Ultrasonography in rheumatoid arthritis: what rheumatologists should know

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ABSTRACT

Ultrasonography has recently gained prestige as an adjuvant method for the diagnosis and therapeutic follow-up of rheumatoid arthritis, although radiography remains the imaging modality traditionally and widely used for those purposes. The great advantage of the ultrasonographic study, which has motivated enthusiastic research in the area, resides in its capacity to detect synovitis and bone erosion at a pre-radiographic phase, which has been increasingly valued in preventing late and definitive structural damage. Because that is a relatively new subject, several scientific articles have been published in recent years about the potential applications of ultrasonography in individuals with rheumatoid arthritis, some of which directed to researchers and others to clinical rheumatologists. This study aimed at assessing the currently available bibliography on the subject and at describing only the concepts that are of practical applicability in the daily routine of clinical rheumatologists.

Keywords: ultrasonography, rheumatoid arthritis, review, color Doppler ultrasonography.

INTRODUCTION

Rheumatoid arthritis (RA) is a multifactorial, symmetric, peripheral, chronic polyarthritis, whose prevalence is estimated as 1% of the population. The synovial membrane is the target structure of the autoimmune attack. Most patients have a cyclic course of clinical remissions and relapses, which tends to result in progressive joint destruction and deformity. Radiography has been traditionally used in the search for imaging diagnostic criteria and in patients' follow-up. However, radiographically demonstrable findings, such as joint space reduction, subluxation, or bone erosion, represent irreparable anatomic changes. However, specialized literature has recently recommended an emphasis on RA screening and early treatment, aimed at preventing the progression to irremediable late deformity.[1] The theoretical motivation for searching for an early diagnosis lies in the greater metabolic activity of the disease's early stages.[2] That phase represents an important window of opportunity to prevent definitive structural damage. Ultrasonography enables the specific follow-up of that group of patients, by demonstrating pre-radiographic changes still at a reversible phase or even already irreversible small changes. As an alternative, magnetic resonance imaging can also detect initial RA changes, but with its inherent limitations of cost and availability (Table 1).

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Table 1
Comparison between different imaging diagnostic methods regarding their capacity to detect some of the most common abnormalities in individuals with initial rheumatoid arthritis

	Radiography	Ultrasonography	Magnetic resonance imaging
Bone edema	—	—	+++
Synovitis	+	++	+++
Bone erosion[39]	+	++	++

— absent / + low / ++ intermediate / +++ high

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ULTRASONOGRAPHY FOR ASSESSING SYNOVITIS

Synovitis, either proliferative or exudative, is the earliest change that can be ultrasonographically graded. Its quantification via grayscale ultrasound usually uses a semiquantitative scale with three levels of intensity, indicating mild, moderate or marked synovial changes[3,4] (Figure 1).

On imaging, proliferative synovitis manifests as distension of the articular capsule by a poorly compressed, hypoechoic tissue, which initially tends to establish in the following joints: metacarpophalangeal, metatarsophalangeal or proximal interphalangeal (Figure 2 A and B). The search for occasional synovial vascularization on color or power Doppler imaging is very useful complementary information for therapeutic monitoring, because increased blood flow is present during the active phase of disease. In addition, spectral analysis of the pathologic flow reveals a pattern of low resistance in the acute active phase and elevated resistance in the chronic active phase[5–8] (Figure 2 E, F and G). The cutoff point of the several quantitative indices to characterize high or low resistance is currently controversial and object of much study in the literature, although an absent or reverse diastolic flow surely indicates high resistance.

