Why Point of Care Ultrasound Is More than the Modern Rheumatologist's Stethoscope

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Abstract

Point of care ultrasound (POCUS) imaging is a valuable tool in assisting clinicians to assess and manage patients in the acute and elective care environment. In modern rheumatology practice, POCUS has been increasingly used due to its effective role in identifying signs of acute inflammation, particularly with the use of power Doppler signals. There is growing evidence to support the utility of ultrasound (US) in the early and accurate diagnosis of inflammatory arthritis. This can prompt early initiation or escalation of disease-modifying treatment. It can also help to explain non-response to ongoing treatment and rule out other causes of joint symptoms.

The role of US in diagnosing giant cell arteritis, particularly with the 'halo sign', is well-recognised as the first-line investigation modality due its non-invasive and quick-access features in comparison to temporal artery biopsy.

US can also enhance the precision of intra-articular steroid injections. Acknowledging that there can be discrepancies in the use of US in real-life clinical practice, due to reliance on operator dependence and interpretation of findings, the Outcome Measures in Rheumatology (OMERACT) Ultrasound Working Group have agreed on standardised definitions and scoring symptoms for pathophysiological manifestations in rheumatic diseases.

Further research is needed to improve understanding of the predictive role of US assessment in treat-to-target strategies and in the follow-up of patients, particularly in psoriatic arthritis. It is the authors' hope that modern rheumatologists will increasingly integrate POCUS as a complementary diagnostic and interventional tool in clinical practice to improve patient outcomes.

Key Points

1. Point of care ultrasound (POCUS) is an important tool for the modern rheumatologist and can be used in daily practice and by the bedside.

2. POCUS enhances diagnostic capability for the practising rheumatologist, enabling quicker treatment decisions.

3. POCUS can be used in a variety of rheumatological diseases ranging from inflammatory arthritis to giant cell arteritis/large vessel vasculitis.

INTRODUCTION

Ultrasound (US) is a very helpful clinical tool in rheumatology due to its low cost, portability, and accessibility for point of care US (POCUS), and it is deemed to be the modern-day rheumatologist's stethoscope.[1,2] It is non-invasive and safe for patients due to the lack of ionising radiation, which enables repeated assessments if needed.

A stethoscope was originally designed to auscultate patients' cardiovascular and respiratory systems, which is particularly relevant in rheumatology when reviewing patients with extra-articular manifestations of rheumatological conditions, such as interstitial lung disease. However, it has many limitations, including a lack of visualisation of underlying structures and, as a result, possible misinterpretation of pathological disease states.

POCUS, in appropriately skilled hands, offers a more dynamic and accurate assessment of structures in motion, and modalities such as power or colour Doppler can depict blood flow in active disease states and provide live information, which is helpful when making advanced treatment decisions.[1] Furthermore, musculoskeletal US (MSUS) can be used to clarify any discrepancy between patient-reported symptoms and a clinician's assessment.

US improves the detection of extra-synovial pathologies, such as tenosynovitis, and thickened pulleys that may be challenging to clinically assess, and helps avoid over or under estimation of clinical synovitis.[3,4] MSUS can help clinicians investigate reasons for a lack of treatment response by identifying any ongoing inflammation or other joint issues to explain the patient's ongoing symptoms. In patients who struggle with treatment compliance, visualisation of their joints and disease status via US in 'real time' can facilitate discussions on consequences of a lack of treatment.[5] Therefore, due to its powerful diagnostic and interventional utility, it is more than a stethoscope. POCUS in rheumatology practice lends itself well to being incorporated as part of an early inflammatory arthritis disease monitoring clinic and giant cell arteritis (GCA) Fast Track clinics.

