

Comparison of ultrasonography and magnetic resonance imaging for the assessment of clinically defined knee enthesitis in spondyloarthritis

S.Z. Aydin¹, A.L. Tan²,
R. Hodgson², A. Grainger²,
P. Emery², R.J. Wakefield²,
D. McGonagle²

¹Istanbul Medeniyet University, Goztepe Training and Research Hospital, Istanbul, Turkey;

²Leeds Institute of Rheumatic and Musculoskeletal Medicine and Leeds NIHR Musculoskeletal Biomedical Research Unit, University of Leeds and Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom.

Sibel Zehra Aydin, MD

Ai Lyn Tan, MD, MRCP

Richard Hodgson, PhD, FRCR

Andrew Grainger, MRCP, FRCR

Paul Emery, MA, MD, FRCP

Richard J. Wakefield, BM, MD, MRCP

Dennis McGonagle, PhD, FRCPI

Please address correspondence to:

Dennis McGonagle,

Academic Unit of Musculoskeletal Disease, University of Leeds,

Chapel Allerton Hospital

LS7 4SA Leeds, United Kingdom.

E-mail: drsibelaydin@gmail.com

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ABSTRACT

Objective. *Ultrasonography (US) and magnetic resonance imaging (MRI) are increasingly used imaging techniques for visualising entheses, however few studies have made a direct comparison of each. This study aimed to compare each technique for the detection of enthesitis in patients with spondyloarthritis (SpA) related knee swelling in order to make a lesion by lesion comparison.*

Methods. *Consecutive SpA patients with knee synovitis were recruited: each had clinical assessment for enthesitis at 8 sites in the involved knee joint followed by US and MRI examinations. Inflammatory and structural changes at tendon and ligament insertions were scored and a lesion by lesion comparison was made.*

Results. *21 patients were recruited. Clinically defined involved knee joint enthesitis was evident in 18 of 21 (86%) patients in 61 of 168 (36%) evaluated sites. Clinical enthesitis was associated with more hypoechogenicity (16 vs. 4%, $p=0.007$) and thickening (16 vs. 6%, $p=0.03$) by US compared to non-tender sites. Considering all MRI findings only increased signal in the surrounding tissues was higher at tender sites (41 vs. 20%, $p=0.01$) and the insertions points themselves showed little abnormality. The positive agreements between individual lesions by both methods was very low (10-26%) with low kappa values (0.06-0.18) with no correlations between the MRI and US scores ($r^2=0.059$).*

Conclusion. *The difficulty in procuring "gold standard" histological validation in synovial joints makes the assessment of enthesitis using clinical and current imaging protocols of limited utility for diagnostic purposes.*

Introduction

Spondyloarthritis (SpA) is considered to be a predominantly enthesitis based disease and therefore the accurate detection of enthesitis is vital for both diagnosis and disease monitoring (1, 2). Clinical examination currently remains the conventional method of assessment of enthesitis based on the presence of tenderness and/or swelling. However, discordance with modern imaging techniques such as ultrasound (US) and

magnetic resonance imaging (MRI) has previously been demonstrated challenging the accuracy of clinical examination. This is particularly so in knees that are clinically swollen where it is more difficult to isolate enthesal sites. Until now, a gold standard method for the assessment of entheses has not been defined. Radiography is insensitive for showing early bone changes and both radiography and computed tomography are insensitive for showing soft tissue enthesal changes.

In recent years, both US and MRI have shown potential for the assessment of enthesitis in patients with SpA. Both techniques are able to simultaneously visualise soft tissue and bone changes although MRI has the advantage of identifying peri-enthesal bone marrow oedema which is thought to represent an important aspect of the enthesitis related lesion (3-11). The relative merits of each technique for detecting enthesal pathology have not been widely studied (12, 13). The objective of this study was first to compare each technique with the standard of clinical examination for the presence/absence of enthesitis and second, to perform a lesion by lesion assessment of the inflammatory and structural components of enthesitis. SpA patients with clinically swollen knees were chosen as it was considered that it was these patients were the greatest diagnostic confusion might arise.

Methods

Patient selection

Patients were recruited from the rheumatology outpatient clinics in the Leeds Teaching Hospital Trusts. All patients fulfilled the European Spondyloarthropathy Study Group criteria (14) and presented with a swollen knee. The study was approved by the Local Research Ethics Committee and written informed consent was obtained from all patients.

Clinical assessment of enthesitis

The entheses around the more symptomatic knee was evaluated by an investigator (AT) prior to the imaging examinations. Sites were chosen only if they were accessible by US (quadri-

Competing interests: none declared.

ceps insertion, patellar tendon origin/insertion, origins/insertions of medial and lateral collateral ligaments (MCL and LCL) and semimembranosus tendon (SMT) insertion). Clinical enthesitis was diagnosed if there was tenderness and/or swelling.

