

## The use of musculoskeletal ultrasound of the wrist and hand in the assessment of treatment response in rheumatoid arthritis patients

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### Abstract

**Objective:** Rheumatoid arthritis is a debilitating disease with accrual of joint damage during each flare of the disease that progresses to considerable functional disability. Early treatment is thus aimed to achieve remission status so as to reduce the progression of joint damage. Currently the disease activity parameter DAS28 (amongst others) is used to define a remission status and thus demonstrate the efficacy of a treatment regimen, however musculoskeletal ultrasound (MSUS) is proving to be superior at determining the amount of inflammation within joints by grading synovial hypertrophy and neo-vascularization of the inflamed synovium. This article is thus intended to shed light on the usefulness of musculoskeletal ultrasound both greyscale and Doppler in the determination of treatment response in rheumatoid arthritis patients.

**Design:** This article will elaborate the importance and effectiveness of musculoskeletal ultrasound. Thus it will involve a discussion on the need for an effective tool to detect inflammatory activity, the ability of ultrasound to detect and grade the disease activity i.e. being sensitive to change, the various scoring systems currently used, and lastly a comparison of musculoskeletal ultrasound to other modalities and clinical and serological evaluation.

**Data source and extraction:** Published studies, reviews and guidelines regarding the use of musculoskeletal ultrasound of the wrist/hand in assessing treatment response in rheumatoid arthritis patients were sourced through the internet and library searches and the relevant data extracted.

**Conclusion:** Musculoskeletal ultrasound of the wrist and hand is a highly effective and sensitive to change

tool for demonstrating the amount of inflammation within joints and can give an objective assessment of the difference in inflammatory activity between a given time period, thus enabling us to gauge the treatment efficacy of a particular regimen.

**Key words:** Rheumatoid arthritis, Musculoskeletal ultrasound, Synovitis, Tenosynovitis, Erosions

### Introduction

Rheumatoid Arthritis (RA) is a chronic progressive autoimmune disease that is characterized mainly by joint inflammation leading to joint destruction with subsequent functional disability and premature mortality. It can involve both large and small joints having intraarticular and periarticular manifestations. The inflammation essentially involves the synovial lining within joints and tendons causing damage to bone, cartilage, tendons and ligaments<sup>1</sup>.

Treatment with Disease-Modifying Anti Rheumatic Drugs (DMARDs) has been demonstrated to retard the progression of the disease but response to therapy needs to be assessed in order to set in place the optimal regimen to bring about a remission status. The gold standard currently used to measure the amount of disease activity are disease activity scores involving subjective clinical assessment, serological tests and health assessment questionnaires<sup>2</sup>. The most commonly used and accepted clinical scoring system is the DAS28<sup>3</sup>.

However, pitfalls involving the use of the DAS28, include discrepancies between the Erythrocyte Sedimentation Rate (ESR) value and the joint counts, whereby a low initial ESR with a relatively small change may give a misleadingly high gradient in the scores denoting improvement that may

not be reflected in the clinical status of the patient or a high initial ESR with significant serological and clinical improvement, which will again not be portrayed in the DAS28 results. There may also be variability when assessing joints that are swollen or tender in between different examiners<sup>4</sup>. Moreover, there is a subset of patients who still have disease progression despite achieving clinical remission status<sup>5</sup>.

Magnetic Resonance Imaging (MRI) and radiographic evaluation have also been used as adjuncts to clinical exam but both have their drawbacks with radiographs having low sensitivity for soft tissue damage and MRI being expensive and inaccessible to many. In the past ten years however, musculoskeletal ultrasound (MSUS) has gained importance in objectively assessing and monitoring disease activity in rheumatoid arthritis patients, mainly because of its greater sensitivity to detect synovial inflammation than either clinical or radiographic evaluation<sup>6</sup>.

Musculoskeletal ultrasound is a convenient method of directly visualizing the articular and periarticular pathology in rheumatoid arthritis as it helps to accurately visualize the extent of synovial thickening within joints and tendon sheaths, and gives a direct correlation to clinical assessment. High frequency MSUS giving a greater anatomic resolution with its high sensitivity to image soft tissues namely the synovium and the tendons, can thus detect early inflammatory changes, such as synovitis, tenosynovitis, erosions and cartilage loss<sup>7</sup>.

According to Backhaus *et al*<sup>8</sup> musculoskeletal ultrasound (MSUS) is a valuable imaging tool that can be used in the detection of early soft tissue lesions and early erosive bone changes. In the Western countries, MSUS has thus become an established method in the evaluation of changes in superficial musculoskeletal structures, and is being increasingly used in rheumatologic practice<sup>8</sup>.