There are several limitations to using MSUS that have to be considered. Deeper structures such as the hips are difficult to image accurately. Image resolution is reduced and power Doppler (PD) signal may be undetectable, making it difficult to assess pathology correctly. It is not useful in assessing axial manifestations of spondyloarthritis,[6] and MRI, CT, or X-ray are the preferred imaging modalities in this context. MSUS is highly operator dependent, which can cause variable quality and interpretation of images obtained.[1] Standardisation of scanning protocols and definitions of pathological findings in rheumatological conditions (Table 1), alongside high-quality training of sonographers, are crucial to reduce discrepancies of MSUS reports.[7,8] Operator-dependent influences of acquiring and interpreting the images can provide the highest rate of error when assessing for synovitis. This could be due to the standard and type of machine that is used (high end versus handheld, for example), greyscale (GS) and Doppler settings, as well as the lack of use of a standardised approach.[8] To minimise this, significant

Table 1: Common features on ultrasound based on Outcome Measures in Rheumatology.[7]

Synovitis	Presence of hypoechoic synovial hypertrophy regardless of effusion or any grade of Doppler signal.
Tenosynovitis	Abnormal anechoic and/or hypoechoic tendon sheath widening, which can be due to presence of abnormal fluid and/or hypertrophy.
Erosions	Intra-articular and/or extra-articular discontinuity of bone surface (on two perpendicular planes).
Osteophytes	Step-up bony prominence at margins of bone (on two perpendicular planes).
Enthesitis	Hypoechoic (lack of homogenous fibrillar pattern and loss of tightly packed echogenic lines after correcting for anisotropy) and/or thickened insertion of tendon close to bone (<2 mm from cortex) with Doppler signal if active; may show erosions, enthesophytes, or calcification if damaged.
Gout (double contour sign)	Abnormal hyperechoic band over superficial margin of articular hyaline cartilage, independent of angle of insonation; can be irregular or regular, continuous or intermittent, and distinguished from cartilage interface sign.
Gout (tophi)	Circumscribed, inhomogeneous, hyperechoic (and/or hypoechoic aggregation), may be surrounded by small anechoic rim.

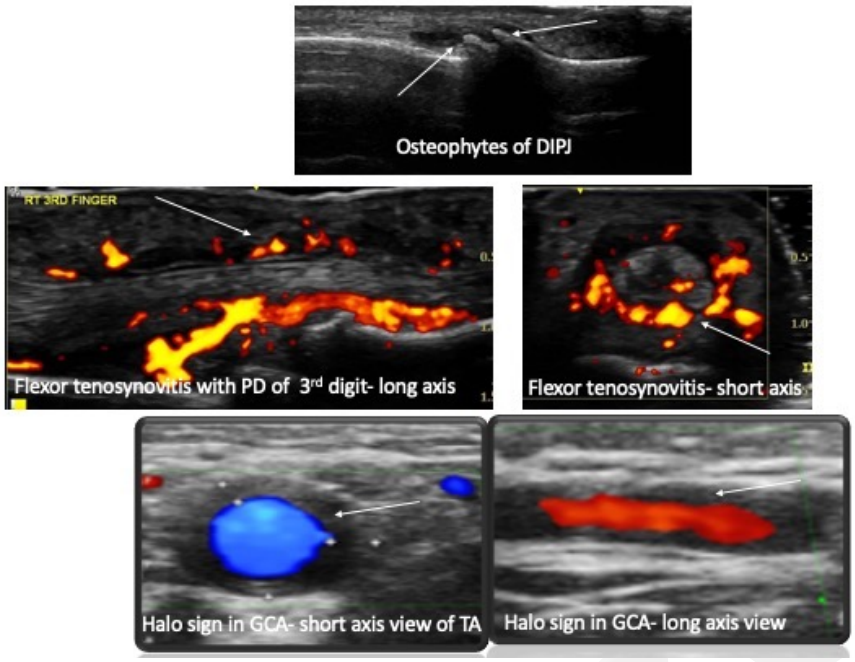
training time is required. With this in mind, the European Alliance of Associations for Rheumatology (EULAR) Outcome Measures in Rheumatology (OMERACT) US task force have developed a highly reliable, standardised, international, and consensus-based rheumatoid arthritis (RA) US synovitis scoring system in the development of US as an outcome measurement tool for joint inflammation assessment in patients with RA. This scoring system evaluates GS and PD using semi-quantitative scoring (0–3), along with a combined score.[8] The combined score provides a severity grading score. The application of the proposed EULAR-OMERACT score, as well as a standardised scanning approach for synovitis in RA, can improve the intra-observer reliability both in clinical trials and routine care.[8] Further work is also needed on the optimal number and type of joints that can be examined to evaluate for inflammatory arthritis in a POCUS setting. This, however, remains a major challenge in the wider uptake of US in routine practice. Others include the length of time to train as a competent practitioner, a lack of suitable trainers and training centres, and availability and accessibility to high end US systems.

