

Comparison between the roles of musculoskeletal ultrasound and magnetic resonance imaging in detection of joint inflammation and destruction in rheumatoid arthritis

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Background

Detection of early signs of synovitis and bone erosions by modern radiological techniques such as musculoskeletal ultrasound (US) and MRI has gained a great interest, as early diagnosis and treatment to target for patients of rheumatoid arthritis (RA) has its impact on disease control.

Aim

The aim of the following study is to detect the ability of US compared with MRI for the early detection of joint synovitis and bone erosion in RA patients.

Patients and methods

Six hundred joints (second to fifth metacarpophalangeal joints and second to fifth proximal interphalangeal joints) were examined in 50 patients with RA diagnosis. Clinical assessment, noncontrast MRI, US, and conventional radiography were performed for synovitis and bone erosion evaluation.

Results and conclusion

We concluded that both US and MRI had high ability to detect inflamed joints with close agreement but favoring the US, especially with the added value of power Doppler US where it can reflect increased vascularity associated with inflammation and also with higher scores for these affected joints than that shown by MRI. On the other hand, the study has found that although both US and MRI had high ability to detect erosions with close agreement, the MRI favorably had higher scores for joint erosions compared with the scores shown by US.

Keywords:

bone erosion, magnetic resonance imaging, rheumatoid arthritis, synovitis, ultrasonography

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Introduction

Rheumatoid arthritis (RA) is one of the most common autoimmune rheumatic diseases, affecting one in 100 individuals worldwide. It is considered a complex systemic multifactorial inflammatory process with predilection for the joints. If left untreated, RA leads to deformity, considerable disability, and major comorbid conditions, including cardiovascular disease and increased mortality [1]. The cause of RA is unknown; however, the progressive clarification in the pathogenesis and the subsequent biopharmaceutical discoveries have led to the establishment of more effective medications with improved outcomes [2]. These effective medications are biologic response modifiers, and they have been proven to markedly reduce signs and symptoms of the disease so that better outcomes are expected and reported. The current treatment strategy, which reflects this progress, is to initiate aggressive treatment approach to the disease soon after diagnosis is made and to escalate the therapy, guided by a continuous assessment of disease activity [3]. The impressive achievements in controlling RA have needed parallel development of the methods that are suitable to assess

the results of the new medications [4]. Thus, the current treatment goal for RA is to achieve a state of disease remission or low disease activity [5]. Three clinical domains are usually considered in making this assessment: signs and symptoms of inflammation, functional impairment, and structural joint damage [6].

The optimal management of RA requires tools that allow early and accurate disease diagnosis, prediction of poor prognosis, and responsive monitoring of therapeutic outcomes. Traditionally, conventional radiography (CR) has been the imaging modality most frequently used in RA disease assessment, and it remains to be widely in use both in clinical and research settings. It is useful in detecting bony structural abnormalities such as erosions, periarticular osteopenia, and joint space narrowing (JSN). It can be used to assess multiple joints in a short time frame. However, the main limitation of CR has been its lack of sensitivity in

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detecting RA joint structural changes, especially in early disease assessment. Accordingly, the more sensitive imaging modalities such as MRI and ultrasound (US) have become increasingly required [7].

Diagnostic high-frequency US is an US-based diagnostic imaging technique used to visualize subcutaneous body structures including tendons, muscles, joints, vessels, and internal organs for possible pathology or lesions. US is effective for imaging soft tissues of the body [8]. It has greatly improved musculoskeletal imaging in rheumatology. Several studies have demonstrated that high-frequency US is accurate for detecting joint effusion and synovitis, compared with other imaging modalities and direct arthroscopic visualization [9]. US is more sensitive and reproducible than clinical evaluation in assessing joint inflammation [10]. In addition, it is sensitive in the detection of rheumatoid erosions, allowing earlier diagnosis of progressive RA [11].

