

Ultrasound of the osteoarthritic joint

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ABSTRACT

Ultrasound (US) has acquired an increasing role in the assessment of joint and periarticular abnormalities in osteoarthritis (OA). It is able to image a large set of abnormalities in this disease which include both inflammatory and structural changes at different peripheral joint sites and it is helpful in guiding local procedures that can be easily and safely performed with optimal patient's tolerance. US is a feasible imaging modality that has become a bedside procedure in the rheumatology clinical practice, thus filling the gap between clinical and radiographic evaluations of patients with OA. The present review focuses and summarises the currently available data on the applications of US in OA.

Introduction

The use of ultrasound (US) to image the joints in osteoarthritis (OA) has widely increased over the last decade. This is due to the capability of US to assess most of the structures involved in OA and their pathology at peripheral joint sites. US offers an overall evaluation and follow-up of the joints in OA and allows a clear depiction of articular cartilage, bony cortex, synovial recesses, tendons, ligaments, bursae and peripheral aspect of the menisci. US of the peripheral joints can be easily carried out at the time of consultation and at different joint sites during the same scanning session, allowing an immediate correlation between clinical and imaging findings, which may improve the diagnosis and management of patients with OA, thus providing useful information to the rheumatologist ultrasonographer, and filling the gap between clinical and radiological evaluation (1) (2) (3). Moreover, US can be routinely used in the clinical practice to guide diagnostic or therapeutic local procedures in the OA joints and peri-articular structures.

Some technical issues of US reduce its diagnostic capabilities, including limited acoustic windows for cartilage and bony cortex assessment in some joints and low sensitivity of current Doppler modes in deep/large joints which are those frequently affected by OA. However, being a relatively inexpensive, safe and quick-to-perform imaging modality, it is nowadays considered a bedside procedure in the evaluation of patients with OA.

The present review focuses and summarises the currently available data on the applications of US in OA.

Figures 1-4 show the most relevant abnormalities detected by US in OA.

Methods

A literature review focussing on the role of US in OA was performed in PubMed and EMBASE. Studies in English, including living adults with symptomatic OA of the most commonly involved peripheral joints (*i.e.* knee, hip, hand and foot) were analysed. Randomised controlled trials, controlled clinical trials, longitudinal and cross-sectional cohort studies, case-control and diagnostic studies were eligible for inclusion. Systematic reviews and meta-analyses and case reports were excluded.

Which lesions and which joints

US is able to image a large set of abnormalities in OA which include both inflammatory and structural changes at peripheral joint sites (1). A list of the most relevant US-detected lesions and their definitions is reported in Table I.

US of the osteoarthritic hip

The hip joint is frequently involved in OA, with different disease clinical features and variable natural history. Hip OA is traditionally imaged using conventional radiography that demonstrates characteristic structural lesions but has a number of limitations in visu-

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alising soft tissue abnormalities (4) (5). In OA, US is able to detect a wide set of abnormalities both at joint level and in the periarticular soft tissues. However, its role in assessing hip OA has been only rarely defined (4) and the majority of reports present in the literature in the field has been mainly focused on the use of US for guiding hip joint injections (6) (7), for assessing the efficacy of image-guided intra-articular corticosteroid injection (8) and for evaluating the presence of effusion in joints treated with hyaluronic acid injections (9).

In terms of prevalence of US-detectable abnormalities in the hip joints, 75 patients with OA have been recently investigated (4), US detecting effusion, synovial hypertrophy and osteophytes in most cases while Doppler signal was rarely found. At periarticular level, trochanteric bursitis and gluteus tendinopathy were frequent findings, while iliopsoas tendinopathy and iliopsoas bursitis were rarely present. Correlations with clinical findings and measures of disease severity showed that the presence of hip pain significantly correlated with the presence of effusion. Age and disease duration significantly correlated with the presence of osteophytes. Various US-detected abnormalities were found also in asymptomatic patients. Statistically significant differences between the symptomatic and asymptomatic patients were registered for effusion. Thus, US was demonstrated to be a useful imaging tool for analysing both inflammatory and structural damage lesions as well as for differentiating the involvement of joint structures and periarticular soft tissues. In addition, even in the presence of limitations in imaging the whole joint due to reduced width of acousting windows, US was able to detect a wide set of abnormalities also in asymptomatic patients, confirming that it is more sensitive than clinical examination in detecting musculoskeletal involvement in hip OA (4).

