# Portuguese recommendations for the use of ultrasound in rheumatology

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## ABSTRACT

**Introduction:** Ultrasound (US) is a relatively cheap, easily available and reliable method to improve the care of rheumatic patients. However, its use in rheumatology practice is very heterogeneous and needs to be standardized.

**Objectives:** To develop recommendations for the use of US in rheumatic diseases endorsed by the Portuguese Society of Rheumatology.

**Methods:** A systematic literature review of the available recommendations on the use of ultrasound in rheumatic diseases was performed and presented in a Portuguese Society of Rheumatology meeting to a subgroup of rheumatologists and rheumatology trainees with special interest in the subject. The most important topics to be addressed were selected and assigned to subgroups for literature review and draft recommendations. Following an iterative process of consensus, the final recommendations were developed, and their level of agreement voted anonymously online. A recommendation was approved when the average level of agreement was ≥ 7.5 in a 10-point Likert scale.

**Results:** Fourteen recommendations were produced regarding nine rheumatology topics: rheumatoid arthritis, spondyloarthritis, connective tissue diseases, polymyalgia rheumatica, vasculitis, crystal-deposition diseases, soft tissue rheumatism, osteoarthritis and ultrasound-guided procedures.

**Conclusion:** We developed an up-to-date guidance in the form of recommendations for the use of US in nine different areas of rheumatology. As US is an important imaging modality with increasing use in the rheumatology setting, and there are frequent technological advances in the US machines and probes, in parallel with continuous associated research, these recommendations should be regularly updated.

**Keywords:** Ultrasound-guided procedures; recommendations; ultrasound.

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## INTRODUCTION

The use of ultrasound (US) for the diagnosis and management of rheumatic diseases is relatively recent, when compared with other areas of medicine, but its use is of undoubtful usefulness in the diagnosis, disease activity monitoring, prognosis and treatment of this group of pathologies. US is a relatively cheap, easily available and, in many settings, reliable method to improve the care of rheumatic patients. The use of US in rheumatology clinical practice is very heterogeneous and needs to be standardized. Recommendations are helpful to accomplish this goal. This paper aims to develop the Portuguese recommendations for the use of US by rheumatologists.

## METHODS

Firstly, the authors reviewed which recommendations had been already published regarding the use of US in the setting of rheumatic diseases, particularly focused on musculoskeletal diseases. SS, FT and JP, with the help of HD performed a systematic literature review in PUBMED using the following code ("Musculoskeletal Diseases/ultrasonography"[Mesh]) OR (("Arthritis/ultrasonography"[Mesh]) OR "Tendinopathy/ultrasonography"[Mesh])) Filters: Consensus Development Conference; Guideline; Practice Guideline; Systematic Reviews; Meta-Analysis; Recommendations; Humans; English; Portuguese; Spanish. From the one hundred and sixty (160) manuscripts resulting from this, 147 were excluded after abstract review and one was excluded after full paper review. Exclusions were mostly because those papers were not recommendations nor guidelines. The resulting 12 manuscripts were then presented in a meeting of the Portuguese Society of Rheumatology (October 2016) to a sub-group of rheumatologists and rheumatology trainees with special interest in US[1-12]. It was decided that the development of recommendations should follow the main areas of rheumatology in which US had shown greater importance: rheumatoid arthritis (RA), spondyloarthritis (SpA), connective tissue diseases, polymyalgia rheumatica, vasculitis, crystal-deposition diseases, soft tissue rheumatism, osteoarthritis and ultrasound-guided (USG) procedures. All these topics were assigned to different subgroups of rheumatologists and rheumatology trainees to perform literature review and draft recommendations.

In a meeting, on May 2017, the published evidence was presented for each topic to all co-authors for consensus agreement on how the recommendations should be written. In a final phase, the recommendations were anonymously voted online to define the agreement rate among the Portuguese Society of Rheumatology. For each recommendation voting 0 means total disagreement and 10 total agreement. A recommendation was approved when the average level of agreement was ≥ 7.5 in a 0 to 10-point Likert scale. Due to the broad nature of these recommendations, the level of evidence was not defined.

## RESULTS

### RHEUMATOID ARTHRITIS

**Recommendation 1 - In rheumatoid arthritis, ultrasound is superior to clinical examination in the detection of joint inflammation and should be used when there is clinical doubt. Ultrasound may be used for differential diagnosis between rheumatoid arthritis and other arthritides.**

US provides added value for the detection of synovitis and can be highly useful in patients with questionable findings on joint examination or in cases requiring a more accurate assessment of inflammatory activity.

We identified 42 studies comparing US and clinical examination in the detection of inflammation in various joints. In general, US detected joint inflammation more frequently than clinical examination; the mean detection rate for synovitis at the hand and wrist was 2.18-fold higher for US, regardless of the duration of RA[1, 13-23].

The presence of synovitis and erosions in US is a valuable finding for the diagnosis of RA (to differentiate from healthy individuals), as is tenosynovitis, although, in the latter, the number of studies is much smaller[24,25]. On the other hand, the utility of US for the diagnosis of early undifferentiated arthritis has also been demonstrated[25]. However, the results concerning the ability to discriminate between RA from other inflammatory arthritis are inconsistent[23,26,27]. Nevertheless, based on clinical experience, the members of the panel considered that US may be useful in establishing the differential diagnosis with other arthritis.

