3 (7.1%)	0

JIA: juvenile idiopathic arthritis; MSUS: muskuloskeletal ultrasound.

Table V. Therapeutic decisions changes in JIA patients after MSUS.

	n=14	
	Systemic (n=9)	Local (n=6)
Introduction or increased sDMARD	3	-
Introduction or increased bDMARD	1	-
Reduction or discontinuation sDMARD	3	
Reduction or discontinuation bDMARD	1	-
Start NSAID	2	-
Intra-articularjoint injection	-	6

sDMARD: synthetic disease-modifying antirheumatic drugs; bDMARD: biologic disease-modifying anti-rheumatic drugs; NSAID: non-steroidal anti-inflammatory drugs; JIA: juvenile idiopathc arthritis; MSUS: musculoskeletal ultrasound.

Discussion

Some literature has described MSUS in paediatric rheumatology; little, though, to the best of our knowledge, evaluates its impact on daily clinical practice. In an effort to determine to what extent MSUS can influence standard diagnostic procedure, we performed MSUS in 65 out of 111 juvenile patients assessed and found that more than half underwent changes in local diagnosis, treatment decisions or both with the inclusion of MSUS data.

The patient cohort is representative of our usual clinical practice with almost half of child patients diagnosed with JIA, many other children with connective tissue diseases or other frequent paediatric conditions such as reactive arthritis or hip transient synovitis.

Joints were evaluated based on current or previous clinical symptoms with most being referred for additional MSUS assessment (14). With respects to the new child patients in this group, more research is warranted before solid conclusions can be drawn, owing to the limited number (15).

The added value of MSUS in our daily clinical practice is evidenced by the number of diagnoses altered as a result of MSUS examination when this data is considered alongside clinical assessment. Nevertheless, the transversal nature of the study does not enable us to draw solid conclusions as to efficacy of treatment response; a longitudunal study would be needed to address such issues more fully. Nevertheless, MSUS helped us not only to take treatment decisions but also to increase and decrease drug dosage as well as proving useful guiding the injection of intra-articular corticoid.

The mean joints assessed by MSUS was 1.4, both in JIA patients and patients with other rheumatic diseases. Bearing in mind MSUS was recommended to shed light on doubts concerning both global and local diagnosis, a mean av-

erage of 1.4 scanned joints should be feasible in daily practice.

Some limitations of our study should be addressed. The MSUS assessment was performed by just one ultrasonographer and thus we did not assess the reliability of the procedure. In addition, we used adult MSUS scanning guidelines given the lack of stardardised scanning methods in children. Furthermore, we showed mainly changes in local diagnosis and treatment decisions, however we do not know if those changes led to a better outcome for our patients due to the transversal nature of the study. In fact, there are only a few studies on the impact of MSUS findings on JIA outcomes (15). Moreover, comprehensive clinical and MSUS examination was not performed as the joints examined by the consultant rheumatologist were done so according to past or current clinical history. There was also a certain amount of subjectivity involved in the selection of joints sent for scanning. This is understandable and in part unavoidable given the lack of universal guidelines governing such procedures, however, the consultant's considerable clinical experience must be taken into account. Nevertheless, this study focused on the influence of MSUS on routine clinical practice in a busy outpatient clinic. Thus, MSUS assessment was clinically driven and therefore, we consider, appropriate for the context of the study. Finally, the number of new patients was too limited to draw solid conclusions from the study group.

MSUS, therefore, can be considered a tool which can bring evidence to light of hitherto undetected subclinical joint inflammation in JIA child patients increasing confidence in local musculoskeletal diagnosis in paediatric rheumatology. MSUS assessment changed local diagnosis, treatment decisions or both in some of our child patients suggesting a potential role of MSUS in the assessment of joints in children. Further longitudinal studies are needed to confirm the usefulness and impact of MSUS on paediatric rheumatology.

References

1. 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.
2. MAGNI-MANZONI S, COLLADO P, JOUSSE-JOULIN S *et al*.: Paediatric Ultrasound Group of the OMERACT Ultrasound Task Force. Current state of musculoskeletal ultrasound in paediatric rheumatology: results of an international survey. *Rheumatology* (Oxford) 2014; 53: 491-6.
3. COLLADO P, JOUSSE-JOULIN S, ALCALDE M, NAREDO E, D'AGOSTINO MA: "Is ultrasound a validated imaging tool for the diagnosis and management of synovitis in juvenile idiopathic arthritis? A systematic literature review" *Arthritis Care Res* 2012; 64: 1011-9.
4. COLLADO RAMOS P: Ultrasound imaging in juvenile idiopathic arthritis for the rheumatologist. *Clin Exp Rheumatol* 2014; 32: S34-41.
5. SAEED A, KHAN M, MORRISSEY S, KANE D, FRASER AD: Impact of outpatient clinic ultrasound imaging in the diagnosis and treatment for shoulder impingement: a randomized prospective study. *Rheumatol Int* 2014; 34: 503-9.
6. DALE J, PURVES D, MC CONNACHIE A, MCINNES I, PORTER D: Tightening up? Impact of musculoskeletal ultrasound disease activity assessment on early rheumatoid arthritis patients treated using a treat to target strategy. *Arthritis Care Res* (Hoboken) 2014; 66: 19-26.
7. CEPONIS A, ONISHI M, BLUESTEIN HG, KALUNIAN K, TOWNSEND J, KAVANAUGH A: Utility of the ultrasound examination of the hand and wrist joints in the management of established rheumatoid arthritis. *Arthritis Care Res* (Hoboken) 2014; 66: 236-44.
8. D'AGOSTINO MA, AYRAL X, BARON G, RAVAUD P, BREBAN M, DOUGADOS M: Impact of ultrasound imaging on local corticosteroid injections of symptomatic ankle, hind-, and mid-foot in chronic inflammatory diseases. *Arthritis Rheum* 2005; 53: 284-92.
9. NARANJO A, JIMÉNEZ-NÚÑEZ FG, MEDINA-LUEZAS J *et al*.: Impact of the use of musculoskeletal ultrasound by rheumatologists in patients with shoulder and hand complaints compared with traditional clinical care. *Clin Exp Rheumatol* 2012; 30: 768-71.
10. KARIM Z, WAKEFIELD RJ, CONAGHAN PG *et al*.: The impact of ultrasonography on diagnosis and management of patients with musculoskeletal conditions. *Arthritis Rheum* 2001; 44: 2932–3.
11. KAY JC, HIGGS JB, BATTAFARANO DF: Utility of musculoskeletal ultrasound in a department of defense rheumatology practice: a four-year retrospective experience. *Arthritis Care Res* (Hoboken) 2014; 66: 14-8.
12. MICU MC, ALCALDE M, SÁENZ JI *et al*.: Impact of musculoskeletal ultrasound in an outpatient rheumatology clinic. *Arthritis Care Res* (Hoboken). 2013; 65: 615-21.
13. M BACKHAUS, G-R BURMESTER, T GERBER *et al*.: Guidelines for musculoskeletal ultrasound in rheumatology. *Ann Rheum Dis* 2001; 60: 641-9.
14. BUGNIMIOTTO E, SILVA V, DE FREITAS TAVARES DA SILVA C *et al*.: Do patients with juvenile idiopathic arthritis in remission exhibit active synovitis on joint ultrasound? *Rheumatol Int* 2014; 34: 937-45.
15. MAGNI-MANZONI S, SCIRÈ CA, RAVELLI A *et al*.: Ultrasound-detected synovial abnormalities are frequent in clinically inactive juvenile idiopathic arthritis, but do not predict a flare of synovitis. *Ann Rheum Dis* 2013; 72: 223-8.