US

US examinations were performed by an experienced rheumatologist (RJW) trained in musculoskeletal US who was blinded to the clinical examination and MRI findings. The most symptomatic knee was scanned by using a Philips 5000 employing either a linear 12-5 or 15-8 MHz probe, depending on the site and patient habitus. Patients were placed with either the knee flexed at 30 degrees or extended to allow better visualisation of the entheses (15), however for the SMT the patient was positioned in a prone position. Grayscale (GS) tendon/ligament changes were recorded including the loss of echogenicity within the fibrillary echotexture, increased thickness and, intra-substance calcification-in addition to bony changes (enthesophytes and bone erosions) as well as bursal enlargement. The findings were graded semi-quantitatively between 0–3 (0-none, 1-mild, 2-moderate, 3-significant). US scores for inflammation (including hypoechoogenicity, thickening and bursal enlargement) and damage (enthesophytes, erosions and calcifications) were calculated separately. A total US score was obtained by adding all findings as previously reported (16).

MRI

The same knee as US was scanned using a Philips Gyroscan ACS NT 1.5 T scanner. T1W, T2 SPIR, TI SPIR pre and post Gd-DTPA were performed. MRI scans were scored for the same sites by two radiologists on a consensus basis (RH and AG) blinded to the clinical and US data according to the following findings: The presence of soft tissue signal around the ligaments and tendons, increased intrasubstance signal, thickening, enthesal bone marrow oedema. All findings were graded as present or absent (scored 0 or 1), and a final summative MRI score was obtained by adding each finding.

Table I. Prevalence of clinical and imaging abnormalities depending on the site (percentage of abnormalities).

	Q-I	PT-O	PT-I	LCL-O	LCL-I	MCL-O	MCL-I	SMT-I
Clinical								
Tenderness	43	52	14	33	5	57	24	62
US findings								
≥1 abnormality by US	29	14	14	48	19	48	0	48
Hypoechoogenicity	0	5	0	24	5	29	0	5
Thickening	0	5	0	33	10	24	0	5
Bursal enlargement	0	0	5	0	0	0	0	0
Erosions	5	0	10	33	10	19	0	43
Enthesophytes	19	10	5	5	0	5	0	0
Calcifications	5	0	0	0	0	0	0	0
MRI findings								
≥1 abnormality by MRI	14	33	33	48	10	76	42	37
Soft tissue signal	10	24	24	35	5	75	39	37
Intrasubstance signal	10	19	10	19	5	0	0	35
thickening	0	5	5	0	5	0	0	10
BME	0	20	5	21	0	26	11	0

Q-I: quadriceps insertion; PT-O: patellar tendon origin; PT-I: patellar tendon insertion; LCL-O: lateral collateral ligament origin; LCL-I: lateral collateral ligament insertion; MCL-O: medial collateral ligament origin; MCL-I: medial collateral ligament insertion; SMT-I: semimembranosus tendon insertion. Numbers are given as percentages.

Statistics

Data are expressed either as frequencies or means (\pm standard deviation (SD)). The prevalence of individual lesions with or without tenderness was compared by using a chi-square test. The concordance between different lesions by both imaging modalities was evaluated using positive and negative agreements and kappa analysis (17). Correlations between MRI and US scores were analysed by Pearson correlation test. Statistical analysis was performed with the package MedCalc software (V.9.2 for Windows).

Results

Twenty-one SpA patients were recruited to the study. Thirteen of these patients had psoriatic arthritis according to the Classification of Psoriatic Arthritis (CASPAR) criteria (18), 3 had reactive arthritis and 5 had undifferentiated SpA. The female/male ratio was 13/8. Mean (SD) age of patients was 41.1 (17.9) years with a disease duration of 18.5 (21.5) months. The mean swollen joint count was 1.7 (0.9). ESR value was 20 (11) mm/h and CRP was 38.5 (59.4) mg/l.

The prevalence of clinical enthesitis

Nineteen patients had clinical enthesitis at one or more sites. The enthesal

sites were found to be tender and/or swollen with physical examination in 5 to 62% of the sites. Some sites were more frequently affected than others with the SMT insertion being the most common (62%) and the LCL insertion the least common (5%) (Table I).

The prevalence of imaging findings

US: Only one patient did not have enthesitis on US. Within the investigated entheses, the frequency of finding at least one abnormality by US was highest at the LCL-origin (48%), MCL-origin (48%) and SMT level (48%) and lowest for the MCL insertion. US detected relatively more abnormalities related to inflammation in the LCL and MCL origins when compared to the quadriceps and patellar tendons. For the SMT insertion, most of the abnormalities were related to damage (Table I).