In another interesting study, focused on the evaluation of the prevalence of iliopsoas bursitis in patients suffering from symptomatic Kellgren-Lawrence grade II-III-IV hip OA, 2.2% out of the 860 patients who were assessed result-

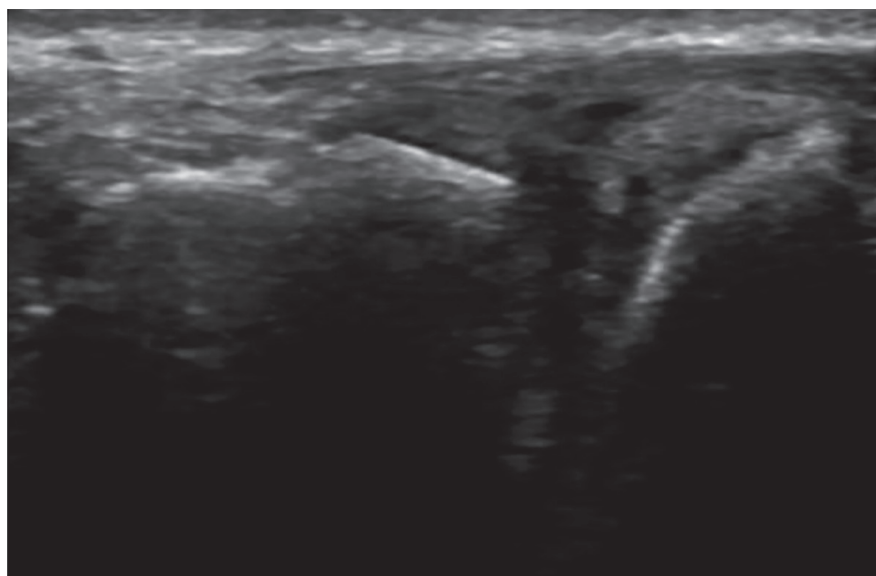


Fig. 1. Ultrasound of the first carpo-metacarpal joint in hand OA, showing the presence of osteophytes.

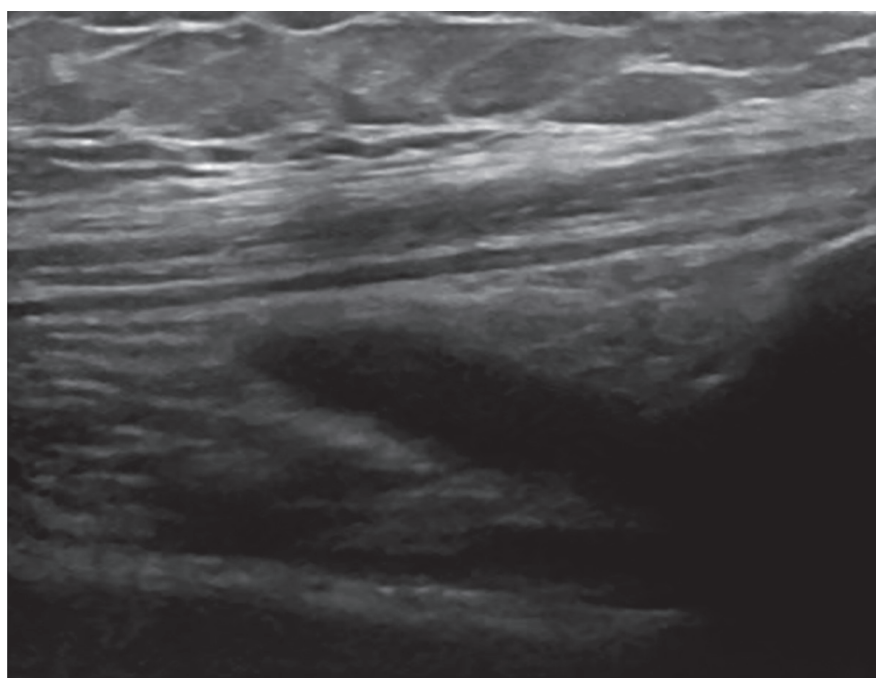


Fig. 2. Ultrasound of the knee in OA, showing the presence of mild effusion in the suprapatellar recess.

ed to be positive for that abnormality and US showed high reproducibility (k values: 1) (10). In terms of US-guided treatment, Atchia and colleagues recently demonstrated the high efficacy of a single US-guided injection for the treatment of hip OA in 77 patients and reported that synovitis on US is a biomarker of response to injection (7).

