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7

Role of ultrasound imaging in individuals at risk of RA

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A B S T R A C T

Early diagnosis and treatment improves outcomes for patients with rheumatoid arthritis (RA). Studies have shown that musculoskeletal ultrasound is more sensitive than clinical examination in identifying synovitis. This review aims to address the role of ultrasound in identifying (1) patients with early inflammatory arthritis (IA) at risk of progression to RA and (2) those without clinical synovitis at risk of progression to early IA and therefore early RA.

Introduction

Early diagnosis and early treatment with disease-modifying antirheumatic drugs of rheumatoid arthritis (RA) reduces inflammation, thereby limiting disease progression, joint damage and loss of function [1–3]. Early effective treatment has also been associated with the ability to achieve remission and the possibility of treatment reduction without flaring [4]. Increasing emphasis has therefore been placed on the identification of patients with RA in the earliest stages [5].

The 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria, which have superseded the 1987 ACR RA criteria [6], were developed to enable

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early classification of patients with RA [7]. Work has also been done to classify individuals in the phases before the development of clinical inflammatory arthritis (IA) aiming to identify patients at the very earliest stages of the disease [8]. Known risk factors for the development of RA include certain genetic profiles (e.g. the presence of HLA-DR shared epitope), environmental factors (e.g. smoking) and autoantibodies (e.g. rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA)). Studies have shown that autoantibodies including RF and ACPA may be present several years before clinically apparent disease [9].

In clinical practice, the presence of joint swelling, together with raised inflammatory markers and the presence of RA autoantibodies or bone erosions on X-ray, is helpful to diagnose RA. In the very early stages of the disease, however, patients may present with nonspecific musculoskeletal (MSK) symptoms without clinical synovitis, and inflammatory markers and X-rays may be normal [10,11]. This has important implications for early diagnosis.

Studies have shown that ultrasound is more sensitive than clinical examination for identifying minimal synovitis [12,13]. By using greyscale (GS) images, even minimal synovial thickening and joint effusion can be clearly delineated, and the use of Doppler mode, in particular power Doppler (PD), enables the identification of synovial tissue hyperaemia [14]. Ultrasound is also more sensitive than X-ray in detecting RA joint erosions as the cortical bone profile, when accessible, is magnified [15]. The greater sensitivity relates to its ability to detect smaller erosions and the multi-planar capability of ultrasound (compared to the two-dimensional image with X-ray). Ultrasound can also differentiate between joint synovitis and other causes of clinical swelling, such as bursitis and tenosynovitis [16], and is therefore a useful imaging modality to assist in the diagnosis of patients with joint inflammation [17].

This review addresses the role of ultrasound in individuals with early IA at risk of progression to RA and those with MSK symptoms without synovitis at risk of progression to early IA (and early RA).

Ultrasound in individuals with early inflammatory arthritis

The role of ultrasound in determining disease persistence and progression to RA in patients presenting with early IA has been evaluated in a number of published studies (Table 1) [18–26].

Ozgul et al. addressed the role of GS ultrasound compared to bone scintigraphy and clinical evaluation alone in 51 patients with early IA who did not fulfil the 1987 ACR RA criteria [18]. After 2 years, 64.7% (n = 33) developed RA. Those with GS changes fulfilled the criteria for RA at an earlier stage than those without. Wrist involvement was documented in the majority of patients who developed RA (right wrist 90.9%; left wrist 81.8%). Findings on bone scintigraphy, however, did not correlate with progression to RA.

In a prospective study of 149 patients with recent-onset UA, Salaffi et al. investigated the role of PD ultrasound to predict the development of RA [20]. A prediction rule was developed using a combination of clinical parameters, serological biomarkers and PD of the wrists, metacarpophalangeal joints (MCPs), and metatarsophalangeal joints (MTPs). After 12 months, 41.6% (n = 62) patients developed RA according to the 1987 ACR criteria [7]. The presence of PD in 2–3 joints or >3 joints increased the odds of progression to RA to 17.55 (95% CI 4.71 to 65.50) and 48.71 (95% CI 8.74 to 271.72), respectively. The prediction rule had a high discriminative ability for the development of RA (area under the curve (AUC) 0.92, 95% CI 0.86 to 0.95, $p < 0.001$).

GS ultrasound and PD assessments of 38 joints was evaluated by Filer et al. in 58 patients with clinically apparent synovitis in at least one joint with less than 3 months of symptoms duration [21]. Ultrasound findings were compared to the Leiden rule for the prediction of RA [27]. After 18 months, 50% (n = 29) patients developed RA (1987 ACR criteria), 22.4% (n = 13) developed non-RA persistent disease and 27.6% (n = 16) resolved. Both GS and PD findings predicted the development of RA. PD counts in particular were found to be superior to global ultrasound scores when combined with clinical features and serology from the Leiden rule (AUC 0.96 vs 0.91) [27].

Ultrasound of the wrists and hands has also been shown to be of value in assisting the diagnosis of RA according to the 2010 ACR/EULAR criteria in a cohort of 69 patients with early IA [22]. After a follow-up period of at least 6 months, 53.6% (n = 37) were diagnosed with RA. Kawashiri et al. found moderate to high PD signal in particular, which was useful for early RA recognition (sensitivity 81.1%, specificity

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