### **The characteristic of being 'sensitive to change'**

The main pathology which is synovitis involves synovial proliferation and hypertrophy together with synovial hypervascularisation and angiogenesis both of which can be detected by greyscale and Doppler Ultrasound (US) respectively.

Greyscale US giving a greater anatomic detail helps to quantify the amount of synovial proliferation and hypertrophy. Doppler ultrasound indicates the amount of neovascularization within the synovium and gives a reliable indicator of the amount of inflammation that is present within a particular joint<sup>6</sup>. Thus enabling an objective assessment of the joint whereby the inflammation present can be quantified and compared to future exams. This makes musculoskeletal ultrasound 'sensitive to change'.

### **Grading of synovitis and tenosynovitis**

To denote the extent of synovial inflammation, a grading system has been utilized using greyscale and Doppler ultrasound which assesses the amount of synovial thickening and vascularity within the synovium<sup>9</sup>. The semi quantitative score for greyscale synovitis is graded from zero to three, ranging from no thickening to marked thickening of the synovium<sup>9</sup>.

Specifically, grade one is whereby there is a hypoechoic line implying mild distention of synovium, under the capsule of the joint. Grade two is where there is moderate synovial thickening which elevates the joint capsule parallel to the joint. Marked distention of the joint capsule with thickened hypoechoic synovium is characteristic of grade three<sup>8</sup>.

Doppler synovitis is scored according to the amount of vascularity within the synovium and is graded from zero to three ranging from absence of vascularity at zero to vascularity observed in greater than half of the synovial area at grade three<sup>9</sup>.

Tenosynovitis on MSUS is delineated by the presence of thick hypoechoic peri-tendinous synovial tissue with or without fluid, observed in orthogonal planes. It may also exhibit vascularity on Doppler scan<sup>10</sup>. The semi quantitative Doppler tenosynovitis score is graded from zero to three ranging from absence of vascularity to marked pathological synovial vascularity within the peri-tendinous synovium<sup>11</sup>. The most common tendons involved in RA within the hand are the extensor carpi ulnaris and second to fourth flexor tendons of the hand<sup>12</sup>.

Bone erosions also commonly seen in RA, are observed as discontinuous signal of the bony margin within the joint which is seen in orthogonal planes<sup>10</sup>. These erosions are mostly observed within either the metacarpal heads at the ulnar and radial joint aspects. They are most common in the second and fifth metacarpophalangeal joints while the 4<sup>th</sup> metacarpophalangeal joint is reported to be the least frequently involved<sup>13</sup>.

### **Examples of proposed scoring systems**

The characteristic of MSUS namely sensitivity to change of ultrasound (US) detected synovitis has been investigated in several studies and various scoring systems have been applied to grade the therapeutic response of different regimens.

A semi-quantitative US synovitis score called ScUSI was developed by Loeuille *et al*<sup>14</sup> for both Grey Scale US (GSUS) and Power Doppler US (PDUS) evaluating 7 joint regions (wrist, 2<sup>nd</sup> and 3<sup>rd</sup> metacarpophalangeal (MCP) joints and 2<sup>nd</sup>, 3<sup>rd</sup> and 5<sup>th</sup> metatarsophalangeal (MTP) joints) and compared results of this score with the radiographic sharp score and the disease activity parameter DAS28. They found the ultrasound synovitis

to be a better predictive factor in the detection of destructive joint processes than the DAS28.

Another scoring system called s4 which is a semi quantitative synovitis score involving the greyscale and Doppler examination of 8 joints of 4 fingers (second through fifth MCP and Proximal Interphalangeal (PIP) joints) was used by Hensch *et al*<sup>15</sup>, and showed that GSUS and PDUS are precise in detecting and monitoring synovial inflammation in patients with active RA during treatment with Tumor Necrosis Factor  $\alpha$  (TNF  $\alpha$ ) inhibitors. This scoring system reflected changes in inflammatory processes earlier than DAS28 and correlated well with C Reactive Protein (CRP) and DAS28.

A novel 7 joint score involving the greyscale and Doppler evaluation of 7 joints (the wrist, MCP2, MCP3, PIP2, PIP3, MTP2, MTP5 of the clinically dominant hand and foot) was used by Bakhaus *et al*<sup>8</sup> to study the treatment response in RA patients receiving DMARDs and/or TNF inhibitors which showed a significant correlation between changes in synovitis seen in GSUS and PDUS and DAS28 changes through 3 and 6 months.

### Comparison of MSUS to other imaging modalities

MSUS both greyscale and Doppler, is comparable to Magnetic Resonance Imaging (MRI) in sensitivity and specificity for the detection of synovitis, tenosynovitis and even erosions. This comes with the added advantage of affordability and accessibility for MSUS. Furthermore, Doppler US has also been shown to give results that are comparable to inflammation depicted in post contrast MRI.