MRI: Only one patient did not demonstrate enthesitis on MRI. MRI detected abnormalities were also more frequent (Like US) at the level of LCL-origin (48%), MCL-origin (76%) and SMT level (37%). At the level of MCL insertion, MRI detected at least one abnormality in 42% of the patients. The most common MRI abnormalities were the presence of surrounding soft tissue signal, followed by bone marrow oedema. Oedema was mostly observed at the

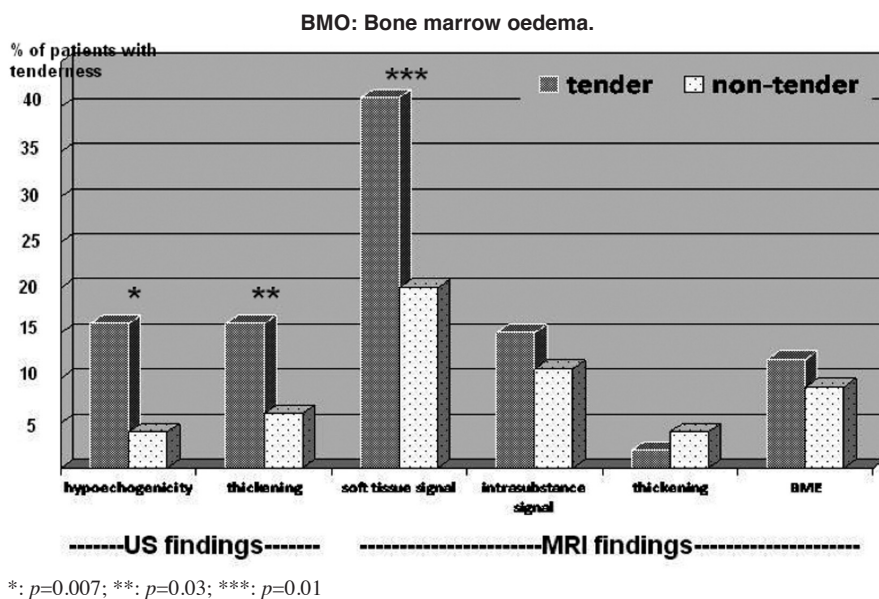


Fig. 1. US and MRI abnormalities related to inflammation according to tenderness.

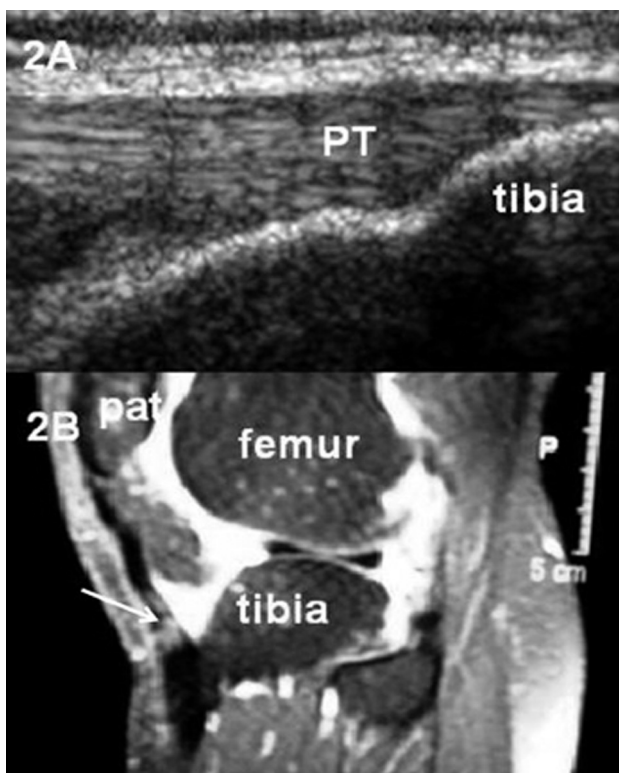


Fig. 2. The longitudinal US scan (1A) and sagittal T1 weighted MRI (1B) scan of the patellar tendon (PT) insertion of a patient with SpA. The US revealed normal fibrillary echotexture whereas there is increased intrasubstance signal on MRI (arrow). pat: patella.

level of origins (PT origin, MCL origin and LCL origin) rather than the level of insertions (20–26% vs. 0–1%) (Table I).

Comparison of imaging findings with physical examination

When the soft tissue US findings pertaining to inflammation were compared, clinically, tender sites had more hypochoogenicity (16 vs. 4%; $p=0.007$)

and thickening (16 vs. 6%; $p=0.03$) compared to the non-tender sites (Fig. 1).