MRI can directly visualize the bone and soft tissues in three dimensions, and it has the potential to measure inflammatory activity and joint destruction, where synovitis volume and bone marrow edema (BME) are suitable for serial measurement. The Outcome Measure in Rheumatoid Arthritis Clinical Trials (OMERACT) rheumatoid arthritis magnetic resonance imaging system is designed to allow straightforward, reproducible scoring of these features [12]. MRI provides information that reflects synovial affection and may be a precise marker of synovitis. BME is an important determinant of structural and functional outcomes [13]. The main 'activity' findings detected by MRI include synovitis, tenosynovitis, and BME, whereas the 'damage' findings include bony erosions and JSN [7].

Patients and methods

A total number of 600 joints including radiocarpal, ulnar carpal, distal radioulnar, and intercarpal compartments of the wrist joint, second to fifth metacarpophalangeal (MCP) joints, and second to fifth proximal interphalangeal (PIP) joints in 50 patients with approved RA diagnosis according to the American College of Rheumatology 1987 criteria were included in the study. Before inclusion in the study, written informed consent was obtained from all patients after explaining the study process in detail. The study was approved by the local ethical committee of Ain Shams University and conducted according to the Declaration of Helsinki and subsequent revisions.

Joints were assessed for swelling that may be due to bony thickening, synovial membrane thickening or joint effusion, temperature, deformity, tenderness with its site and severity, and range of motion. In addition, assessment of disease activity using the modified disease activity score 28 (DAS28) [14] was performed.

Plain radiography of both hands was performed for the detection of erosions and JSN, and it was scored using the modified Genant scoring system [15].

High-resolution ultrasonography

B-mode gray scale scanning technique was performed using a Philips HD 100 unit, manufactured by Philips Medical Systems, Bothell, WA, USA) by means of a 7–13-MHz linear array transducer. It was performed for the more affected hand and wrist joints where scanning was done for a total of 12 joints:

- (1) The second through fifth MCP joints.
- (2) The second through fifth PIP joints.
- (3) The radiocarpal, ulnar carpal, distal radioulnar, and intercarpal compartments of the wrist joint.

Joint effusion, synovitis, and bone erosions in the synovial membrane of the preselected joints were evaluated. Grading of the findings was carried out using the scores described by Szkudlarek *et al.* [16].

Magnetic resonance imaging assessment

MRI was performed for the same joints, which were evaluated by US examination for all patients. Imaging was performed with the 1.5-T MRI system (Achieva; Philips medical Systems, Andover, MA, USA). All images were obtained with the use of a dedicated extremity coil. A protocol was followed, in which images were obtained in the coronal and axial planes (through each joint and including the most anterior and posterior planes). Axial T1-weighted (TR/TE, 300 ms/14 ms), axial T2-weighted (TR/TE, 4500 ms/93.5 ms), coronal T2-weighted sequence, coronal STIR (TR/TE, 4500 ms/30 ms), and water-selective excitation three dimensional (WATSc) sequence images were obtained. The examinations were evaluated for the absence, presence, amount, and localization of joint pathology, with emphasis on the synovitis and bony erosions according to the OMERACT [17] and scored according to the OMERACT rheumatoid arthritis MRI scoring system [18].

Statistical analysis

Statistical analysis was performed using SPSS software (version 15.0). For evaluating the effect of disease severity, the patients were divided into four groups

according to the DAS28 scoring system. Agreement and correlation between imaging modalities were reported by means of a κ test. Wilcoxon signed-rank test was used to evaluate the difference between the magnitudes and signs of paired observations by comparing the distributions for positive and negative differences of the ranks of their absolute values.

Results

The age of the study population ranged from 26 to 64 years, with mean age \pm SD of 43.18 \pm 10.55 years. The study population showed that 86% of the patients were female (43 patients), whereas 14% were male (seven patients).