HOW USEFUL IS ULTRASOUND IN RHEUMATOLOGY PRACTICE?

US can be useful in the RA continuum, as extensively shown in a review by Di Matteo et al.[9] For those who are at risk of RA (positive or negative autoantibodies with musculoskeletal symptoms but without clinical synovitis, i.e., subclinical synovitis), US can help to detect subclinical inflammation and/or joint damage (erosive disease) to guide prediction of developing inflammatory arthritis, and provides risk stratification for initiating disease-modifying antirheumatic drugs or biological treatment. Early detection and subsequent treatment in the apparent 'window of opportunity' has shown to positively improve disease outcomes and is the basis of Early Inflammatory Arthritis clinics.

In undifferentiated arthritis, US can help differentiate the development of RA or other types of inflammatory arthritis, such as psoriatic arthritis (PsA). This is supported by various studies, such as in Gutierrez et al.,[10] whereby US showed inflammation at the peritenon finger extensor tendon of metacarpophalangeal joints (Figure 1) in a majority of patients with PsA, but in none with RA. Furthermore, Zabotti et al.[11] has shown that the detection of one or more extra-synovial US feature provided a sensitivity of 68.0% and a high specificity of 88.1% in diagnosing PsA compared to RA. Extra-synovial changes tend to be more specific for PsA. In addition to peri-tendinous inflammation, this includes dermal soft tissue oedema, enthesopathy at deep flexor tendon insertion on the distal phalanx, capsular enthesophytes, juxta-articular

Figure 1: Pathological ultrasound in rheumatology.



DIPJ: distal interphalangeal joint; GCA: giant cell arteritis; PD: power Doppler.

periosteal reaction, metacarpophalangeal peri-extensor tenonitis. and thickening of the finger pulleys.

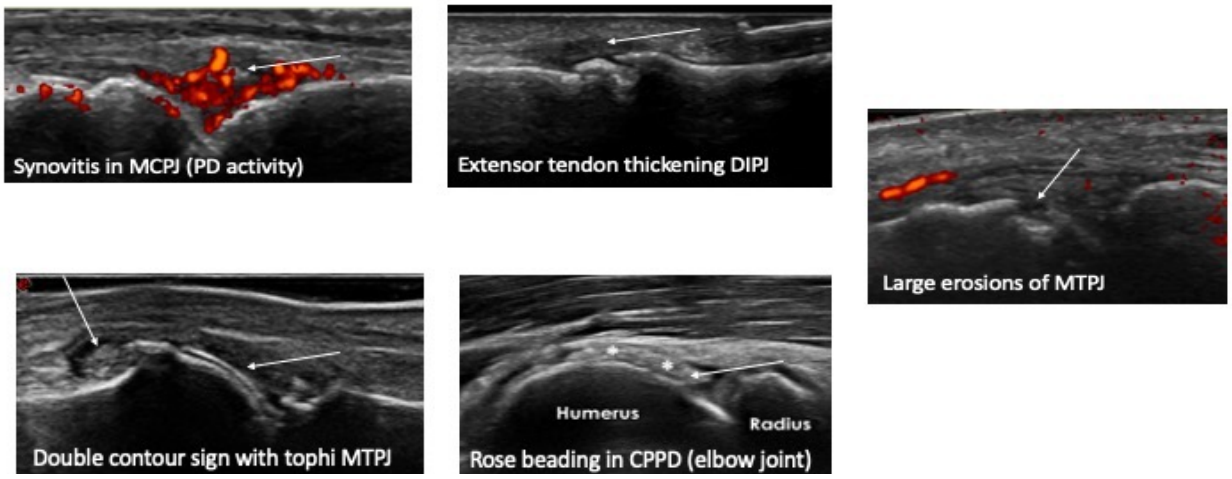
US can accurately detect unique findings in crystal arthropathies such as the double contour sign or gouty tophi (Figure 2). In patients with polymyalgia rheumatica, bilateral subacromial subdeltoid bursitis, long head biceps tendon tenosynovitis, trochanteric bursitis, and glenohumeral or hip joint effusions are typically seen on MSUS. It can also be helpful in diagnosing patients presenting with non-inflammatory joint conditions such as osteoarthritis, fibromyalgia syndrome, and tendinopathies.