Previously, Robinson *et al.* evaluated by US capsular thickness, joint effusion, ilio-psoas bursitis, ilio-psoas tendinitis and osteophytes and dem-

onstrated a good clinical effectiveness and dose response of image-guided intra-articular corticosteroid injections in 120 patients with hip OA (8).

Renneson-Rey and colleagues demonstrated that US-detected joint effusion was associated with worse pain and functional impairment at baseline but had no influence on the clinical response to intra-articular Hylan GF-20 in 55 patients affected by hip OA (9). Finally, the administration of intra-articular hyaluronans under US-guidance

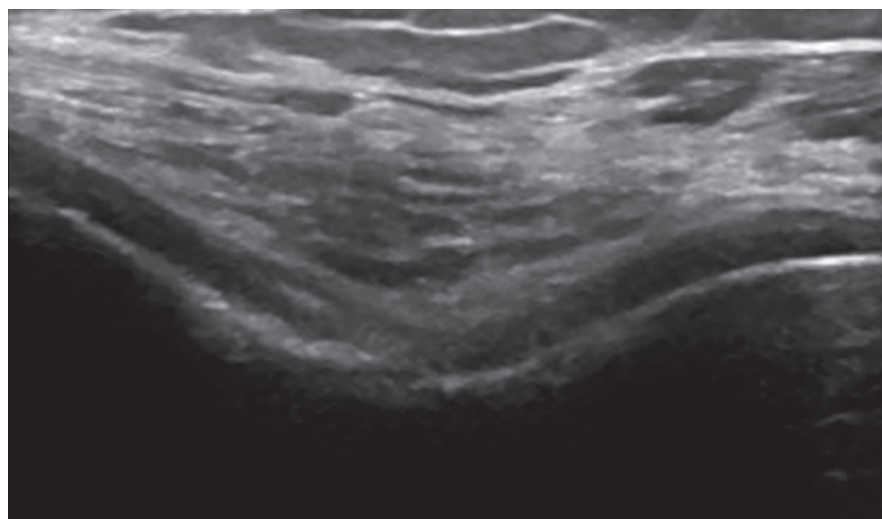


Fig. 3. Ultrasound of the femoral hyaline cartilage in knee in OA, showing irregularities of cartilage margins, inhomogeneity of the echotexture with loss of the anechoic structure, and thinning of the cartilage layer.

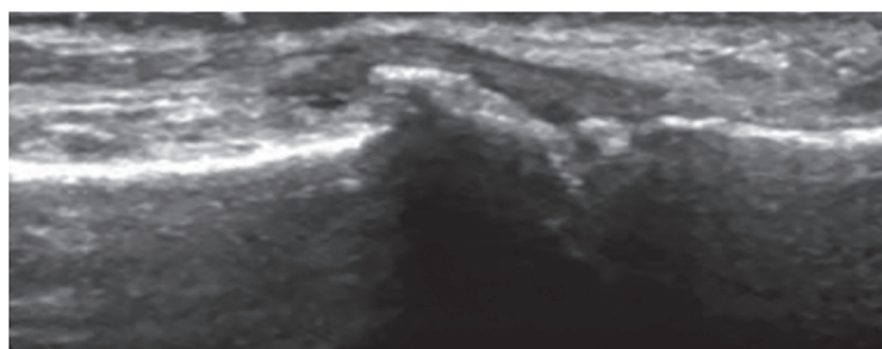


Fig. 4. Ultrasound of the third proximal interphalangeal joint in hand OA, showing the presence of osteophytes and synovial hypertrophy.

Table I. Definitions of US-detected pathology in OA.

Cartilage lesions	loss of sharpness and/or irregularities of the superficial/deep margin, loss of normal anechoic echostructure, focal and asymmetric thinning up to the complete absence of the cartilaginous layer.
Osteophyte	a step-up of the bony prominence at the end of the normal bone contour, or at the margins of the joint seen in two perpendicular planes, with or without acoustic shadow.
Erosion	an intra-articular discontinuity of the bone surface that is visible in two perpendicular planes.
Effusion	abnormal hypoechoic or anechoic intra-articular material that can be displaced and compressed, but does not exhibit a Doppler signal.
Synovial hypertrophy	abnormal hypoechoic intra-articular tissue that is non-displaceable and poorly compressible and which may exhibit a Doppler signal.

resulted to be a safe technique for treatment of hip OA in 1906 patients (11).