All patients had a history of diagnosed RA not less than 6 months. As regards their disease duration, it ranged from 0.5 to 15 years, with a median of 4.15 and an interquartile range (IQR) of 1.7–7.25. The duration of morning stiffness ranged from 10 to 60 min, with a median of 18.75 and an IQR of 12.5–36.65. Their clinical examination as assessed by the 28 joint counts [19] revealed that the number of swollen joints ranged from 0 to 14 joint, with a median of 3.25 and an IQR of 1.65–6.4. In addition, the number of tender joints ranged from 0 to 17 joints, with a median of 3 and an IQR of 1–7.4. According to their DAS28 score,

patients were divided into four groups, with 20 patients in the remission group (scoring ≤ 2.6), eight patients in low disease activity group (scoring >2.6 and ≤ 3.2), 12 patients in the moderate disease activity group (scoring >3.2 and ≤ 5.1), and 10 patients in high disease activity group (scoring DAS28 >5.1).

Both US and MRI were able to detect the presence and the degree of synovitis and bone erosions, as given below.

Detection of synovitis

We compared the number of joints that showed active inflammation clinically in the clinically more affected hand with the number of joints that revealed inflammation radiologically; it was 23% (104 of 450) for the clinical examination and 39% (235 of 600) and 29% (173 of 600) for US and MRI findings, respectively.

The Wilcoxon signed-rank test was performed to find the difference between the number of joints showing synovitis on MRI and that on US among patients of each group (Table 1):

Wilcoxon test showed that in 32 patients the number of joints that exhibited synovitis by US was more than number revealed by MRI (negative ranks), whereas in

Table 1 Difference between ultrasound and magnetic resonance imaging synovitis joint count

	N	Mean rank	Sum of ranks	Z	P value
MRI synovitis joint count (N=12)–gray scale US synovitis joint count (N=12)					
Remission					
Negative ranks	10 ^a	9.25	92.50	-1.912	>0.05 (NS)
Positive ranks	5 ^b	5.50	27.50		
Ties	5 ^c				
Total	20				
LDA					
Negative ranks	6 ^a	3.50	21.00	-2.32	>0.05 (NS)
Positive ranks	0 ^b	0.00	0.00		
Ties	2 ^c				
Total	8				
MDA					
Negative ranks	11 ^a	6.00	66.00	-2.9	<0.05 (S)
Positive ranks	0 ^b	0.00	0.00		
Ties	1 ^c				
Total	12				
HDA					
Negative ranks	5 ^a	7.70	38.50	-1.136	>0.05 (NS)
Positive ranks	5 ^b	3.30	16.50		
Ties	0 ^c				
Total	10				

HDA, high disease activity; LDA, low disease activity; MDA, moderate disease activity; S, significant; US, ultrasound. ^aThe number of joints showing synovitis on MRI fewer than the number showing synovitis on US (MRI<US). ^bThe number of joints showing synovitis on MRI more than the number shown on US (MRI>US). ^cThe number of joints showing synovitis on MRI equal to the number shown on US (MRI=US).

10 patients the number of joints revealed by MRI was more than that revealed by US (positive ranks), and in the other eight patients both methods showed the same number of joints (ties).

Wilcoxon test showed that the number of patients showing US synovitis more than MRI synovitis (negative ranks) are higher than those showing MRI synovitis more than US synovitis (positive ranks), although there was no significant difference between the numbers of joints detected by both radiological methods in three of the studied groups.

Wilcoxon signed-rank test was used to find the difference between the synovitis scores described by US and MRI. The result is shown in Table 2.

Table 2 Ultrasound and magnetic resonance imaging synovitis score difference among study groups

	Median (IQR)	Range	P [^]
US	3.0 (1.8–6.3)	0.0–22.0	0.061
MRI	3.0 (2.0–4.3)	0.0–9.0	
Difference (MRI–US)	0.5 (3.5–14.0)	0.0–17.0	

IQR, interquartile range; US, ultrasound. [^]Wilcoxon signed-rank test (P: nonsignificant, >0.05; significant, <0.05; highly significant, <0.001).

MRI and US synovitis scores were significantly different among the studied cases, being significantly higher among US scores.

Detection of joint destruction

We compared the number of joints that showed bony erosions by conventional radiography in the clinically more affected hand to the number of joints that revealed erosions by US and MRI; it was 19% (133 of 700, 14 areas in each patient), 26.8% (161 of 600), and 34% (204 of 600) in clinical examination, US, and MRI findings, respectively.

