Application of Ultrasound in Assessment of Biologics Efficacy in Patients with Rheumatoid Arthritis

CME Credits

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Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease, which is characterized by synovitis and extra-articular inflammation, leading to joint destruction and deformity and increased morbidity and mortality. The prevalence of RA is estimated to be 1% globally, 0.53%–0.55% in the United States in 2014 and is more prevalent in middle-aged female and elderly patients.[1] The diagnosis of RA is based on the 1987 American College of Rheumatology (ACR) revised classification criteria or the ACR/EULAR 2010 RA classification criteria,[2] which focused on specific clinical manifestations, immunological tests for rheumatoid factor and anti-cyclic citrullinated peptide antibodies, and inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein. However, with the widespread application of ultrasound in RA recently, it has become a helpful tool for facilitating early diagnosis of RA. The ultrasound features of RA include synovial hypertrophy associated with increased Doppler signals, cortical bone erosion, extensor carpi ulnaris tenosynovitis, and posterior tibialis tenosynovitis among affected joints.[3] Recently, our ultrasound research team developed a 40-joint ultrasound program (proximal interphalangeal joints, metacarpophalangeal [MCP] joints, wrists, elbows, shoulders, knees, ankles, and metatarsophalangeal joints), to enhance the early detection and early intervention for RA and to promote long-term remission of RA.[4]

The mainstream treatments of RA include disease-modifying anti-rheumatic drugs (DMARDs). For those difficult-to-treat or DMARDs refractory RA patients, biologic agents such as anti-tumor necrosis factor-α (e.g., etanercept, adalimumab, golimumab, and certolizumab), anti-interleukin-6 (e.g., tocilizumab), anti-CD80/CD86 (e.g., abatacept), and JAK inhibitor (e.g., tofacitinib, baricitinib, and upadacitinib) should be considered. For the evaluation of biologics treatment response, the 28-joint disease activity score (DAS28)-ESR is commonly used for clinical assessment. The DAS28-ESR assesses the tender joint count of 28 joints (TJC, 0–28), the swollen joint count of 28 joints (SJC, 0–28), ESR (mm/h), and the patient global health (GH, 0–100 mm) and is calculated by the following formula: DAS28-ESR = 0.56 $\sqrt{}$(TJC) +0.28 $\sqrt{}$(SJC) + 0.70 Ln (ESR) + 0.014 (GH). A DAS28-ESR score <2.6 indicates clinical remission. Nevertheless, there are numerous potential confounders that influence DAS28-ESR scores, raising doubts about the use of this indicator. A tool to replace clinical assessment is therefore essential. Recent studies demonstrated that ultrasound detected more patients with RA relapse than did clinical assessment in terms of RA disease activities and treatments response of biologics.[5]

According to the policy of Taiwan's National Health Insurance Administration, clinically remitted RA patients after biologics should receive biologic dose reduction due to the concern of increased risk of serious infection and the enormous cost of long-term use.[6] Nonetheless, there are some RA patients who remain clinical remission after biologics dose reduction but not in image remission.[7] These groups of patients may not achieve true remission of RA and there is a clear need to titrate up the dose of biologics or modify medications. We had performed an ultrasound study at baseline before biologic dose reduction and at week 24 after dose reduction. We graded synovitis using the Outcome Measurement in Rheumatology Clinical Trials criteria and scored synovitis by grayscale (GS, scores 0–3, included both synovial hypertrophy and effusion) and power Doppler (PD, scores 0–3) status.[8] Total score (from 0 to 24) was the sum of the scores of eight joints (bilateral

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Received: 02-07-2021 **Accepted:** 06-08-2021 **Available Online:** 06-01-2022

Access this article online

Quick Response Code:

Website: www.jmuonline.org

DOI: 10.4103/JMU.JMU_147_21

How to cite this article: Chen YJ, Lai KL. Application of ultrasound in assessment of biologics efficacy in patients with rheumatoid arthritis. J Med Ultrasound 2022;30:79-80.

MCP2, MCP3, wrists, and elbows). Clinical relapse was defined as an increase in DAS28 of o1.2. GS ultrasound relapse was defined as an increase in total GS score of o2, and PD ultrasound relapse was defined as an increase in total PD score of o1 [Figure 1]. At week 24, the relapse rates of clinical, GS ultrasound, and PD ultrasound were 15.8%, 31.6%, and 63.2%, respectively [Figure 1].[9]

Based on the findings from previous studies and our results, it is feasible to use ultrasound to determine the treatment response of biologics in patients with RA and to facilitate the detection of occult inflammation after biologic dose reduction. Therefore, we can adjust the dose of biologics in RA patients who are clinically remitted but not image remitted to avoid joint deformity and future disability.

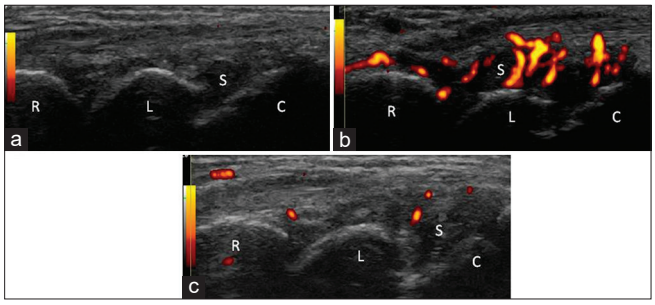

Figure 1: Serial ultrasound assessments of right wrist in a 37-year-old female patient with RA (long-axis dorsal view). (a) At month 12 of full-dose biologics treatment: No PD flow. (b) At week 24 after biologics dose reduction: Synovial PD flows significantly increased. (c) 20 weeks later after titrating back to full dose of biologics: Synovial PD flows decreased. S: Hypertrophied synovium, R: Radius, L: Lunate bone, C: Capitate bone, PD: Power Doppler. RA: Rheumatoid arthritis

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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