**Recommendation 2 - In rheumatoid arthritis, ultrasound can detect synovitis even when the disease is in clinical remission. Ultrasound may be used to assess subclinical inflammation and response to treatment.**

US can provide added value to physical examination in patients with RA in remission.

Subclinical synovitis detected in Doppler mode, even when the disease is in clinical remission, may predict the development of relapses or new flares over the short-to-medium term, as well as progression of structural damage[27-29].

There is a good correlation between different models of US evaluation, including comprehensive and reduced joint counts, in patients with RA in clinical remission[30].

US is more sensitive than clinical examination to monitor therapeutic response, regardless of the first-line therapeutic modalities (synthetic or biological disease modifying anti-rheumatic drugs [DMARD]; disease activity; disease duration or the presence of factors associated with a good or poor prognosis[22, 31-36].

**Recommendation 3 - In rheumatoid arthritis, the presence of synovitis, tenosynovitis and erosions detected by ultrasound predicts joint damage and may be used to assess prognosis.**

Baseline synovitis or tenosynovitis detected by US seems to be predictive of erosive progression at 1 year (OR 7.18) and 3 years (OR 3.4)[37,38]. Baseline erosions on ultrasound appear to be predictive of further erosions at 6 months[38-41].

Apart from being superior to physical examination to detect synovitis and tenosynovitis, US is comparable with magnetic resonance imaging (MRI) and radiography to detect erosions and all these findings predict development and/or progression of structural damage, which is even more evident when there is Doppler signal[41,43-45].

## SPONDYLOARTHRITIS

**Recommendation 4 - In spondyloarthritis, ultrasound may be used for the diagnosis and monitoring of arthritis, bursitis, tenosynovitis and enthesitis. There is currently no evidence to recommend Ultrasound in the assessment of axial disease involvement.**

Enthesitis is a major feature of SpA, and US can improve its diagnosis.

Gray scale (GS) findings consist of loss of normal fibrillar echogenicity of the tendon insertion, with an increased thickness of the insertion, or intralesional focal changes of the tendon insertion, such as calcific deposits, fibrous scars and periosteal changes. These are often nonspecific and can be found in several causes of enthesopathy such as mechanic, metabolic and inflammatory[46-55]. Nevertheless, power Doppler (PD) US[56-62], and its proximity to cortical bone profile (2mm), are the most discriminative feature distinguishing enthesitis of SpA from other inflammatory and noninflammatory joint diseases, according to OMERACT consensus[63].

In 9 studies regarding the diagnosis of enthesitis in SpA, 4 of them in psoriatic arthritis(PsA)/Psoriasis, sensitivity and specificity ranged from 76% to 98%, and 48% to 90%, respectively[59,60,62,64-69]. The discrepancies in methods, the lack of comparison with a gold standard, such as biopsy, and the lack of evaluation of a real prognostic value of entheseal lesions detected by ultrasound, makes it difficult to compare several studies efficiently. Currently, there is an absence of consensus on the best enthesitis score to use, and whether different methods should be applied for diagnostic and monitoring purposes[46,59,65,69-72]. However, it is well known that lower limb enthesis are most commonly affected, and the best diagnostic performance is achieved by using combined entheseal GS and PD US modalities[73,74].

Regarding the monitoring of disease activity, there are several literature reports supporting the use of US in monitoring SpA, namely enthesitis. Many of these studies showed correlation between GS and PD findings with various aspects used in disease monitoring such as painful or tender enthesis, Bath Ankilosing Spondylitis Disease Activity Index (BASDAI), Bath Ankilosing Spondylitis Functional Index (BASFI), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)[61,75-79]. Regarding treatment response two studies showed a significant reduction of PD and GS enthesis abnormalities (tendon hypoechogenicity and/or thickening and bursitis) in SpA patients treated with anti-tumor necrosis factor (TNF) drugs. These studies have the limitation for a relative short time period of follow-up (2 and 6 months, respectively)[73,80].

The evidence regarding the assessment of synovitis is mostly limited to PsA patients[81-83]. The SOLAR score, sonography of large joints in Rheumatology, validated for rheumatoid arthritis, includes the evaluation of the shoulder, elbow, hip and knee, can be used for monitoring AS and PsA patients with peripheral involvement of medium or large joints[84].

Although there is some scarce evidence on the potential use of US for diagnosing active sacroiliitis, namely through the use of contrast-enhanced US, the panel decided that it was not robust enough to recommend its use in axial disease[85-88].

**Recommendation 5 – Musculoskeletal ultrasound may be used for the diagnosis and monitoring of arthritis, bursitis, tenosynovitis or enthesitis in patients with psoriatic arthritis. It is not recommended to evaluate axial involvement or structural damage.**

Although PsA is a subtype of SpA, the panel found useful to produce a recommendation on PsA, taking its individual features into account.

As previously mentioned, four studies demonstrated the usefulness of US in the diagnosis of enthesitis in PsA patients[63, 67-69].

Regarding arthritis, Milosavljevic J *et al*. showed that US was effective in demonstrating PsA involvement of the hands and wrists and more sensitive than clinical examination in detecting pathology[80]. Other authors have shown that US can differentiate RA from PsA in early arthritis patients, mainly at the metacarpophalangeal joint level – PsA patients presented more evidence of extensor peritenon inflammation[82]. Lin Z *et al.* also showed that US proved valuable in detecting soft tissue inflammation and enthesitis in the fingers of PsA patients that were distinctive from RA patients[83].