US of the osteoarthritic knee

Thanks to its progressive technical advances and technological developments,

US has markedly increased its ability to image different anatomic structures and their abnormalities in the finest details in knee OA, and an increasing number of studies focusing on the US assessment of different abnormalities both

within the joint and in the surrounding musculoskeletal soft tissues has been registered over the last years (12).

Particularly, a wide interest has been focused on the US assessment of the popliteal fossa in OA, with the evaluation of different aspects related to the presence of Baker's cysts.

The effects of intra-articular knee joint steroid injections in 30 patients with OA have been analysed by Acebes *et al.* who demonstrated a reduction in Baker's cysts dimensions as well as in cyst wall thickness after a single intra-articular injection of 40 mg triamcinolone acetonide at knee joint level (13).

An interesting recent study focusing on the reliability of clinical examination and US for detecting Baker's cyst, showed that, in 110 patients with knee OA and in non-OA individuals, US was more sensitive than clinical assessment which cannot accurately assess the popliteal fossa (14).

Forty patients with knee OA complicated with symptomatic Baker's cysts were recently studied also by Bandinelli and colleagues who performed an interesting longitudinal US and clinical follow-up assessment of the response to Baker's cysts injection with steroids and demonstrated that US-guided steroid direct injection reduced US measures and clinics of Baker's cysts, in particular, when steroid is directly infiltrated into the cysts (15).

One hundred and ninety-six patients with chronic knee osteoarthritic pain were previously evaluated for Baker's cysts in another study analysing clinical, US, radiographic and scintigraphic assessments and demonstrating that Baker's cysts are a common US findings and are associated with synovitis and its grade, as shown by early-phase bone scintigraphy. Clinical variables, radiographic damage and knee joint effusions cannot predict the presence of Baker's cysts in those knees (16).

US features and clinical response to a single session of US-guided aspiration and corticosteroid injection in 32 patients with knee OA and Baker's cysts were recently analysed by Koroglu *et al.* who classified Baker's cysts as simple and complex by US prior to the treatment and demonstrated that cyst

aspiration with corticosteroid injection yields clinical improvement and cyst volume reduction (17).

Finally, the response to horizontal therapy, aspiration and corticosteroid injection alone or in combination, in terms of pain relief and functional improvement, was recently assessed in 60 OA patients complicated with Baker's cysts and treatment demonstrated to be effective particularly after combined use of horizontal therapy and steroid injection (18).

In terms of prevalence of sonographic-detected abnormalities in OA, an interesting study analysed 82 patients with knee involvement and evaluated the correlations between US findings and clinical data, demonstrating that both inflammatory abnormalities and structural damage lesions were frequent findings in knee OA. Interestingly, statistically significant correlations were present between US inflammatory findings and the main clinical tests for OA, confirming that US has a relevant role in the global evaluation of patients with knee OA (12).

The prevalence of US inflammation and correlations with clinical findings were also assessed in a multicentre study which was performed in 600 patients with painful knee OA. US inflammatory findings correlated with advanced radiographic disease and with clinical signs and symptoms suggestive of an inflammatory flare (19).

The clinical and sonographic factors associated with painful episodes in patients with knee OA were analysed by de Miguel *et al.* in 101 patients. Among a number of inflammatory abnormalities that were assessed effusion, Baker's cyst, and higher BMI were found to be risk factors of painful flare (20).

The correlation between clinical and ultrasonographic findings in 100 chronic painful primary knee OA patients referred with acute flare-ups and the impact of diagnostic US to determine the origin of pain in these patients were recently investigated by Esen *et al.* US-detected inflammatory abnormalities were significantly more frequently observed in the painful knees with significant correlation with the Kellgren-Lawrence grade (21).

US findings in 50 patients with knee OA were investigated in a comparative study with clinical and radiographic assessment by Naredo and colleagues who demonstrated the presence of effusion, Baker's cysts and medial meniscal protrusion with medial collateral ligament displacement in most patients. Meniscal protrusion and ligament involvement resulted to be associated with knee pain (22).

In terms of diagnosis, the diagnostic value of colour Doppler US in patients with inflammatory arthritis *versus* OA of the knee joint was recently analysed by Beitinger *et al.* in 106 patients. The US findings were compared to synovial fluid analysis in order to differentiate inflammatory and non-inflammatory disease but, even though Doppler synovitis score resulted to be significantly more severe in inflammatory arthritis, high synovial Doppler activity could be observed also in OA patients sporadically, without any definitive Doppler threshold that clearly separated OA from inflammatory patients (23).