Additionally, in patients with established RA, POCUS can be used as an extension to clinical examination by monitoring response to therapy and/or helping clinicians to reconsider the primary diagnosis and ongoing management. It is also useful for patients who develop new symptoms as to whether they are related to active disease or non-inflammatory causes. It can help monitor progression of any structural damage, i.e., joint erosions (Figure 2), and/or disease relapse after tapering of treatment.[9]

US is effective in the diagnosis of GCA and is recommended as the first-line imaging modality by the EULAR Large Vessel Vasculitis guidelines.[12] Integration of US as part of a Fast Track Pathway (GCA) enables a rapid diagnosis of GCA and subsequent treatment. A service evaluation of Fast Track GCA clinics by Kamperidis et al.[13] showed that out of 94% of patients scanned, 30% were diagnosed with GCA, which enabled prompt and appropriate steroid-weaning regimens in confirmed cases and discontinuation of steroids in excluded cases. This consequently reduced the demand for outpatient clinics, theatre slots, and staff for temporal artery biopsy and, more crucially, minimised complications of GCA such as blindness or prolonged steroid treatment.

Furthermore, US can help in the accurate placement of steroid needle injections, avoid complications, and possibly improve short-term outcomes.[14]

Figure 2: Pathological ultrasound in rheumatology including giant cell arteritis.



CPPD: calcium pyrophosphate deposition; DIPJ: distal interphalangeal joint; MCPJ: metacarpophalangeal joint; PD: power Doppler.

BASICS OF ULTRASOUND

US images are formed by a transducer emitting and receiving high-frequency sound waves. The waves generated by the transducer transform electrical potentials into mechanical vibrations, and vice versa. They travel through different densities of tissues, and the transducer receives reflected echoes, which are converted to computer images displayed as GS.[1] US gel is used as coupling medium to improve US pulse penetration, as it has similar impedance to human tissue.[15]

B (brightness/GS) mode frequency is first optimised based on the target structure's depth and any soft tissue features. This provides morphological information of the anatomical site. For example, if thickened tissue (high impedance) overlies structure, such as in psoriasis, lower frequency enables better sound penetration. B mode gain can then be adjusted for brightness of returning echoes.[1]

There are two main modes of Doppler imaging (which displays blood flow), including PD and colour Doppler, which allows for the evaluation of blood flow based on the reflection of sound waves (due to movement of red blood cells). PD mode is especially useful in rheumatologic MSUS as it integrates all Doppler signals, regardless of direction, and detects slow blood flow. Detection of increased blood flow by Doppler is an indirect sign of inflammation in structures such as joints, tendons or enthesis, or even erosions. Echogenicity (displayed as brightness) differentiates structures based on the proportion of waves reflected in comparison to subdermal fat (Table 2).

For rheumatological practice, linear transducers are often used to cover medium and higher frequencies. Usually, frequencies between 5–20 MHz are used in rheumatology settings, so more than one probe is usually needed in clinical practice.[15] Higher frequency probes enhance image resolution but decrease wave penetration to allow assessment of small joints and superficial entheses or tendons such as finger joints and wrists, whereby linear and/or hockey probes are recommended. Lower frequency probes are preferred for examining deeper structures such as the hip, whereby linear and/or curved probes are recommended.[16]

Table 2: Differences in echogenicity representing various structures in musculoskeletal ultrasound.[1]

Hyperechoic	Increased reflection (appears white) such as in skin, bone, and tendon (fibrillar pattern in longitudinal view).
Hypoechoic	Less reflection (appears grey) such as in synovial proliferation and nerves.
Anechoic	No or very minimal reflection (appears black) such as in synovial fluid and blood vessels.