The Wilcoxon signed-rank test was performed to find the difference between the number of joints showing bony erosions on MRI and the number showing bony erosions on US among patients of each group (Table 3).

The Wilcoxon test showed that in nine patients the number of joints that exhibited erosions by US was more than the number of joints revealed by MRI (negative ranks), whereas in 30 patients the number of joints revealed by MRI was more than that revealed by US (positive ranks), and in the other 11 patients both methods showed the same number of joints (ties).

Table 3 Difference between ultrasound and magnetic resonance imaging synovitis joint count

	N	Mean rank	Sum of ranks	Z	P value
MRI erosion count (N=12)–US erosion count (N=12)					
Remission					
Negative ranks	3 ^a	9.33	28.00	-1.206	>0.05 (NS)
Positive ranks	10 ^b	6.30	63.00		
Ties	7 ^c				
Total	20				
LDA					
Negative ranks	0 ^a	0.00	0.00	-2.5	<0.05 (S)
Positive ranks	7 ^b	4.00	28.00		
Ties	1 ^c				
Total	8				
MDA					
Negative ranks	4 ^a	4.25	17.00	-1.1	>0.05 (NS)
Positive ranks	6 ^b	6.33	38.00		
Ties	2 ^c				
Total	12				
HAD					
Negative ranks	2 ^a	4.00	8.00	-1.811	>0.05 (NS)
Positive ranks	7 ^b	5.29	37.00		
Ties	1 ^c				
Total	10				

HDA, high disease activity; LDA, low disease activity; MDA, moderate disease activity; S, significant; US, ultrasound. ^aThe number of joints showing erosion on MRI fewer than the number showing erosion on US (MRI<US). ^bThe number of joints showing erosion on MRI more than the number shown on US (MRI>US). ^cThe number of joints showing erosion on MRI equal to the number shown on US (MRI=US).

Wilcoxon test showed that the number of patients showing MRI erosion more than US erosion (positive ranks) are higher than those showing US erosion more than MRI erosion (negative ranks), although there was no significant difference between the numbers of joints detected by both radiological methods in three of the studied groups.

Wilcoxon signed-rank test was used to find the difference between the erosion scores described by US and MRI. The results are shown in Table 4.

MRI and US erosion scores were significantly different among the studied cases, with MRI scores being significantly higher.

Discussion

As the remission was defined according to DAS28 score, which depends mainly on clinical examination together with erythrocyte sedimentation rate of the patient, only three patients who were free of joint affection showed no evidence of synovitis either by US and power doppler US (PD) and also by MRI. They can be considered to be in true remission. In addition, the same three patients were in remission when assessed by the stricter American college of rheumatology (ACR) criteria and simplified disease activity index (SDAI) scores. The other three patients who showed no synovitis by US had synovitis by MRI in one of their examined joints. This was in agreement with Brown *et al.* [20], who explained that the current measures used to assess disease activity in RA, which largely rely on subjective clinical symptoms, joint examination findings, and laboratory measures of acute-phase reactants, are not sufficiently sensitive to exclude ongoing inflammation in patients with low levels of disease activity. In addition, it agreed with the results of Brown *et al.* [21] when he concluded that it is still possible to detect Doppler activity and synovitis in joints of patients in clinical remission applying both DAS28 and ACR criteria of remission. This also was in agreement with Colebatch *et al.* [22], who concluded that synovitis is frequently found by imaging, such as by US or MRI, in patients considered to be in remission,

and is associated with adverse clinical and functional outcomes.

In our study, we concluded that 85% of the patients showing remission according to DAS28 showed inflammatory signs in at least one of their examined joints, which was evident by either B-mode US alone or combined with PD or by MRI or even both techniques. Also patients who had high disease activity according to clinical scores had higher number of inflamed joints detected radiologically than those detected clinically. This indicates that the clinical assessment alone or combined with activity scores is not accurate and cannot be dependable, and that the modern radiological techniques can reveal hidden inflammation that can affect the course of the disease and the decision of treatment. In addition, it can affect patients' outcome and their quality of life.