## SYSTEMIC LUPUS ERYTHEMATOSUS, SJOGREN'S SYNDROME, SYSTEMIC SCLEROSIS AND INFLAMMATORY MYOPATHIES

**Recommendation 6 - In systemic lupus erythematosus, Sjögren's syndrome and systemic sclerosis patients, ultrasound may be used to assess musculoskeletal involvement, being more sensitive in the detection of inflammatory findings than physical examination.**

Regarding systemic lupus erythematosus (SLE), three systematic reviews, collected evidence on joint and tendon involvement[89-91]. In one review including 610 SLE patients, effusion was identified in 602 (53,5%) joints, synovial hypertrophy in 150 (13,3%), tenosynovitis in 210 (18,7%) and bone erosions in 73 (6,5%) cases[89]. In another review including 459 patients, mostly asymptomatic, wrist and hands were the most frequent joints studied, and synovitis and tenosynovitis reported in 25-94% and 28-65%, respectively; PD in 10-82% and erosions in 2-41% of patients[90]. This evidence suggests a potential role of US in identifying subclinical disease. Additionally, two studies showed that US abnormalities depended on the SLE arthropathy subtype (non-deforming, x-ray non-erosive arthropathy, Jaccoud s arthropathy or Rhupus syndrome), with a higher incidence of inflammatory changes and erosions in the Rhupus sub-group[91]. US has also been used to assess efficacy of therapy in controlling arthritis in patients with SLE under biologic DMARDs[92,93].

Musculoskeletal involvement in Systemic Sclerosis (SSc) patients may be underestimated by the concomitant skin disease, which can make the clinical examination difficult[94]. Three reviews on the use of US in SSc have shown that: 1) US is superior to conventional x-ray in identifying digital calcifications and erosions; 2) US is more sensitive in detecting hand and wrist inflammation than clinical examination; 3) inflammatory joint and tendon disease in SSc patients can be persistent, as showed in a 6-month prospective study; 4) SSc patients frequently have thicker A1 pulley and thicker wrist, knee and ankle retinaculae thickness than healthy subjects[91,95,96]. The potential role of US in the multi-target assessment of SSc, regarding skin and lung involvement, has been explored recently[96].

According to a review of five papers, which included 16 to 60 patients with Sjögren's Syndrome (SjS), US detected synovitis in 5-76% of patients, significantly more prevalent than in healthy controls. The distribution of joint involvement was similar to RA, frequently polyarticular and symmetrical, and erosions were also detected[91,97-101]. US can also identify subclinical synovitis in 16% of joints of SjS patients, 2% with PD[101]. Not surprisingly, patients with secondary SjS with RA are more prone to have synovitis detected by US than those with primary SjS[100,102]. In addition, patients with SjS and fibromyalgia usually have normal enthesis and tendons in typical fibromyalgia tendon tender points[99].

**Recommendation 7 - Ultrasound can be used to assess salivary glands' involvement in Sjögren's Syndrome and may be performed to support the diagnosis.**

The use of US in the study of salivary glands (SGUS) has attracted considerable attention given it is an accessible, safe, noninvasive and reliable technique for detecting morphological abnormalities in patients with primary SjS[103-105]. SGUS may evaluate parenchyma heterogeneity/inhomogeneity, gland size, hypoechogenic areas, hyperechogenic bands, borders definition, blood flow changes and the presence of periglandular or intraglandular lymph nodes. Of these, inhomogeneity has the best diagnostic accuracy and was correlated with disease duration[105-108].

Different SGUS scoring systems, which include one or more of the US findings described above, have been developed, but none is validated for use in clinical practice.

Comparing with other imaging methods, SGUS showed good correlation to sialography, scintigraphy and MRI, in terms of diagnostic accuracy[103,109]. When compared to biopsy, US showed lower sensitivity and similar specificity[107]. In a recent meta-analysis, including 29 studies, the pooled specificity of SGUS in distinguishing SjS patients from controls was high (92%), and the pooled sensitivity only moderate (69%)[110,111]. Some studies were also performed in secondary SjS, with similar diagnostic sensitivity[108].

Cornec *et al.* have shown that the addition of a SGUS score based on glandular echostructure to the 2012 ACR classification criteria notably improved the diagnostic performance[112,113]. There are also some reports on the role of SGUS in prognosis (lymphoma risk) and response to treatment (rituximab)[114-116].

In conclusion, the SGUS is apparently useful in detecting structural abnormalities of salivary glands in SjS patients, but we need an international consensual scoring system to standardize the method; the intra- and inter-rater reliability must be evaluated in larger studies; and its role in the follow-up and monitoring response to therapy is far from established[105,107,111,117,118].

**Recommendation 8 - In inflammatory myopathies, ultrasound may be useful to detect muscle changes and identify biopsy site, despite the lack of strong evidence.**

Although muscle biopsy is the gold standard to confirm the diagnosis of inflammatory myopathies, it can lead to false-negatives because inflammation may be spotty[119]. US, as other imaging techniques (e.g. MRI), can detect muscle changes in the acute and chronic phases of the disease, assess the extension and severity of muscle damage, and assist in directing the biopsy site. MRI is still considered more sensitive than US in detecting muscle edema and in guiding muscle biopsy, but it is expensive, less accessible and contraindicated in some patients[119-122].

There are few controlled studies reporting the usefulness of US in inflammatory myopathies, but some non-controlled studies have shown that, in the acute phase, muscles (focally or diffusely) can appear thickened, and with areas of hypoechogenicity. PD signal is more common in early disease and correlates with disease activity. Higher echogenicity and more pronounced atrophy are more common findings in the chronic stages of myositis[91,123,124].