The course of a wide set of US abnormalities in 55 knee OA patients was assessed in a 1 year follow up study by Bevers *et al.* who evaluated different inflammatory and structural US features at three time points during 1 year and demonstrated that inflammatory abnormalities (*i.e.* effusion and synovial hypertrophy) occurred in over 40% of patients at some time in the year of follow-up and showed a fluctuating pattern, while meniscal protrusion and Baker's cyst were more stable features (24).

More recently, the same authors investigated the association between different US features and radiographic and clinical progression after a 2-year follow-up in 125 knee OA patients and demonstrated a longitudinal association between Baker's cyst and synovial hypertrophy with clinical and radiographic progression (25).

Recently, among a number of common US-detected abnormalities, synovial pathology was found to correlate with the severity of radiographic knee OA more than with symptoms in 243 patients (26). The association of US features with pain in patients with knee OA was also investigated by Wu *et al.* in 54 patients

whose US inflammation features, including effusion and synovitis, were positively linearly associated with knee pain. In addition, synovitis was degree-dependently associated with pain at rest and with the presence of medial knee pain (27).

In terms of predictive value, the role of US in predicting the response to intra-articular corticosteroid injection in primary OA of the knee was assessed by Pendleton and colleagues who demonstrated that in 86 patients US was more sensitive than clinical examination at detecting inflammation in knee OA and peri-articular structures as well as that the presence of effusion or synovitis did not predict response to intra-articular steroids (28).

The predictive value of US features for the effects of intra-articular steroids in knee OA were also investigated in 62 patients by Bevers *et al.* who showed that no patient, disease or US characteristic of inflammation turned out to be a reliable and clinically meaningful predictor for the effects of intra-articular steroids after 4 weeks (29).

Chao *et al.* previously assessed whether inflammation on US was predictive of clinical response to intra-articular corticosteroid injections in 79 patients with knee OA who received either an intra-articular injection of triamcinolone acetonide in the treatment group or saline in the placebo group. Intra-articular corticosteroid were demonstrated to be an effective short-term treatment for symptomatic knee OA compared to placebo and patients with non-inflammatory characteristics on US had a more prolonged benefit from corticosteroids compared to inflammatory patients (30).

Clinical and ultrasonographic predictors of joint replacement for knee OA were analysed by Conaghan *et al.* in a EULAR multicentre study performed in a cohort of 531 patients with painful OA knee. Significant progression to joint replacement was reported and, in addition to severity of radiographic damage and pain, US-detected effusion resulted to be a predictor of subsequent joint replacement (31).

In terms of accuracy of intra-articular injections, recently, the accuracy of

blind versus US-guided suprapatellar bursal injection were investigated by Park and colleagues who demonstrated that in 99 patients intra-articular injections through the suprapatellar bursa under US guidance increased the accuracy of knee joint injections (32).

The accuracy of US-guided intra-articular injections at 3 different sites in knee OA was again investigated the same authors who demonstrated in 126 joints that injections in the midlateral or superolateral recesses increased the accuracy of knee joint injections (33).

In terms of reliability in the detection of both inflammatory and structural abnormalities, US has been recently demonstrated to be reliable between ultrasonographers with different level of experience. In 9 patients with varied severity of knee OA, the analysis of a wide set of lesions demonstrated that, when a standardised scanning technique and agreed definition of pathology are used, US is a reliable tool even if it is used by sonographers with limited experience (34).

A recent OMERACT study focused on inflammatory and structural abnormalities in 13 patients with knee OA demonstrated from moderate to good intra- and inter-observer reliability in terms of inflammatory assessment and from fair to good intra- and inter-observer agreement for structural damage evaluation. Once again, the use of a standardised scanning protocol assures a reliable assessment of US in knee OA (35).

In terms of treatment effect, the efficacy of a bradykinin receptor 2 antagonist was evaluated by contrast-enhanced US and compared with contrast-enhanced MR in a study which assessed 41 patients with painful knee OA. US and MR had good agreement in assessing inflammatory changes and both demonstrated an analgesic effect of icatibant, representing a good model for evaluation of an inflammatory process in knee OA (36) (37).

Concerning meniscal involvement in OA, meniscal displacement was recently assessed in 78 patients by Kawaguchi and colleagues who found in medial meniscus significantly displaced by weight bearing in knees with K/L grades 1–3 OA. A significant associa-

tion with an increased pathology at the 1-year follow-up was also demonstrated (38).