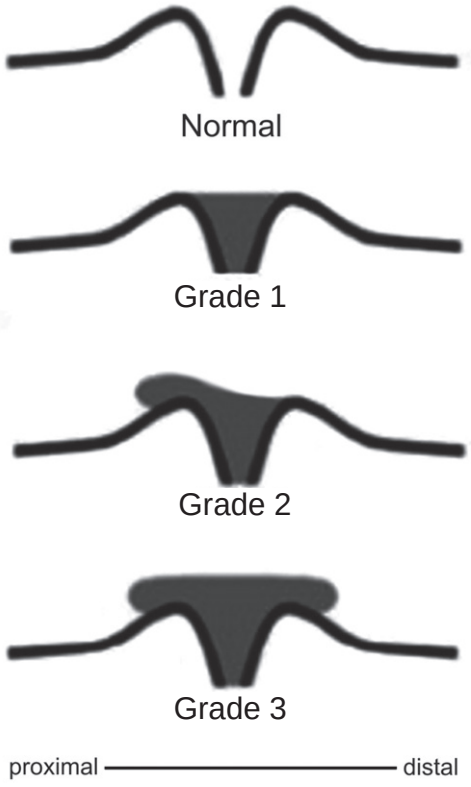

Figure 1
Synovitis grading in metacarpophalangeal, metatarsophalangeal and interphalangeal joints on ultrasonography. Note that normal synovium is imperceptible. Initially, the articular capsule distension is proximal, only progressing distally in more severe cases. Modified from Fernandes et al.[40]

Although proliferative synovitis and exudative synovitis (joint effusion) can only be differentiated via gray scales in last-generation equipment (Figure 3 A, B and C), in most cases the major diagnostic clue is synovial fluid compressibility (Figure 3, D, E and F). An insignificant amount of fluid in the plantar or dorsal recess of metatarsophalangeal joints is a normal finding, which should not be considered pathological.

Synovitis of the distal radioulnar joint, usually extending to the ulnar styloid process and contiguous structures, is such a characteristic finding that it is even considered pathognomonic of RA (Figure 4 A and B). Usually, but not always, the change is bilateral. On the dorsal face of the intercarpal joints, that finding is equally considered typical (Figure 4 C and D). Synovitis can also affect synovial sheaths. In fact, the histopathological analysis of the synovial tendon sheath reveals an incredible similarity with that of the joint synovium in individuals with RA, including hyperplasia of the lining cells and leukocyte infiltration, mainly CD4+ T cells and CD68+ macrophages.[9] Thus, the differential diagnosis with systemic inflammatory arthropathy should be considered in the presence of synovitis in unusual sheaths, rarely associated with trauma or overuse, such as that of the long flexor of the thumb (Figure 4 E and F), extensor carpi ulnaris, and flexor carpi radialis (Figure 4 G and H). Distally, the most affected sheaths are those of the extensor tendons of the second and third fingers.[10–12] Synovitis in the tendon sheaths of the toes is rare, being usually associated with systemic inflammatory arthropathy, either in the flexor (Figure 4 I and J) or extensor (Figure 4 K and L) region.

Ultrasonography can be used to monitor the response to treatment by assessing the reduction in synovitis intensity on the grayscale test and/or in synovial vascularization by use of color or power Doppler imaging.[13] Several ultrasonographic scores of synovial impairment have been proposed in the literature and all have been mainly aimed at detecting changes in the inflammatory activity by assessing the smallest possible number of joints to reduce the time of exam.[14–18] In our opinion, such protocols are still primarily aimed at the communication between researchers, their use