This was proven by Szkudlarek *et al*<sup>16</sup> who found a good to excellent sensitivity and specificity of MSUS, both greyscale and Power Doppler as compared to MRI, for the detection of synovitis at metatarsophalangeal and metacarpophalangeal joints. A good agreement between US and MRI in the detection of greyscale synovitis at MCP and PIP joints was also reported by Scheel *et al*<sup>18</sup>.

With regards to the comparison between Doppler ultrasound and contrast MRI, Terslev *et al*<sup>19</sup> depicted a high significant association between Doppler US indices of inflammation and post-contrast MRI scores at wrist and hand joints; whereas Fukae *et al*<sup>20</sup> found a good correlation between the measurements of Doppler synovitis and the enhancement rate of MRI in MCP and PIP joints.

Accordingly, even for the detection of tenosynovitis, the accuracy of MSUS is comparable to MRI. A number of studies have compared US and MRI evaluation of tenosynovitis and have shown MSUS to have a high specificity, and a fair to moderate sensitivity for detecting tenosynovitis<sup>21</sup>. In a study conducted by

Naredo *et al*<sup>23</sup>, MSUS detected more tendon effusion than MRI at wrist and hand tendons.

In addition, MSUS has also been found to be better than conventional radiography and equal to Magnetic Resonance Imaging (MRI) when it comes to detecting bone erosions<sup>7</sup>.

### MSUS as compared to clinical and serological evaluation

Another advantage of MSUS is that it can be directly correlated to clinical examination and expound further the pathology that is present within. Furthermore, MSUS has also been found to correlate well with serological parameters of disease activity, in fact, even better as compared to clinical exam.

A moderate to good correlation between swelling joints count and MSUS-detected synovitis for both greyscale and Doppler ultrasound was found by Naredo *et al*<sup>23</sup> and in another study, MSUS-detected synovitis was also found to better correlate with ESR and C-Reactive Protein (CRP) than clinically detected synovitis.

The fact that synovitis can still be demonstrated in patients in clinical remission was demonstrated in a study by Scire *et al*<sup>24</sup>, who studied patients with early RA starting conventional synthetic DMARDs treatment, whereby both clinical and MSUS-detected synovitis were significantly correlated with CRP in patients with active disease, but, in patients who achieved the clinical remission status, only Doppler synovitis correlated with CRP. This shows the accuracy of Power Doppler in detecting inflammation even in subclinical arthritis.

### Discussion

Currently the gold standard in our setting for disease activity evaluation is clinical scoring systems. However, these have been stated as being subjective as clinical examination and the perception of swelling and tenderness varies among different examiners as does a patient's own perception of their general health. Serological parameters which again due to gradient differences may not give an accurate analysis of the patient's disease activity. Radiographic evaluation shows changes too late into the disease course and is not sensitive to soft tissue changes. MRI is accurate but expensive and hard to access by many. MSUS is thus an ideal tool in that it is accurate, accessible, available and affordable. It gives an accurate anatomic depiction of the disease activity and further helps to grade the inflammation within joints and tendons and also helps to indicate the amount of bone damage.

### Conclusion

Musculoskeletal ultrasound is an important tool with high sensitivity and specificity for the early detection of destructive inflammatory processes in rheumatoid

arthritis. Given the dire consequences of undeterred progression of the disease it is incumbent to embrace MSUS in the routine follow up of patients to ensure the institution of an optimal treatment regimen for each and every patient.