Contrast-enhanced US allows more accuracy for muscle perfusion. Two controlled studies showed that patients with myositis had higher blood velocity, blood flow and blood volume than healthy controls. The blood flow was the best measure for diagnosis of dermatomyositis (DM) and polymyositis (PM), with a sensitivity of 73% and specificity of 91%[119,125].

In 2016, Yoshida *et al.* determined in 14 patients with inflammatory myopathies that PD US was useful for the detection of fasciitis in most of the DM patients (6/7 patients) and in none of the PM patients. Positive PD US findings in DM patients were confirmed by histology in all 6 patients and by MRI in 4. In one patient, PD US was helpful in monitoring response to therapy. Larger studies are still needed to confirm these findings and to address whether PD US can replace MRI or biopsy[126].

## POLYMYALGIA RHEUMATICA

**Recommendation 9 - Ultrasound can be used to confirm the diagnosis of polymyalgia rheumatica and to differentiate it from other inflammatory arthropathies or periarticular diseases.**

Three main reviews evaluated the prevalence of US abnormalities in patients with polymyalgia rheumatica (PMR) and their diagnostic value[127-129]. Heterogeneity among the included studies was large (numbers varied from 13 to 57 patients) and the most frequent US findings were subacromial-subdeltoid (SAD) bursitis, long head of biceps (LHB) tenosynovitis and glenohumeral synovitis, in the shoulder, and hip synovitis, trochanteric bursitis, iliopsoas and ischiogluteal bursitis, in the hip[126-130].

Regarding the shoulder findings, SAD bursitis is the US abnormality more commonly found, with prevalence varying from 65 to 100% and it is considered the hallmark of PMR, providing the best diagnostic accuracy (if bilateral, it is the most specific finding)[130-133]]. Lower frequencies found in older studies might be explained by steroid treatment[134-136]. LHB tenosynovitis and glenohumeral synovitis were less frequent (60--85% of untreated PMR patients)[137,138].

Regarding hip involvement, US detected hip synovitis in 25-52% PMR patients[130,133,137,138]. One study found trochanteric bursitis in 100% of untreated PMR patients (90% bilateral), but these results were never replicated. Iliopsoas bursitis appeared in 30%, and ischiogluteal bursitis in 20% of cases[139]. Peripheral arthritis is less often found (18-38%)[130].

Establishing the clinical diagnosis as the gold-standard, a meta-analysis has shown that SAD bursitis had 80% sensitivity and 68% specificity for the diagnosis of PMR; the values for bilateral SAD bursitis were 66% and 89%, for glenohumeral synovitis 62% and 58%, and for hip synovitis 33% and 78%[129].

US is comparable to MRI in the detection of SAD bursitis, LHB tenosynovitis, and trochanteric bursitis, but has lower accuracy for glenohumeral synovitis, hip synovitis and iliopsoas bursitis[132,133,139].

US also seems to be useful in detecting inflammatory findings in PMR patients with low ESR, and in detecting subclinical findings in patients in clinical remission, therefore it may be superior for monitoring disease activity when compared with clinical and laboratory markers[132,137,140].

The addiction of US to the PMR classification criteria improves its performance in terms of specificity. US findings are useful in discriminating PMR patients from patients with non-RA shoulder conditions, but less so in discriminating PMR from RA[128,141].

## VASCULITIS

**Recommendation 10 - In giant cell arteritis a non-compressible 'halo' sign is the most important ultrasound finding for diagnosis. It is recommended that patients with suspected giant cell arteritis, or giant cell arteritis flare, undergo rapid access ultrasound of at least the temporal and axillary arteries, performed in a high-quality equipment by sonographers with expertise in vascular ultrasound.**

US is a valuable imaging modality for patients with suspected giant cell arteritis (GCA) or GCA flare[142]. Three meta-analyses have reported a high sensitivity and specificity for its diagnosis, when compared to temporal artery biopsy (TAB) or the 1990 ACR classification criteria[143-145]. A recent multicentric study analyzed 381 patients with newly suspected GCA who underwent both ultrasound of the temporal and axillary arteries and TAB, within 10 days of starting high-doses of corticosteroids[146]. Ultrasound showed superior sensitivity but lower specificity than TAB for diagnosing GCA (59% vs. 39% and 81% vs. 100%, respectively); however, strategies combining clinical judgement with both tests have shown to be more cost-effective, with higher sensitivity/specificity. Performing ultrasound in all cases of suspected GCA, followed by TAB only in patients with negative ultrasound but high-risk of having GCA showed a diagnostic sensitivity of 94% and specificity of 77%. Therefore, it is currently recommended that, in patients with high clinical suspicion of GCA and positive ultrasound, there is no need for additional testing to confirm diagnosis and that, in cases of low clinical probability and negative ultrasound, alternative diagnoses must be considered[147].

Ultrasound should be performed in a timely manner and by experienced ultrasonographers[148]. A non-compressible 'halo' sign, defined as a homogenous, hypoechoic wall thickening, well delineated towards the luminal side, visible both in longitudinal and transverse planes, is the most important ultrasound finding suggestive of GCA[149]. The halo sign has been reported to disappear after a mean of 2-3 weeks following corticosteroid initiation[150-152] and the sensitivity for its detection rapidly decreases under treatment[152]. Fast-track clinics with rapid access to ultrasound are therefore recommended and have already shown to improve clinical outcomes, particularly visual loss[153-154].