Within the MRI findings only increased signal in the surrounding tissues was found to be significantly higher at clinically tender sites (41 vs 20%; $p=0.01$). All the other MRI findings were found at similar rates independent from tenderness (Fig. 1).

Comparison of MRI and US

No correlations were found between the MRI and US scores ($r^2=0.059$). When analysed separately, MRI scores were independent of US scores with respect to both inflammation and damage ($r^2=0.002$ and 0.085 , respectively). Employing as lesion by lesion comparison, the positive agreement rates of different findings of US and MRI were between 10–26%. All comparisons resulted with poor agreements with low kappa values (0.06–0.18) (Fig. 2).

Discussion

In recent years US and MRI have been increasingly used to evaluate patients with suspected enthesitis. At peripheral sites of isolated enthesitis there is less diagnostic difficulty clinically; however a major challenge is the recognition of enthesitis in swollen joints in SpA. This study has shown a poor level of agreement between clinical examination and both US and MRI and between US and MRI themselves. Overall ultrasound detected more abnormalities than MRI.

Ultrasound has been shown to be more specific in detecting synovitis compared to MRI (19, 20); in terms of enthesitis, it appeared that both modalities were measuring different things with US depicting true enthesitis related changes whereas MRI showed changes in peri-enthesal soft tissues. This is consistent with a recent finding where US was shown to be more sensitive at detecting tenosynovitis compared to MRI (21). The peri-enthesal soft tissue changes on MRI could be related to severe enthesitis or to synovitis itself with extension of inflammatory changes into the soft tissues. This may have accounted for the discrepancies between both imaging modalities. The presence of soft tissue changes around insertions on MRI that are associated with clinical tenderness at insertions may therefore be related to synovitis in some cases.

In the current study, both imaging findings also detected less enthesitis than physical examination. This is in contrast to Bandinelli *et al.* who showed there were more ultrasound enthesal changes than clinical examination (22), but their cohort had early disease,

whilst the subjects in this study were not limited to early disease, and had clinically swollen joints. Clinical assessment of enthesitis in patients with synovitis can be difficult and misleading, due to proximity of most entheses to inflamed synovial tissues, leading to the false positivity of physical examination. This finding demonstrates the importance of using imaging modalities in patients with synovitis for differential diagnosis.

Most of the previous studies focusing on entheses of the knee joints in SpA using either imaging modalities only examined the quadriceps and patellar tendon insertions. On the other hand, ligament insertions are also a target for inflammation in SpA and highly under-investigated. We had seen that both MRI and US detected frequent abnormalities related to inflammation at the level of origins and insertions of MCL and LCL (except US for MCL insertion) being even more frequent than quadriceps and patellar entheses. Including these structures as a part of the assessment is likely to improve our knowledge about the pathogenesis and extension of disease in SpA and clinically relevant as patients not infrequently have symptoms at those sites.

Our study had some limitations. Although this study used intravenous gadolinium based contrast agent to enhance MRI of the knee entheses, its role is yet to be established in this context. We only included SpA patients who presented with joint effusion. However, asymmetrical synovitis of the lower limbs is a characteristic feature of SpA and therefore is a common presentation. Including the non-swollen contralateral knee in this study could possibly show any true enthesitis without the influence of synovitis. However, only some of the patients had unilateral swollen knees with some others having bilateral swollen knees. In addition, although it would be feasible to perform US on both knees, it was not possible to perform MRI on both knees concurrently which was limited by the size of the knee coil. Structural thickening on US was determined subjectively, and not measuring PD signal in our US assessment may be considered as a limitation. According to our experience, the

positivity of PD signal at the sites that were assessed in this study is a very rare finding and not even reported in the literature. Therefore we would not expect PD to change our results. We used optimal positions of the knee for both US and MRI to best show abnormalities; this resulted in knee positions that are not identical for both techniques because we exploited the capability of US to scan dynamically, whilst the knee was scanned in a fixed position on MRI which contrast was used.

In conclusion, both US and MRI found frequent abnormalities at or adjacent to most entheses around the knee. However there was a significant discrepancy between individual lesions using both imaging modalities. We believe that this is attributable to the fact that perienthesal tenderness does not necessarily mean enthesitis but synovitis in some cases and soft tissue involvement in a synovial joint has the risk of masking some MRI features of enthesitis. This study highlights the difficulties in the clinical and imaging assessment of enthesitis in synovial joints. Given the difficulties with histological studies in this setting then a gold standard is unlikely. The clinical and imaging assessment of enthesitis in diseased synovial joints remain problematic.

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