ULTRASOUND IN RHEUMATOID ARTHRITIS

Several studies have shown that, although only a minority of 'at-risk' individuals have US changes (high score of GS and PD findings) at baseline, these findings are significantly predictive of progression to RA.[17] In a study by van der Ven M et al.,[18] patients with arthralgia but no synovitis on MSUS had a high negative predictive value for development of inflammatory arthritis over a year. In the ESPOIR cohort, MSUS identified erosions in those with early arthritis, which predicted radiographic erosions 2 years on.[19] These patients can be risk stratified to more aggressive treatment.

In patients with sustained remission, studies have found that both MSUS findings of synovitis (including Doppler activity; Figure 2) and hypertrophy may be predictive of unsuccessful tapering or cessation of treatment.[20,21]

US has shown to be useful in monitoring treatment-related changes to synovitis and tenosynovitis, including monitoring response to disease-modifying antirheumatic drugs, biologics, or topical treatment (intra-articular injections). It can help in those patients not responding to treatment and those with long-standing disease with new symptoms, i.e., either progressive joint damage, new inflammatory disease, or non-inflammatory sequelae of primary disease.

Several studies have shown that some patients with RA who are in clinical remission do not achieve good functional outcomes and show progression of radiographic disease. This may be due to persistent subclinical synovitis, and US could help identify this.[1] Those in remission with subclinical synovitis are at higher risk of disease flare. However, while subclinical inflammation can be seen in up to approximately 90% of patients with RA in remission, only a minority will have flares or radiographic progression. Therefore, the clinical significance of subclinical synovitis remains unclear, especially in the long term. At the same time, in a patient who is symptomatic, a completely normal MSUS without concerning GS or PD findings can be reassuring and prevent over-treatment.[1]

Using a treat-to-target (T2T) approach has good evidence for the best outcomes in RA, but it remains to be proven whether clinical remission or radiographic remission using US is sufficient. Two large RCTs, TASER and ARCTIC, have demonstrated that a treatment strategy based on US assessment did not lead to an improved clinical outcome in comparison with a conventional clinical T2T approach. Patients in the US tight control group were overtreated without any significant clinical improvement, although radiographic structural progression was reduced. These studies may have been underpowered to show a true difference between the groups, and they did have some other methodological flaws: for example, there was a lack of wrist assessment in the TASER study and the sonographer was also the treating physician in the ARCTIC study, which could impact the results, but these do highlight that further studies are needed in this regard.[22,23]

Ultrasound in Psoriatic Arthritis

US can detect subclinical elementary lesions that may help diagnose PsA, especially in patients with psoriasis. MSUS was used in a study by Elnady et al.,[24] which showed that in patients with

psoriasis, there was a higher prevalence of baseline enthesitis and PD scores in those who developed PsA compared to those who did not.[24] MSUS has also improved specificity from 54.4% to 90.4% in screening for early PsA in 140 patients with psoriasis and arthralgia, and no longer suspected in 45 out of 46 PsA patients.[25] Koppikar et al.[1] found that over 25% of patients with musculoskeletal complaints, but no prior diagnosis of PsA, had at least two joints with sonographic inflammation.[1]

Currently, there is insufficient evidence to prove the utility of MSUS in the disease monitoring of PsA, but there has been a study by Ruta et al.[26] showing PD evidence of subclinical synovitis as a predictor of PsA flare at 6 months in those who are in clinical remission. A study of patients with PsA in remission showed residual US subclinical inflammation in peripheral tissues; a joint or enthesis positive PD signal was found in about 19% and 24% of patients, respectively.[1]

Ultrasound in Crystal Arthritis

US can be used to differentiate between urate deposition and chondrocalcinosis in crystal arthritis. Calcium pyrophosphate crystals tend to localise within the cartilage and show up as hyperechoic dots or lines, the so called 'rose beading' sign (Figure 2),[27] and are noted to be reliable findings in the knee, wrist, and acromioclavicular joint.[28] Monosodium urate crystals localise either at the interface between cartilage and synovium (as a double contour sign), in the synovium (as micro-calculi), or in the soft tissue/tendon around the joint, and also show up as hyperechoic.[29]

With regard to disease monitoring, a study by Peiteado et al.[30] showed that US is sensitive in assessing response to urate-lowering therapy, but there was still persistent tophi burden at 2 years despite clinical control.

