Utility in Clinical Trials of Magnetic Resonance Imaging for Psoriatic Arthritis: A Report from the GRAPPA 2014 Annual Meeting

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ABSTRACT. Psoriatic arthritis (PsA) is a heterogeneous disease that involves both peripheral and axial joints and entheses. Magnetic resonance imaging (MRI) allows visualization of the inflammatory components (synovitis, tenosynovitis, enthesitis, periarticular inflammation, and bone marrow edema) as well as structural damage (bone erosion, bone proliferation) in PsA. However, MRI has not been validated as an outcome measure in PsA clinical trials to the same extent as in rheumatoid arthritis. Recently, further validation of the Outcome Measures in Rheumatology (OMERACT) PsA MRI score (PsAMRIS) was presented at the 2014 annual meeting of the Group for Research and Assessment of Psoriatic Arthritis (GRAPPA). In this review, we present the current knowledge within MRI assessment of PsA, particularly peripheral manifestations, as well as different imaging methods and scoring systems, and we discuss future research perspectives. (J Rheumatol 2015;42:1044–7; doi:10.3899/jrheum.150130)

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Psoriatic arthritis (PsA) is a heterogeneous disease that affects axial and peripheral joints and entheses in various patterns throughout the body. The treatment options in PsA have recently improved markedly, making placebo-controlled studies increasingly unethical and emphasizing the need for sensitive outcome measures to accurately assess and compare different treatment strategies.

Magnetic resonance imaging (MRI) can visualize the inflammatory components (synovitis, tenosynovitis, enthesitis, periarticular inflammation, and bone marrow edema) as well as structural damage (bone erosion and bone proliferation) in PsA (Figure 1). Unfortunately, despite the potential of MRI for diagnosing, monitoring, and prognosticating axial and peripheral PsA, MRI in PsA has received much less research scrutiny than MRI in rheumatoid arthritis (RA), ankylosing spondylitis, and axial spondyloarthritis. In this review, we describe our current knowledge and future perspectives on the use of MRI in PsA clinical trials, with a focus on the peripheral disease manifestations.

Methods for MRI Assessment of PsA in Clinical Trials

PsA disease manifestations may be assessed by qualitative, semiquantitative, or quantitative methods. There is no consensus on which joints to assess, and while it should probably be individualized based on the pattern of involvement, most studies have assessed the wrist and fingers[1,2,3,4,5,6].

The international MRI in arthritis group of OMERACT (Outcome Measures in Rheumatology)[7] has recommended that T1-weighted MRI before and after intravenous contrast be acquired to visualize synovitis, tenosynovitis, and periarticular inflammation. These images also should be obtained in coronal and axial planes to visualize erosions. In addition, short-tau inversion recovery or T2-weighted, fat-suppressed images are required to visualize bone marrow edema. To confirm inflammatory changes (synovitis, tenosynovitis, and periarticular inflammation), it is suggested that the sequence be obtained in 2 planes (optimally, axial and sagittal)[7].

Qualitative Methods

Most studies report only qualitative MRI assessments, i.e., presence versus absence of the different pathologies of PsA[8]. The simplicity of this approach may favor implementation in clinical practice, particularly for diagnostic purposes, but the lack of detail, and ensuing lack of sensitivity to change, limits its use in clinical trials when only a few joints are examined by conventional MRI. In contrast, if many joints were assessed, as by whole-body MRI counts of inflamed joints, qualitative assessment of each joint may be sufficient. Whole-body MRI is a new technique that allows imaging of the entire body in 1 examination and has been introduced as a potential method for simultaneous assessment of peripheral and axial joints and entheses[9,10,11]. The method still needs improved image quality and more validation, and it is not yet ready for clinical use; however, it seems extremely promising particularly in PsA, owing to the diverse manifestations of the disease.