US of the osteoarthritic foot

Foot OA is characterised by a number of inflammatory and structural lesions at the level of different of different joint areas but, nonetheless foot involvement is frequent in OA, US reports results to be quite limited on this topic with only a few studies currently available in the literature.

Iagnocco *et al.* recently investigated the prevalence of US abnormalities in the foot of 100 OA patients and compared them with clinical findings, demonstrating the presence of a high number of changes both related to inflammation and structural damage in up to 88% of cases. US resulted to be more sensitive than clinical examination in the detection of inflammatory abnormalities (39).

First metatarsophalangeal joint pain was recently investigated by Keet *et al.* who assessed US-detected synovitis, structural pathology and their relationship to symptoms and function in 33 patients, showing that osteophytes were associated with pain and, together with more severe synovitis, contributed to poorer function (40).

Finally, the efficacy of US-guided steroid injections for pain management of midfoot joint degenerative disease was recently investigated by Drakinaki and colleagues who found good therapeutic results up to 3 months post-injection in the majority of the 63 patients who were treated (41).

US of the osteoarthritic hand

The prevalence of hand OA has been estimated at over 44% in elderly populations, however only a limited number of studies have been focused on the US assessment of the hand in OA and most reports have been developed on radiographic disease, which may not be reflective of symptomatic or clinically relevant OA (42).

In terms of prevalence of inflammatory abnormalities and correlations between inflammation and symptoms, Kortekaas and colleagues found that pain in hand OA was associated with different fea-

tures of inflammation (*i.e.* effusion, synovitis on grey-scale and Doppler) in 55 hand OA patients and demonstrated a high prevalence of pathology by US (43).

In a follow-up study focused on inflammatory US features and performed by the same authors in 25 hand OA patients, inflammatory US findings were seen in nearly all patients at baseline and were stable over time at patient level, but varied on joint level. Pain diminished after 3 months, while associations between painful joints and inflammation increased, emphasising the multifactorial aetiology of pain (44).

In a study on erosive hand OA, US was found detects more joints with inflammation (*i.e.* effusion, synovitis on grey-scale US and Doppler) than clinical examination (*i.e.* soft periarticular or articular tissue swelling, tenderness on palpation, and redness) in 18 patients, thus demonstrating that US can supplement the clinical examination, as US-detected subclinical joint inflammation might accelerate joint damage and thus functional impairment (45).

In an interesting study focused on 22 patients with erosive hand OA Vlychouy *et al.* demonstrated that US evidence of inflammation was frequent and that US is a reliable and a more sensitive imaging modality than x-ray in detecting erosions and osteophytes (46).

The frequency of structural and inflammatory findings in erosive and non-erosive OA was also explored by Wittoek and colleagues, who evaluated 38 patients and also analysed if US can detect more abnormalities than conventional radiography. The study demonstrated that US is capable of detecting erosions in radiographic non-erosive phases and that the highest frequency of synovitis is present in erosive joints but inflammatory findings are common in all anatomical phases of OA (47).

In terms of correlations between US and radiography for structural lesions assessment, Keen *et al.* compared the detection of osteophytosis and joint space narrowing by US and conventional radiography in OA of the hand. Out of the 37 patients who were imaged, both abnormalities resulted to be more frequently detected by US than by

radiography and, particularly, involvement of metacarpophalangeal joints was more common than would have been expected from radiographic studies (42).

Concerning erosive OA, high resolution US was used by Iagnocco and colleagues to detect bone erosions in 110 patients with hand OA. Good concordance between US and radiography in detecting central joint erosions was demonstrated, thus showing that US may be considered a useful technique for the differential diagnosis between erosive OA and classical hand OA (48). The reliability of US and correlations with MRI, radiographs and clinical joint findings was recently analysed in an interesting Norwegian study in which 127 hand OA patients were assessed and US was found to be reliable in assessing osteophytes. Good agreement was also found between osteophytes detected by US and MRI, while US was more sensitive than conventional radiography and clinical examination (49).

In terms of reliability and validity of US in hand OA, Möller *et al.* demonstrated that US measurements of finger joint cartilage performed in 18 patients is reliable and valid, when compared to measurement of joint space width on conventional radiography, thus representing a promising alternative to x-ray (50).