Ultrasound in Osteoarthritis

Typical US features of osteoarthritis are osteophytes, which appear as a hyperechoic shadow (Figure 1), usually with cartilage changes or disappearance and/or synovitis. US is found to be more sensitive (up to eight times more) than plain radiography to delineate osteophytes in smaller joints, such as finger joints, that are localised dorsally.[31]

Ultrasound-Guided Procedures

Multiple RCTs in inflammatory arthritis have shown better accuracy in using US, which can reduce complications of procedure, to guide joint injections, but no short-term benefits as improvement was only seen in 6 weeks.[32,33] However, in a larger RCT of 244 patients with inflammatory arthritis, there were better patient-reported outcomes of 81% reduction in injection pain, and 38% increase in responder rate.[34]

Gutierrez et al.[10] showed similar improvements in functional, clinical, and US scores by using MSUS guidance over the palpation-guided approach in patients with chronic inflammatory arthritis and tenosynovitis. There seems to be a clear benefit of targeting pathologically active joints through MSUS assessment before the guided injection, as treatment efficacy was observed in moderate PD synovitis.[35]

Ultrasound in Sjögren's Syndrome

US also has its role in the diagnosis of connective tissue conditions such as Sjögren's syndrome. US features such as inhomogeneous and hypoechoic structures in submandibular and parotid glands are indicative of Sjögren's. Other pertinent US findings for Sjögren's include atrophic submandibular glands with sagittal diameter <0.8 cm and enlarged parotids with diameter >2 cm. There is a 63% sensitivity and 99% specificity for diagnosis of Sjögren's based on international classification criteria, if two or more of the four glands show this pathological pattern.[36]

Ultrasound in Giant Cell Arteritis

US displays homogenous, hypoechoic circumferential wall thickening (halo sign; Figure 1) with possible features of stenoses or acute occlusions in GCA.[37] Use of Doppler US of temporal arteries has shown a sensitivity of 85% and specificities of more

than 95% in various studies to diagnose GCA.[38] In addition, axillary arteries can be easily examined using US and are found to be more commonly affected in GCA than previously expected.[39]

The extent of vascular inflammation can be quantified based on halo count (number of temporal artery segments and axillary arteries with a halo sign, ranging from 0–8) and halo score (composite index that incorporates both the number of halos and maximum halo thickness in each region, ranging from 0–48). The combination of halo count and halo score has been shown to support a diagnosis of GCA[40] in routine care as they correlate with raised laboratory markers of inflammation and may have a role in monitoring disease activity, especially with the availability of newer biologic treatments.

CONCLUSION

POCUS can be a useful adjunct in facilitating early, confident diagnosis of inflammatory arthritis, and has a role in predicting disease flares and progression, which leads to timely and effective treatment to enhance patient outcomes. In patients with a lack of response to treatment of inflammatory arthritis, US can be used to confirm or refute subclinical inflammation, support patient education with medication compliance, and facilitate shared decision-making on treatment escalation if appropriate.

US can also help to eliminate other causes of musculoskeletal symptoms to avoid misdiagnosis and treatment. There are some limitations in using US, such as operator-dependence, training issues, and a lack of agreement on the number of joints and tendons to include for scoring of disease activity. Further research is also warranted to define its role in the follow-up of rheumatoid arthritis and psoriatic arthritis, especially in T2T strategies.

US has also been proven to be a vital diagnostic tool for other rheumatological conditions such as GCA and Sjögren's syndrome. It can also be used to guide intra-articular steroid injections for precision and response as a common procedure in the management of patients with inflammatory arthritis.

Overall, integrating POCUS into the rheumatology clinic is proving to be more than a modern rheumatologist's stethoscope as, in trained hands, it can enhance efficiency by reducing clinic visits, improve patients' education of disease management, and improve patient outcomes.

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