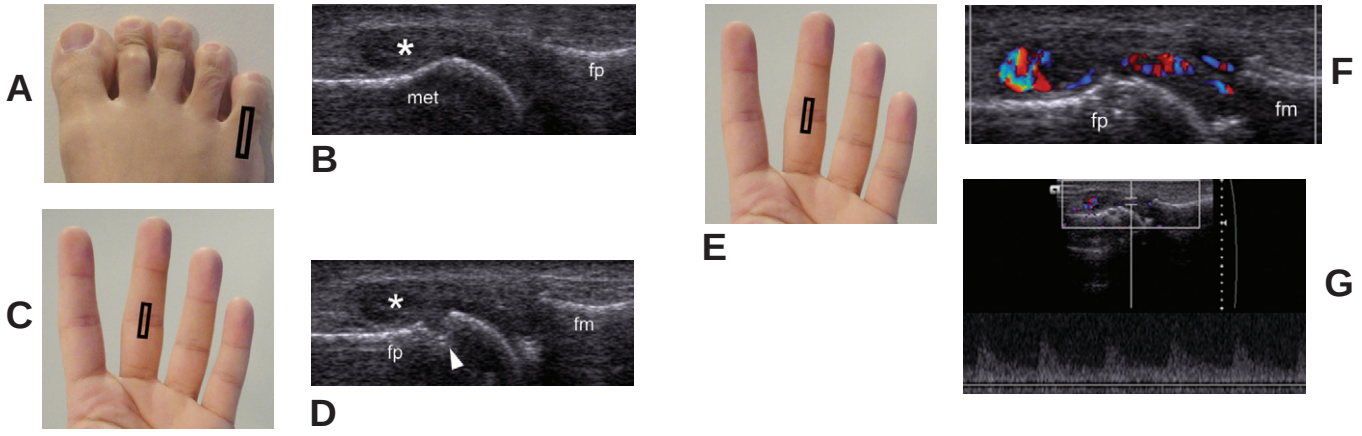

Figure 2
Ultrasonographic manifestations of rheumatoid arthritis. **(A)** Positioning of the transducer. **(B)** Corresponding image demonstrating the head of the metatarsal bone (met), the base of the proximal phalanx (fp) and typical proliferative synovitis (*), grade 2/3, affecting the metatarsophalangeal joint of the fifth toe. Synovitis is the earliest ultrasonographic change that can be demonstrated in individuals with rheumatoid arthritis, being a strong predictor of erosion. **(C)** Positioning of the transducer. **(D)** Corresponding image of the proximal interphalangeal joint, demonstrating the head of the proximal phalanx (fp), the base of the middle phalanx (fm) and typical proliferative synovitis (*), grade 2/3, and a small bone erosion (arrow head). **(E)** Positioning of the transducer. **(F)** Corresponding image of the proximal interphalangeal joint, showing flow inside the synovium, indicating disease activity. **(G)** Corresponding spectral analysis demonstrating anterograde diastolic synovial flow. The spectral analysis of synovial flow helps to differentiate the active acute phase, which has low resistance index, from the active chronic phase, which has high resistance index.[5–8] The appropriate adjustment of the equipment should prioritize the search for low velocity flow, with reduced wall filter, reduced frequency of pulse repetition (around 800 Hz) and color gain at high levels. Care should be taken not to excessively compress the transducer against the epidermal surface, whose small vessels can collapse, temporarily interrupting flow.[41]

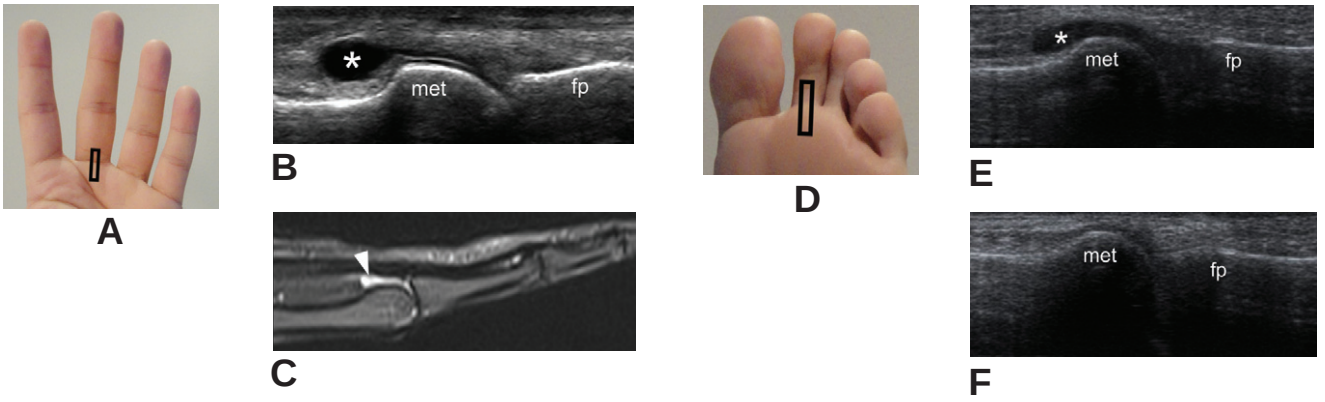

Figure 3
Differentiation between joint effusion and synovitis. **(A)** Positioning of the transducer. **(B)** Corresponding image demonstrating the head of the metacarpal bone (met), base of the proximal phalanx (fp) and distension of the articular capsule by anechoic fluid (*). **(C)** Magnetic resonance imaging, sagittal plane, STIR-weighted image, confirming joint effusion (arrow head). **(D)** Positioning of the transducer. **(E)** Corresponding image at the level of the metatarsophalangeal joint, demonstrating the head of the metatarsal bone (met), base of the proximal phalanx (fp) and distension of the articular capsule by hypoechoic material (*), compatible with grade 2 synovitis or effusion. **(F)** Compressive study, showing the wide compressibility of the finding (arrow head), because of its fluid content, indicating effusion rather than synovial proliferation.