Reliability and validity of US were also assessed in another interesting study by Wittoek *et al.* who evaluated both soft tissue and destructive changes in OA of the interphalangeal finger joints, comparing US findings with MRI and conventional radiography. Nine patients with erosive and 5 with non-erosive disease were studied and US and MRI were found to be more sensitive in detecting erosions than conventional radiography in erosive OA. A high agreement between US and MRI in the assessment of bone erosions, osteophytes and synovitis was present. A high percentage of inflammatory changes was found in erosive, and in smaller amount in non-erosive OA, both confirmed by MRI. Good interobserver reliability of US was obtained for all variables (51). The reliability of US in detecting cartilage abnormalities in hand OA patients was recently assessed by Iagnocco *et al.*

who demonstrated that US is a reliable imaging modality for the detection of cartilage lesions in 8 patients with metacarpo-falangeal joint pathology (52). In terms of effectiveness, response of symptoms and synovitis to intra-muscular methylprednisolone in hand OA was assessed by US in 36 patients. The results showed that despite parenteral corticosteroids were associated with a statistically significant reduction in symptoms, no statistically significant reduction in US-detected synovial inflammation was found (53).

In an interesting comparative efficacy study performed in 88 patients by Monfort and colleagues, US was used to guide intra-articular injections with hyaluronic acid and corticoid in OA of the first carpo-metacarpal joint. The authors demonstrated that both hyaluronic acid and betamethasone were effective and well-tolerated for the management of rhizarthrosis (54).

In addition, in a study aiming to ascertain whether joint injection with local anaesthetic and steroid was of predictive value in disease progression in thumb carpo-metacarpal OA, 43 patients were assessed at an average follow up of 24 months and 32% of them who resulted to do not respond favourably to injection at one week were found to likely to progress to surgery in the first year after the injection (55). Finally, inflammatory features, especially when persistently present, have been recently demonstrated to be independently associated with radiological progression in 56 patients with hand OA after 2.3 years, thus indicating a role of inflammation in the aetiology of structural damage in hand OA (55).

US of the osteoarthritic shoulder

Shoulder OA is not frequent at glenohumeral level but it involves quite often the acromioclavicular joint. In 2015, the effects of palpation versus US-guided acromioclavicular joint intra-articular steroid injections have been analysed in a retrospective study focused on 100 patients and US guided injections for the treatment of symptomatic OA resulted in better pain and functional status improvement than palpation-guided therapy at 6 months follow-up (56).

Previously, US was used to guide intra-articular and peri-articular acromioclavicular joint injections in 101 patients with symptomatic OA which both resulted to be clinically effective (57).

Discussion

The most relevant indications of US in OA include detection of articular cartilage damage, bony cortex abnormalities, joint inflammation and peri-articular soft tissues involvement. US is more sensitive than clinical evaluation and conventional radiography in the detection of synovitis and cortical lesions respectively (1).

Technological advances in the field of US have lead to the production of high-end equipment that allow a direct visualisation of most joint and peri-articular structures and the demonstration of their involvement in the osteoarthritic joint (3) (59) (60). At different joint sites US has demonstrated to be a valuable tool for the analysis of inflammation as well as for the evaluation of structural lesions (1) (3) (2) (48) (61). Both grey-scale and Doppler modes represent fundamental tools for the correct and extended joint evaluation in OA and, in addition, the application of Doppler mode allows the differentiation between active and non-active disease (1). US can be successfully used as a guide for fluid aspirations, injections, biopsies and other diagnostic and therapeutic procedures, improving their safety and reliability and resulting in an excellent patient tolerance without any radiation burden (1).

In conclusion, US is able to reliably evaluate most of the pathologic conditions in OA and it is a sensitive-to-change tool for the analysis of disease features at follow up and the assessment of response to treatment. OA is the most common rheumatic disease and US allows for a feasible, quick and non-invasive assessment of joint abnormalities during clinical practice with a multiregional evaluation of the musculoskeletal system during the same scanning session (1) (59) (61). On the other hand, US has only partial accessibility to the inner joint structures, resulting in incomplete visualisation of the articular cartilage and bony profile in many

peripheral joints (3). In addition, the assessment of the bone is limited to its cortical portion, with lack of visualisation of the subchondral tissue. Those limitations of US represent clear disadvantages respect to MRI in the imaging of the whole joint in OA, however, the global evaluation of the osteoarthritic joint by US facilitates the diagnosis of the disease and the assessment of its severity in different disease phases (62).

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