In around 50% of patients with GCA, ultrasound assessment has documented large-vessel involvement, particularly of the axillary arteries, which can occur in the absence of temporal arteries involvement and persist for a much longer time, therefore increasing the diagnostic yield for GCA[155-158].

## CRYSTAL-RELATED ARTHRITIDES

**Recommendation 11 - Ultrasound detects monosodium urate and calcium pyrophosphate dehydrate crystals deposition in articular and periarticular structures. It may be used to support the diagnosis of gout and calcium pyrophosphate dehydrate crystals deposition disease and for differential diagnosis with other arthritides.**

Ultrasound is a useful diagnosis method for gout when the gold standard (demonstration of crystals in synovial fluid) is not available[159-160]. The highly sparkling reflectivity of monosodium urate (MSU) and calcium pyrophosphate dehydrate (CPPD) crystals can be easily detected by US, even when only minimal deposits within cartilage and/or tendon sheets are present[104].

There are both gout non-specific and specific US findings[161-162]. The OMERACT group established definitions for the specific findings, namely "double contour sign" (DCS), "aggregates" and "tophi"[161-164] that can be found in all gout stages. Several studies and meta-analysis tested the sensitivity and specificity of DCS and tophi when compared to direct crystal observation by synovial fluid analysis. The prevalence of those US findings ranged from 22-92% for DCS and from 48 to 80% for tophi presence, depending on the US technique applied and on the disease stage (more frequent in longstanding disease)[165]. Both DCS and tophi are highly specific for gout (98-100%)[161, 166,167]. DCS has shown good to excellent intra- and inter-observer agreement and tophi detected by US has shown good construct validity when compared with MRI[161,162,167]. Tophi and erosions in gout are more easily identified by US than by radiography[165].

Recently, a collaborative European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) international project developed new preliminary classification criteria for gout, including an imaging domain that improved the performance when compared with clinical criteria alone (sensitivity 92% and specificity 89%, compared with 85% and 78%, respectively)[168].

Regarding gout follow-up, a correlation was found between uricemia level and US findings through the vanishing of specific gout signs (mainly tophi and DCS) after effective urate-lowering therapy[162,165,169].

Considering CPPD disease, the most specific US findings are: 1) hyperechoic dots or lines within the medium layer of cartilage (almost pathognomonic of chondrocalcinosis), rather than on the surface, as seen in gout; 2) hyperechoic foci ("punctate pattern") in the synovial fluid, menisci and triangular fibrocartilage; 3) linear calcification (often with acoustic shadow) or ovoid- shaped areas in tendons; and 4) homogeneous hyperechoic nodular or oval deposits in bursae or articular recesses[159,160,170].

In two literature reviews, US sensitivity and specificity were calculated using the direct observation of CPP crystals in the synovial fluid as gold standard and found to be high: 90% and > 95%, respectively[160,170-172]. When compared to conventional radiography, US showed a good correlation in the detection of calcifications[159,170].

In conclusion, US in the acute phase of crystal-related arthritides is useful to identify crystal deposition in areas of synovitis, tenosynovitis and, and allows US-guided aspiration of synovial fluid of less accessible involved structures[159-161]. In the inter-critical or asymptomatic chronic stages, US can detect specific signs of gout (DCS, aggregates or tophi) and of CPPD disease (calcified deposits within cartilage and soft tissues) and distinguish between them. Moreover, US can help to differentiate tophi from other subcutaneous nodules[104].

## SOFT TISSUE RHEUMATISM

**Recommendation 12 - Ultrasound may be used for the diagnosis and differential diagnosis in patients with loco-regional symptoms with doubtful clinical examination. It allows the assessment of periarticular tissues, including muscle, tendon, ligament, fascia, aponeurosis, retinaculum, bursa, nerves and subcutaneous tissue.**

The use of US for the diagnosis and treatment of periarticular disease is broad. Soft tissue rheumatism refers to non-systemic, focal pathologic syndromes involving the periarticular tissues, including muscle, tendon, ligament, fascia, aponeurosis, retinaculum, bursa, nerve and subcutaneous tissue[173-175]. In this section, we will review the usefulness of ultrasound in the diagnosis of soft tissue rheumatism per anatomical area, although, as agreed by the working group, the recommendation is broader.

Shoulder: US is mostly used when physical examination is nonconclusive. It is particularly useful to diagnose rotator cuff tears, performing better for full-thickness tears (sensitivity of 95%, and specificity 96%) than for partial-thickness tears (sensitivity of 72%, and specificity 93%). Regarding subacromial bursitis, sensitivity ranges from 79% to 81%, and specificity from 94% to 98%. For tendinopathy, sensitivity ranges from 67% to 93%, specificity from 88% to 100%. Sensitivity for calcifying tendinosis is about 100%, with specificity ranging from 85% to 98%[176]. Evidence is contradictory regarding whether US is superior to MRI for diagnosing partial cuff tears, but seems inferior to MRI arthrography, using surgery (open or arthroscopic) as gold standard[177,178]. There is some evidence on the use of US to diagnose supraspinatus and infraspinatus muscle atrophy, to evaluate surgical shoulder[179-181] and to evaluate subacromial impingement, although the dynamic study is highly operator dependent[182-184]. The experience of the sonographer seems decisive in the accuracy of the diagnosis of rotator cuff tears[185].

Adhesive capsulitis is hardly diagnosed by US, but coracohumeral ligament thickening is a known marker of this disease[186].