## References

1. Czembirek H, Boeck M, Stiskal M. Rheumatoid arthritis: A practical guide to imaging, image interpretation, and clinical objectives. *RadioGraphics*. 2005; **25**(2):381–398.
2. Van der Heijde D, van 't Hof M, van Riel P, *et al.* Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. *Ann Rheum Dis*. 1990; **49**:916–920.
3. Prevoo ML, van't Hof MA, Kuper HH, *et al.* Modified disease activity scores that include twenty-eight joint counts: development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum*. 1995; **38**:44–48.
4. Anderson J, Caplan L, Yazdany J, *et al.* Rheumatoid arthritis disease activity measures: American College of Rheumatology Recommendations for Use in Clinical Practice. 2012 [cited 2019 Mar 21]; Available from: <http://onlinelibrary>.
5. Naredo E, Montoro M. and Janță I. Rheumatoid Arthritis. In: El Meidany Y. Editor. Musculoskeletal ultrasonography in rheumatic diseases. *Springer*. 2015: 57- 80.
6. Naredo E. Doppler ultrasonography in rheumatoid arthritis therapy monitoring. *Int J Clin Rheumatol*. 2009; **4**(1):33–40.
7. Szkudlarek M, Klarlund M, Narvestad E, *et al.* Ultrasonography of the metacarpophalangeal and proximal interphalangeal joints in rheumatoid arthritis: a comparison with magnetic resonance imaging, conventional radiography and clinical examination. *Arthritis Res Ther*. 2006; **8**(2): R52.
8. Backhaus M, Ohrndorf S, Kellner H, *et al.* Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot Project. *Arthritis Rheum*. 2009; **61**(9): 1194–1201.
9. Szkudlarek M, Court-Payen M, Jacobsen S, *et al.* Interobserver agreement in ultrasonography of the finger and toe joints in rheumatoid arthritis. *Arthritis Rheum*. 2003; **48**(4): 955–962.
10. Wakefield RJ, Balint PV, Szkudlarek M, *et al.* Musculoskeletal ultrasound including definitions for ultrasonographic pathology. *J Rheumatol*. 2005; **32**(12):2485–87.
11. Naredo E, D'Agostino MA, Wakefield RJ, *et al.* Reliability of a consensus-based ultrasound score for tenosynovitis in rheumatoid arthritis. *Ann Rheum Dis*. 2013; **72**(8): 1328–34.
12. Filippucci E, Gabba A, Di Geso L, *et al.* Hand tendon involvement in rheumatoid arthritis: an ultrasound study. *Semin Arthritis Rheum*. 2012; **41**(6):752–760.
13. Wakefield RJ, Gibbon WW, Conaghan PG, *et al.* The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis: a comparison with conventional radiography. *Arthritis Rheum*. 2000; **43**(12):2762–70.
14. Loeuille D, Sommier JP, Michel-Batot C, *et al.* ScUSI, an ultrasound inflammatory score, predicts Sharp's progression at 7-months in RA patients [abstract]. *Arthritis Rheum*. 2006; **54** (Suppl): S139.
15. Hensch A, Hermann KG, Scheel AK, *et al.* Impact of B-mode, power Doppler, and contrast enhanced-ultrasonography in RA patients on anti-TNF therapy [abstract]. *Arthritis Rheum*. 2007; **56** (Suppl):S280.
16. Szkudlarek M, Narvestad E, Klarlund M, *et al.* Ultrasonography of the metatarsophalangeal joints in rheumatoid arthritis: comparison with magnetic resonance imaging, conventional radiography, and clinical examination. *Arthritis Rheum*. 2004; **50**(7):2103–12.
17. Szkudlarek M, Court-Payen M, Strandberg C, *et al.* Power Doppler ultrasonography for assessment of synovitis in the metacarpophalangeal joints of patients with rheumatoid arthritis: a comparison with dynamic magnetic resonance imaging. *Arthritis Rheum*. 2001; **44**(9):2018–23.
18. Scheel AK, Hermann KG, Kahler E, *et al.* A novel ultrasonographic synovitis scoring system suitable for analyzing finger joint inflammation in rheumatoid arthritis. *Arthritis Rheum*. 2005; **52**(3):733–743.
19. Terslev L, Torp-Pedersen S, Savnik A, *et al.* Doppler ultrasound and magnetic resonance imaging of synovial inflammation of the hand in rheumatoid arthritis: a comparative study. *Arthritis Rheum*. 2003; **48**(9):2434–41.

20. Fukae J, Kon Y, Henmi M, *et al.* Change of synovial vascularity in a single finger joint assessed by power Doppler sonography correlated with radiographic change in rheumatoid arthritis: comparative study of a novel quantitative score with a semiquantitative score. *Arthritis Care Res.* 2010; **62**(5):657-663.
21. Wakefield RJ, O'Connor PJ, Conaghan PG, *et al.* finger tendon disease in untreated early rheumatoid arthritis, a comparison of ultrasound and magnetic resonance imaging. *Arthritis Rheum.* 2007; **57**(7):1158-64.
22. Hoving JL, Buchbinder R, Hall S, *et al.* A comparison of magnetic resonance imaging, sonography, and radiography of the hand in patients with early rheumatoid arthritis. *J Rheumatol.* 2004; **31**(4):663-675.
23. Naredo E, Bonilla G, Gamero F, *et al.* Assessment of inflammatory activity in rheumatoid arthritis: a comparative study of clinical evaluation with grey scale and power Doppler ultrasonography. *Ann Rheum Dis.* 2005; **64**(3):375-381.
24. Scire CA, Montecucco C, Codullo V, *et al.* Ultrasonographic evaluation of joint involvement in early rheumatoid arthritis in clinical remission: power Doppler signal predicts short-term relapse. *Rheumatology.* 2009; **48**(9):1092-97.