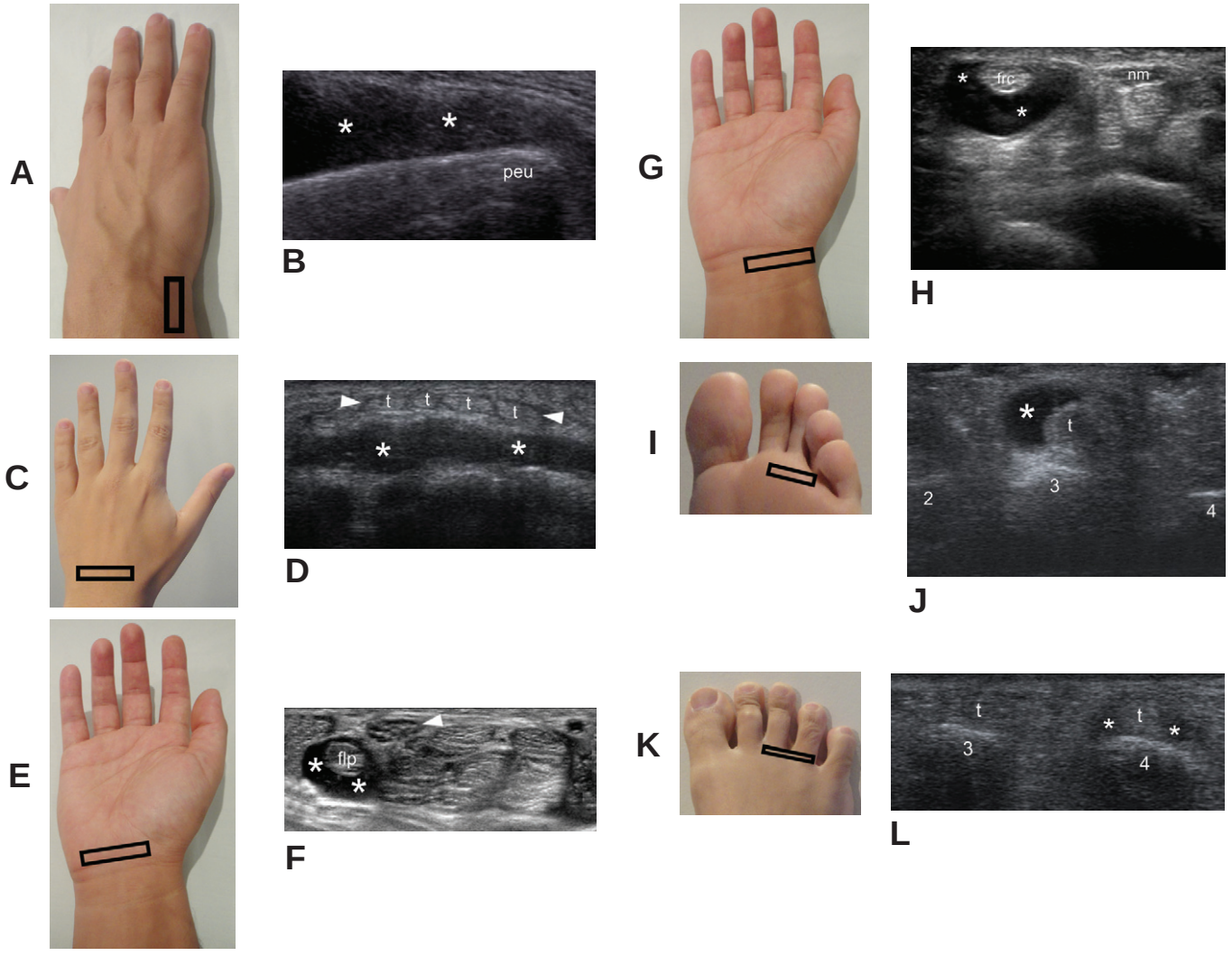

Figure 4
Ultrasonographic manifestations of rheumatoid arthritis. **(A)** Positioning of the transducer. **(B)** Corresponding image revealing extensive proliferative synovitis (*) contiguous with the ulnar styloid process (peu). The deep face of the ligaments that unite the carpal bones is lined by synovial cells, and, in non-sealed sites, the inflammatory process extends to adjacent soft tissues. **(C)** Positioning of the transducer. **(D)** Corresponding image demonstrating the exuberant intercarpal proliferative synovitis (*), which dorsally displaces the tendons (t) of the forth extensor compartment (arrow head). An important differential diagnosis of that image pattern is the short extensor of the fingers muscle, a variant of the normality that can be present in the region and whose echogenicity is similar to that of synovitis. In the differentiating process, the examiner should note that the muscle, unlike synovitis, tends to affect the areas between the tendons of the fourth compartment and not only the tendons' deeper areas. In addition, the dynamic examination during extension of the fingers contracts the muscle mass and tends to increase its cross-sectional area, which does not occur with synovitis. **(E)** Positioning of the transducer. **(F)** Corresponding image demonstrating fluid distension of the radial sheath (*) due to exudative synovitis of the long flexor of the thumb (flp). Note the swollen median nerve (arrow head), due to secondary carpal tunnel syndrome. **(G)** Positioning of the transducer. **(H)** Corresponding image showing excessive fluid (*) surrounding the carpal radial flexor tendon (frc), due to synovitis. Note the median nerve (nm) on the same imaging plane. **(I)** Positioning of the transducer. **(J)** Corresponding image demonstrating fluid distension of the sheath (*) of the flexors (t) of the third finger (3). **(K)** Positioning of the transducer. **(L)** Corresponding image demonstrating fluid distension of the sheath (*) of the extensors (t) of the fourth finger (4).