With regard to the detection of inflammation, although MRI revealed synovitis in three patients who were shown by US as being free of any affection, the total number of joints showing synovitis by US was higher than those revealed by MRI. When we compared the number of joints that showed any sign of inflammation clinically with the number revealed by US and MRI, we found that 39% of the joints examined by US showed signs of affection, whereas 29% of them were revealed by MRI and only 23% showed clinical affection. This reflected the superiority of the recent radiological techniques above the clinical examination. This was in agreement with the study by Mitran *et al.* [23] when they stated that in daily practice several composite indices are used to evaluate disease activity, considering tender and swollen joint count, visual analog scales by patient and physician, and inflammation markers, but sometimes they have lower accuracy because of associated fibromyalgia, depression, deformities that influence joint count, and so on. They also stated that imaging methods, such as musculoskeletal US or magnetic resonance, are precise, more sensitive, and reproducible than clinical evaluation in assessing joint inflammation. Moreover, US can be used as often as required during patient examination, improving the accuracy and precision of clinical data.

When we compared the two radiological techniques, we found that in 64% ($N=32$) of the patients the US revealed higher number of joints with synovitis than by MRI, whereas 20% ($N=10$) of them had more joints by MRI. The other 16% ($N=8$) of the patients showed equal findings by both techniques. At the joint level,

Table 4 Ultrasound and magnetic resonance imaging erosion score among study grades

	Median (IQR)	Range	P [^]
US	3.0 (2.0–5.0)	0.0–13.0	<0.001*
MRI	10.0 (6.8–19.3)	0.0–48.0	
Difference (MRI–US)	7.0 (3.5–14.0)	0.0–40.0	

IQR, interquartile range; US, ultrasound. [^]Wilcoxon signed-rank test. *Means highly significant.

69% of joints showed findings by both techniques, whereas 28.5% showed synovitis by US only and 2.5% by MRI only. There was a significant agreement between US and MRI findings, and the difference between the number of joints detected by both radiological methods in the studied groups was not significant ($P>0.05$). This was close to the results found by Szkudlarek *et al.* [24] where they found that there was 76% agreement between US and MRI (331 of 433 finger joints) in the joints examined for synovitis in 40 RA patients. In addition, it was close to the results described by Rahmani *et al.* [25], where they stated that 66% of joints showed findings by both techniques, whereas 21% showed synovitis by US only and 13% by MRI only.

The median and the IQR of the synovitis scores described by both techniques were significantly different from each other among the studied cases, being significantly higher among US scores ($P=0.061$). This may be because US is better for scanning of small hand joints, whereas MRI cuts are better in the visualization of wrist joint. In addition, we used MRI without contrast, which could have led to missing of some joints that may have revealed inflammation if contrast was used.

We concluded from our results that both radiological techniques had high ability to detect inflamed joints with close agreement but favoring the US, especially when adding the value of the power Doppler activity for better visualization of the inflammation. This was in accordance with Rahmani *et al.* [25] where he stated that US and MRI have an acceptable agreement in detecting synovitis. His results also demonstrated that noncontrast MRI, although not able to differentiate between effusion and synovitis, is still a good predictor of soft tissue abnormality compared with US. However, because MRI as a diagnostic modality is very expensive and usually not easily accessible, US might be a very good diagnostic substitute for patients' screening and inflammation detection with high accessibility in different settings, as it is an easily available instrument with low costs and is also patient friendly. However, one should always take into consideration that this technique is highly dependent on the availability of experienced specialists.

In addition, this was in agreement with Xiao *et al.* [26], who concluded from their study that the two imaging techniques were fairly consistent for detecting arthrosynovitis in MCP, PIP, and wrist joints, and also that US is a reliable method for diagnosing synovitis when compared with MRI results.