US can diagnose biceps tendon tenosynovitis and distinguish inflammatory from noninflammatory pathologies using PD[187]. US can also be used to diagnose biceps tendon rupture, dislocation and tendinosis[188,189], and deltoid and pectoralis tears[190].

Although it is usually not used for evaluating shoulder nerves, US can be useful in the diagnosis of paralabral cysts compressing the suprascapular nerve and in detecting teres minor atrophy, frequently related with axillary nerve entrapment[191,192].

Elbow: There is some evidence of the utility of US on the diagnosis of several soft tissue rheumatisms, such as lateral and medial epicondylitis, olecranon bursitis, triceps tendinosis and enthesopathy[193,194]. US proved useful in identifying the point of maximum tenderness of the extensor carpi radialis brevis tendon at the epicondyle insertion[195]. For the diagnosis of lateral epicondylitis, US is a sensitive (72% to 88%) but rather nonspecific (36% to 48.5%), inferior to MRI in an old study[196-198]. PD correlates with pain[199].

In a case–control study of medial epicondylitis, US demonstrated good agreement with physical examination with 95% sensitivity, 92% specificity, 90% positive predictive value, and 95% negative predictive value[200].

Although there is evidence that the cross-sectional area and length of thickening of the ulnar nerve can correlate with symptoms and electrophysiological aspects of ulnar neuropathy[201,202], the role of US for the diagnosis of this pathology is far from established[203]. The cubital-to-humeral nerve area ratio is a useful diagnostic methodology[204]. US can demonstrate ulnar nerve subluxation, a condition predisposing to ulnar nerve neuropathy[205].

Wrist: Several tendons and tendon sheaths may be involved in wrist pathology. The most commonly soft tissue pathology is the De Quervain's tenosynovitis, for which US reinforces its diagnosis and eases surgery planification[206-208]. In addition, it is possible to identify impingement of extensor tendons in screws of patients with distal radius fracture treated with a volar plate[209].

There is a widespread use of US for the diagnosis of carpal tunnel syndrome (CTS)[208-214]. The most frequently used US parameter include: increased median nerve cross section area (CSA), calculation of the difference between the site of lower CSA (entrapment area) and greatest nerve swelling or its ratio[215]. Ultrasound can even be helpful in the diagnosis of CTS in patients with normal electromyography[216] and can also provide additional diagnostic value in patients with a bifid median nerve and in rheumatoid arthritis patients[217-218].

Wrist ganglia can be thoroughly characterized by US[219].

Hand: Ultrasound can characterize accurately the flexor and extensor system of the fingers and seems accurate for specifically diagnosing ganglions and slightly less for solid lesions such as giant cell tumors of the tendon sheath[219-222]. US also allows the evaluation of the flexor tendon echostructure, being a good method to characterize trigger fingers[223-227].

Hip: The greater trochanteric pain syndrome is very frequent, and its etiological diagnosis is sometimes difficult. Trochanteric bursitis is rare and the role of US for the diagnosis of gluteal tendinopathy is far from established, although it seems the most appropriate first-line imaging method[228-230]. Ultrasound can also be used to establish adductor tendon disease, tears of the rectus femoris, tendinosis of tensor fascia lata, ischial bursitis and labral lesions[231-237]. US is also useful in the diagnosis of some extra-articular causes of snapping hip such as iliotibial band and iliopsoas snapping, which seem to be the most prevalent cause of this syndrome[238-242]. Morel-Lavallée lesions appear by US as hypoechoic or anechoic lesions, compressible, and located between the deep fat and overlying fascia[243]. US can also be useful in the diagnosis of hamstring muscles and insertional lesions[244] and can be as useful as MRI in depicting acute hamstring injuries[245].

Knee: US can be useful in the diagnosis of the Jumper's knee, namely through the detection of Doppler signal in the patellar tendon[246] and can be even superior to MRI in diagnosing this pathology[247], showing high inter-tester reliability[248]. It also helps in the diagnosis of patellar calcifications[249]. Quadriceps and patellar tendon tears can also be easily identified by US[250-257], as well as enthesitis, although with some lack of specific etiological findings[258,259]. In addition, meniscal extrusion can also be identified by US, namely in osteoarthritis patients[260]. US is also useful in the diagnosis of medial collateral ligament lesion[261]. Older studies show worse diagnostic accuracy in detecting ligamentous and meniscal knee pathology[262-264]. In a 2001 study US demonstrated the presence of Baker's cyst with 100% accuracy using MRI as gold standard[265]. There are also some reports on the usage of US for iliotibial band friction syndrome[266].

Ankle and foot: US could identify tibialis posterior tenosynovitis with good sensitivity and specificity when compared with MRI, as well as tendon instability[267-269]. It has also shown to be useful for diagnosing instability and anatomical variation of peroneal tendons[270-272]. Besides, US seems useful for identifying the cause of heel pain, particularly Achilles tendinopathy, according to two case-control studies, and the presence of Doppler findings is useful for diagnosing this entity[273-277]. A meta-analysis proposed that a fascia plantaris with a thickness >4 mm is suggestive of pathology (plantar fasciitis)[278]. US also allows the characterization of ganglia of the ankle and foot[279]. US proved useful in identifying deltoid ligament injuries in patients with bimalleolar fractures, but mostly to clarify lateral ligament and syndesmosis lesions[280-288]. According to a meta-analysis, for Morton's neuroma, US sensitivity is equal to MRI[289]. In rheumatoid arthritis patients, US can detect plantar bursitis as a cause of metatarsalgia[290]. In short, for periarticular pathology of ankle and foot, US represents an accurate, safe and relatively low-cost technique[291].