on routine clinical practice being based on fragile scientific evidence. Ultrasonographic contrast media have also been tested in the search for a better differentiation between active and inactive synovitis, but their use is equally experimental and should not be incorporated to routine clinical practice, at least for now.[19]

ULTRASONOGRAPHY FOR ASSESSING BONE EROSION

Bone erosion results from the colagenase produced on the interface between synovium, bone and joint cartilage, typically observed in the periphery of the joint space, where bone is not covered by cartilage.[20] Erosions develop predominantly during the first two years of disease (in aggressive disease, in the first 6 months)[21] and have a marked predilection for the ulnar styloid process, capitate bone, pyramidal bones, semilunar bones, and radial face of the second and third metacarpophalangeal joints, most notably in the head of metacarpal bones[22] (Figure 2 C and D). Because of the ease of access, the search for erosions in the margins of the metacarpophalangeal and metatarsophalangeal joints of the first and fifth fingers is probably more accurate than the study of the other toes and fingers, which do not allow satisfactory medial and lateral access. It is worth noting that, when assessing the dorsal face of the head of metacarpal and metatarsal bones, a small anatomic bone indentation usually present in those regions should not be considered an erosion[23] (Figure 5).

Semiquantitative scores for different degrees of erosion have already been published aiming at treatment monitoring,[24–27] but they still require more comprehensive studies, confirming their accuracy and reproducibility. In accordance with the literature, we observed that the clinical remission of RA under treatment is usually accompanied by an improvement in synovitis, but not in the erosions already formed.