However, because MRI is expensive and difficult to apply universally, high-resolution US is a safe and noninvasive substitute, it is repeatable, and highly sensitive to joint cavity hydrops and synovial hyperplasia; in addition, it is good for the early diagnosis of RA and for monitoring the response to drug treatment.

With regard to the detection of bone destruction, although US was unable to detect any erosions in 12% ($N=6$) of patients, MRI was able to detect bony erosions in 8% ($N=4$) of them. Only 4% ($N=2$) of the patients had no evidence of bony erosions that could be detected by both radiological techniques, and they belong to the remission group. In addition, the total number of joints showing bony erosions by MRI was higher than those revealed by US.

When we compared the number of joints that showed erosions by CR with the number revealed by US and MRI, we found that 34% of the joints examined by MRI showed signs of erosion, whereas 26.8% of them were revealed by US and only 19% were shown by radiography. This reflected the superiority of the recent radiological techniques above the CR in detection of bony erosions.

Our results showed that in 60% ($N=30$) of the patients the MRI revealed higher number of joints with erosions than by US, whereas 18% ($N=9$) of them had more joints by US. The other 22% ($N=11$) of the patients showed equal findings by both techniques. However, there was no significant difference between the number of joints detected by both radiological methods in three of the studied groups ($P>0.05$).

In addition, we observed that both US and MRI were able to detect more erosions at both patient level and joint levels. US was able to detect erosions in 23% more patients than radiography. MRI was able to detect erosions in 31% more patients. These results correspond to that of Baillet *et al.* [27] who stated that although CR was considered to be the gold standard for imaging in RA its sensitivity for RA diagnosis is very low. Surrogate tools for early RA management have been developed during this last decade, such as MRI and US, allowing assessment of both disease activity and structural damage. The presence of early erosion correlates with structural damage progression and functional capacity. Therefore, early detection and the follow-up of erosions are undoubtedly critical for RA diagnosis, monitoring, and prognostication.

The median and the IQR of the erosion scores described by both techniques were significantly different from each other among the studied cases, being significantly higher among MRI scores ($P < 0.001$).

This was in accordance with Baillet *et al.* [27] who performed a meta-analysis search of 21 studies including 913 patients to evaluate the reproducibility of US and to compare its efficacy with that of MRI for the detection of bone erosion in RA patients. They stated that the difference between US and MRI in detecting bone erosion, either in the number of patients or number of articular sites, was not statistically significant. In addition, they reported that US tended to detect more erosions than MRI in the early RA population at a joint level, whereas MRI tended to be better in established RA at both joint and patient levels when comparing the number of erosions detected by both techniques.

In addition, our result was in accordance with that of Rahmani *et al.* [25], who concluded that there was a high agreement between US and MRI in erosion detection and that it was also higher in patients with more active disease compared with those who had much milder symptoms. He also concluded that MRI is the most accurate and sensitive device for detecting bone erosion compared with other methods, as it could detect more erosions.

Our results confirmed the importance of endorsement of modern imaging techniques in the assessment of RA patients either in identifying the degree of their disease activity according to the inflammatory findings of the joints or in identifying the extent of joint destruction according to the presence and extent of bony erosions. In addition, we supported their superiority above clinical examination, and accordingly the activity scores that depended upon it, and also above the CR.

Conclusion

We concluded that both US and MRI had high ability to detect inflamed joints with close agreement, but favoring the US, especially with the added value of power Doppler US where it can detect increased vascularity associated with inflammation and also with higher scores for these affected joints than the score shown by MRI. We also concluded that both US and MRI had high ability to detect erosions with close agreement but favoring the MRI also with higher scores for these joint areas with erosions than the score shown by US. We recommend that these

methods could be used as a beneficial tool for follow-up of cases under treatment so that treatment will be tailored to target. In addition, future studies are needed to show which of these techniques is more favorable to reflect the therapeutic response. For its cost and availability, we recommend US as a modality of choice to monitor the results of therapy and a better tool for the definition of disease remission and exacerbation. It might also be recommended that the definition of remission should be revised to include the new radiological technique to prevent relapse of the disease.

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Conflicts of interest

There are no conflicts of interest.

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