### OSTEOARTHRITIS

**Recommendation 13 - In osteoarthritis, ultrasound can be used to confirm the diagnosis and distinguish it from other arthritides, despite conventional radiography still being the gold standard. The presence of synovitis or Doppler signal indicates active inflammation. Ultrasound should not be used as a routine imaging in the follow-up and prognosis of osteoarthritis.**

The diagnosis of osteoarthritis (OA) is clinical and less prevalent than radiographic OA. The relevance of radiographic asymptomatic OA is unknown. Imaging is not required to make the diagnosis in patients with typical presentation of OA nor is a substitute for a detailed clinical history and thorough examination. Imaging methods should be used when an alternative diagnosis is considered, or in atypical presentations, to help confirm the diagnosis and/or make alternative or additional diagnosis. Nowadays, there is no sonographic definition of osteoarthritis[292-296].

US is useful to analyse inflammatory changes (synovial hypertrophy, fluid, Doppler signal) and structural changes (osteophytes, cartilage thickness, erosions) and to differentiate the involvement of articular from periarticular structures. It can detect more osteophytes and possibly more erosions than radiography in the hands but doesn't visualize subchondral cysts. In the majority of erosive hand OA inflammation can be identified. In a swollen knee, the presence of meniscal extrusion and joint space narrowing can suggest OA[297-306].

Cartilage quantification by US is objective, reliable and valid when compared with conventional radiography, but evidence of its applicability is lacking[301].

In OA there seems to be a weak correlation between US findings, radiographic grade and symptoms[307]. Regarding response to treatment, evidence is contradictory. The presence of hip synovitis, and ultrasound-guided aspiration of Baker's cyst in patients with knee OA are predictors of response to local steroids injection; oppositely there is evidence that the presence of knee synovitis in knee OA is a negative predictor of local steroid injection[308-313]. For hand and foot OA, searching for predictors of response to intraarticular steroid or hyaluronic acid injection failed[314-316]. For hand OA, inflammatory features do not diminish after administration of parenteral steroids[317].

As a conclusion, in OA, US seems useful mostly for differential diagnosis and to identify concomitant soft tissue rheumatism but less useful to predict treatment response.

### ULTRASOUND-GUIDED PROCEDURES

**Recommendation 14: Ultrasound guidance may improve accuracy of articular and periarticular injections or aspirations, and it is particularly recommended in structures difficult to access.**

USG injection of articular or periarticular structures seems to improve accuracy of the procedure compared to blinded or landmark guided (LMG) injections. Several studies compared USG and LMG injections or aspirations using different accuracy assessments. A better outcome was found in various meta-analysis, including studies with shoulder injections (better results for USG injections of the glenohumeral joint, acromioclavicular joint and biceps tendon sheath, but not for the subacromial space), hip joint, knee joint (injection or arthrocentesis) and elbow joint (in a single trial)[318-321].

Pain related to the procedure appears to be smaller when performing USG procedure, as found in several studies with knee injection or arthrocentesis and in a trial with injection of tenosynovitis in different locations of patients with inflammatory chronic arthritis[320,322].

Regarding efficacy, several meta-analyses showed greater improvement in pain or function scores with USG injections of the subacromial-subdeltoid bursa, biceps tendon sheath, carpal tunnel syndrome, wrist and plantar fascia[318,323-326]. Two trials using injections in different locations of arthritis or tenosynovitis in patients with inflammatory rheumatic diseases also found better results with USG injections[322,327]. However, single studies with injections of the glenohumeral joint in patients with adhesive capsulitis, trigger finger or Morton's neuroma failed to show advantage of the USG arm[318,328,329].

Generally, most studies comparing USG with LMG procedures include a small number of patients, are methodologically heterogeneous or apply subjective outcomes. Although in most cases better efficacy is found in the USG injection arms, this advantage has not been consistent. Moreover, cost-benefit analyses have not been performed in most trials. Nevertheless, studies that evaluated accuracy and applied objective outcomes, found better results when performing USG procedures. Therefore, the group recognized that performing procedures guided by US offers some advantages, particularly in injections or aspirations of structures that are anatomically or technically difficult to access.

## LEVEL OF AGREEMENT

Sixty-six rheumatologists voted anonymously online and the results are shown in Table I. All but one recommendation achieved at least an average of 7.5 of level of agreement. The recommendation regarding the use of US to evaluate the muscle in inflammatory myopathies achieved only 6,9 of average level of agreement and only 48,5% of the voters rated the recommendation 8 or higher. This may be explained by the fact that Portuguese rheumatologists, even those performing US are unfamiliar with the use this technique in this setting. All other recommendations achieve level of agreement higher or equal to 7.5, however, only one recommendation had more than 90% responses 8 or higher, recommendation 14, regarding the use of ultrasound guided procedures, which are now widely used throughout the Portuguese rheumatology practice. Many recommendations had less than 80% responses graded 8 or higher (6 out of 14) which may be related to the fact that, although the recommendations were produced by US rheumatology experts, the online survey could be responded by any rheumatologist. This dispersion of responses may be related with the asymmetrical use of US in rheumatology clinical practice in Portugal.