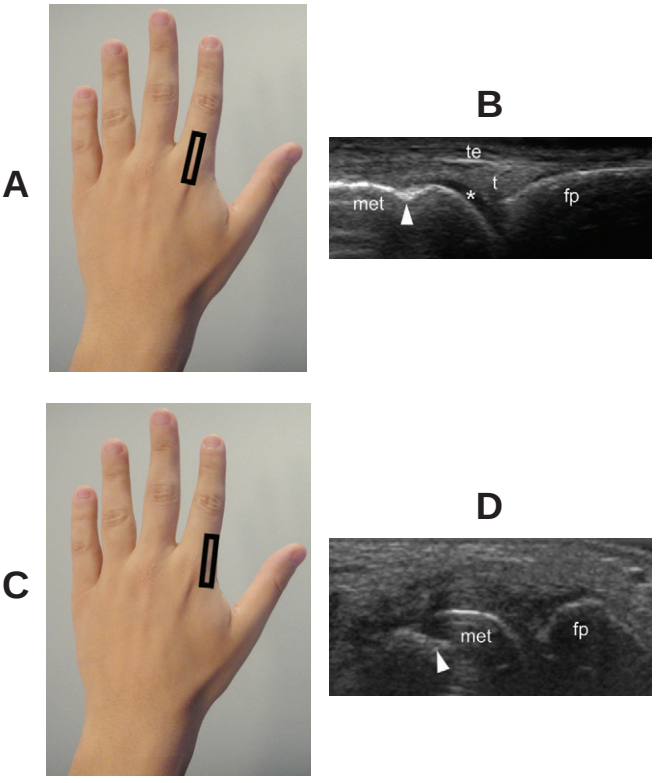

Figure 5
Anatomical trap. **(A)** Positioning of the transducer. **(B)** Corresponding image showing the head of the metacarpal bone (met), the base of the proximal phalanx (fp), joint cartilage (*), the extensor tendon (te) and the dorsal triangular structure (t), and a small anatomical indentation in the head of the metacarpal bone (arrow head), which should not be mistaken for erosion. **(C)** Positioning of the transducer. **(D)** Corresponding image showing the head of the metacarpal bone (met), the base of the proximal phalanx (fp) and bone erosion (arrow head), the latter on a typical location. Note the position of the transducer and the magnitude of the bone anatomical indentation, shallower and more centrally located than erosion.

ULTRASONOGRAPHY FOR THE DIFFERENTIAL DIAGNOSIS OF RHEUMATOID ARTHRITIS

The ultrasonographic documentation of synovitis or bone erosion does not exclusively indicate the diagnosis of RA in its early phase. In fact, spontaneous resolution is observed in half of the cases of synovitis with less than 6 months of evolution.[28,29] In the other half, the course tends to be of a chronic and persistent disease. Some patients with chronic and persistent disease develop full criteria for RA, while others remain with the diagnosis of undifferentiated arthritis. In screening incipient RA, it is worth noting that it should be differentiated from undifferentiated arthritis and other inflammatory polyarthralgias in their initial phase, mainly psoriatic arthritis and systemic lupus erythematosus, whose findings might be similar with identical distribution.[23,30–32] When present, both subcutaneous edema[33–35] and bone erosion in the margins of the distal interphalangeal joint[36,37] suggest psoriatic arthritis as the initial hypothesis. The lack of such findings, however, does not contribute to the differential diagnosis. Based on clinical and serological characteristics, it is currently possible to predict with good accuracy which patients with undifferentiated arthritis will progress to RA, a

task much better performed by the attending physician than by the ultrasonographist.[38]

CONCLUSION

Ultrasonography has recently gained prestige as an adjuvant method for the diagnosis and therapeutic follow-up of RA, although radiography remains the imaging modality traditionally and widely used for those purposes. The great advantage of the ultrasonographic study, which has motivated enthusiastic research in the area, resides in its capacity to detect synovitis and bone erosion at a pre-radiographic phase. That generates information that can be used for diagnostic or therapeutic purposes, with a potential impact on the patients' quality of life.

sugerem artrite psoriásica como hipótese inicial. A ausência desses achados, no entanto, não contribui para o diagnóstico diferencial. Com base em características clínicas e sorológicas, é atualmente possível prognosticar com boa acurácia quais pacientes com artrite indiferenciada progredirão para AR, em uma tarefa mais bem executada pelo médico assistente do que pelo ultrassonografista.[38]

CONCLUSÃO

A ultrassonografia ultimamente vem ganhando prestígio como método adjuvante no diagnóstico e acompanhamento terapêutico da AR, embora a radiografia ainda seja a modalidade de imagem tradicionalmente utilizada em larga escala com esses propósitos. O grande trunfo do estudo ultrassonográfico, que vem motivando pesquisas entusiastas na área, reside em sua capacidade de detectar sinovite e erosão óssea em fase pré-radiográfica, gerando informação que pode ser utilizada com intuito diagnóstico ou terapêutico, de potencial impacto na melhora da qualidade de vida dos pacientes.

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