## CONCLUSION

The use of US in rheumatology had an enormous growth in the last decade. It is now part of the optimal rheumatology care in inflammatory joint diseases, having a role in the diagnosis, prognosis and response to treatment, namely in RA and SpA, but also in other rheumatic diseases, such as SLE, SjS, SSc and inflammatory myopathies. In PMR, US is now included in the classification criteria. Depending on the clinical setting, US is determinant for the accurate diagnosis of loco-regional complains, giving, in most cases, a precise anatomical definition of the cause of pain. More recently, this diagnostic method has also shown its importance in crystal-induced arthritides with distinctive, almost pathognomonic, findings that are very important in the correct differential diagnosis. However, the role of US in rheumatology now goes beyond the musculoskeletal system, being increasingly used for the diagnosis of SjS (characteristic salivary gland findings) and GCA (typical halo sign in the temporal and/or axillary arteries). These recommendations tried to take into account latest literature evidence, but also the current US practice in the Portuguese rheumatology. For this reason, some topics that are in development, such as US of the lung and elastography in SSc, nailfold US in PsA and USG biopsies were not included in this review. The potential development of these techniques may determine a revision of the current recommendations in the future. In addition, it is very important to highlight that US has a very long learning curve; therefore experience in US of the local rheumatologists performing the exam needs to be considered when applying these recommendations.

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**TABLE I. PORTUGUESE RECOMMENDATIONS ON THE USE OF ULTRASSONOGRAPHY IN RHEUMATOLOGY**

| Topic | Reccomendation | Agreement Mean; SD (percentage of responses 8 or higher) |
|---|---|---|
| Rheumatoid arthritis | 1 - In RA, US is superior to clinical examination in the detection of joint inflammation and should be used when there is clinical doubt. US may be used for differential diagnosis between RA and other arthropathies. | 8.2;4.5 (72.7%) |
| | 2 - In RA, US can detect synovitis even when disease is in clinical remission. Ultrasound may be used to assess subclinical inflammation and response to treatment. | 8.6;3.4 (81.8%) |
| | 3 - In RA, the presence of synovitis, tenosynovitis and erosions detected by ultrasound predicts joint damage and may be used to assess prognosis. | 8.8;2.1 (87.9%) |
| Spondyloarthritis | 4 - In spondyloarthritis, ultrasound may be used for the diagnosis and monitoring of arthritis, bursitis, tenosynovitis and enthesitis. There is currently no evidence to recommend US in the assessment of axial disease involvement. | 8.5;3.2 (81.8%) |
| | 5 – Musculoskeletal ultrasound may be used for the diagnosis and monitoring of arthritis, bursitis tenosynovitis or enthesitis in patients with psoriatic arthritis. It is not recommended to evaluate axial involvement or structural damage. | 8.7;2.8 (81.8%) |
| Systemic Lupus Erythematosus, Sjögren's Syndrome, Systemic Sclerosis and Inflammatory Myopathies | 6 - In systemic lupus erythematosus, Sjögren's Syndrome and systemic sclerosis patients, US may be used to assess musculoskeletal involvement, being more sensitive in the detection of inflammatory findings than physical examination. | 8.2;4.1 (69.7%) |
| | 7 - US can be used to assess salivary glands' involvement in Sjögren's Syndrome and may be performed to support the diagnosis. | 8.2;2.8 (69.7%) |
| | 8 - In inflammatory myopathies, ultrasound may be useful to detect muscle changes and identify biopsy site, despite the lack of strong evidence.* | 6.9;5.5 (48.5%) |
| Polymyalgia Rheumatica | 9 - US can be used to confirm the diagnosis of polymyalgia rheumatica and to differentiate from inflammatory arthropathies or periarticular diseases. | 7.6;4.6 (63.6%) |
| Vasculitis | 10 - In GCA a non-compressible 'halo' sign is the most important US finding for diagnosis. It is recommended that patients with suspected GCA, or GCA flare, undergo rapid access US of at least the temporal and axillary arteries, performed in a high-quality equipment by sonographers with expertise in vascular US. | 8.8;2.3 (84.8%) |
| Crystal-related arthropathies | 11 - US detects monosodium urate and CPPD crystals deposition in articular and periarticular structures. It may be used to support the diagnosis of gout and CPPD disease and for differential diagnosis with other arthropathies. | 8.2;2.5 (85.5%) |
| Soft tissue rheumatism | 12 - US may be used for the diagnosis and differential diagnosis in patients with loco-regional symptoms with doubtful clinical examination. It allows the assessment of periarticular tissues, including muscle, tendon, ligament, fascia, aponeurosis, retinaculum, bursa, nerves and subcutaneous tissue. | 8.4;2.1 (88.7%) |

*continues on the next page*

**TABLE I. CONTINUATION**

| Topic | Reccomendation | Agreement Mean; SD (percentage of responses 8 or higher) |
|---|---|---|
| Osteoarthritis | 13 - In osteoarthritis, US can be used to confirm the diagnosis and distinguish it from other arthropathies despite conventional radiography still being the gold standard. The presence of synovitis or Doppler signal indicates active inflammation. US should not be used as a routine imaging in the follow-up and prognosis of osteoarthritis. | 7.5;6.0 (72.6%) |
| Ultrasound-guided procedures | 14 - US guidance may improve accuracy of articular and periarticular injections or aspirations, and it is particularly recommended in structures difficult to access. | 8.9;1.1 (95.2%) |

RA – rheumatoid arthritis; US – ultrasound; GCA – giant cell arteritis; CPPD - calcium pyrophosphate dehydrate
*Recommendation 8 did not achieve enough agreement to be supported.


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