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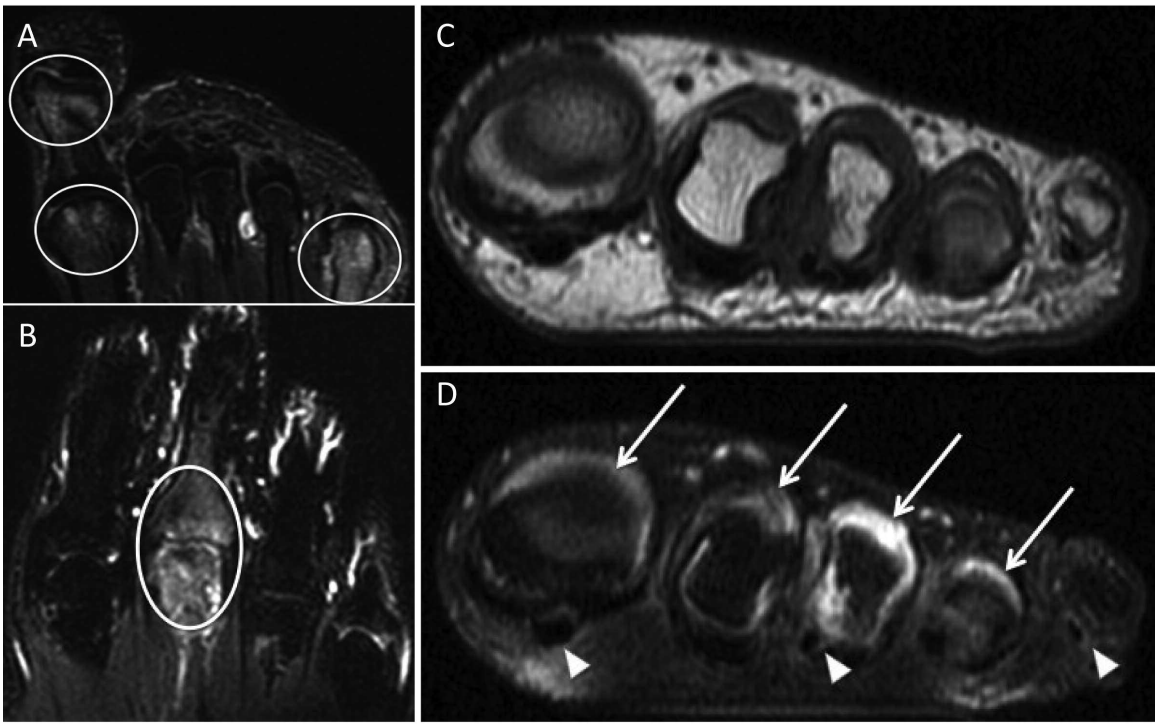

Figure 1. Panels A and B are coronal short-tau inversion recovery images of the foot (A) and hand (B), showing bone marrow edema in the first and fifth metatarsophalangeal (MTP) and first interphalangeal joint of the foot (A) and the third metacarpophalangeal joint of the hand (B). Panels C and D are axial T1-weighted precontrast and fat-suppressed postcontrast sequences of the MTP joints of the foot. The fat-suppressed postcontrast image (D) shows synovitis (arrows) in the first to fourth MTP joints and mild flexor tenosynovitis (arrowheads) at the first, third, and fifth MTP joint.

Quantitative Methods

Quantitative assessment of contrast enhancement by dynamic contrast-enhanced MRI has been reported[1,2,3,4,5,12,13], and allows the assessor to estimate the rate of enhancement on several consecutive fast MRI obtained at the time of contrast injection, using computer software. However, the data from this method are still limited, and its advantage in clinical trials has not yet been documented.

Semiquantitative Methods

Several semiquantitative scoring systems for synovitis, bone marrow edema, and/or erosions have been described[7,14,15], but most of these have been used in only a few patients. In a study of 11 patients with PsA treated with the anti-tumor necrosis factor (TNF) agent adalimumab for 24 weeks, MRI of a wrist or knee showed significant improvements from baseline at 24 weeks in both clinical measures of disease activity and in MRI bone marrow edema and effusion, but not in synovitis[14]. Therapy-induced decreases in dactylitis (clinical and MRI assessments) have also been observed[16].

The OMERACT PsAMRIS

The OMERACT-based international MRI in inflammatory arthritis group has developed the Psoriatic Arthritis Magnetic Resonance Image Score (PsAMRIS) for evaluation of inflammatory and destructive changes in PsA hands[7,17,18]. This is the most validated assessment system available; it has good documented intrareader and interreader reliability for status scores of all variables. For inflammatory variables, the intrareader and interreader reliability was high for change scores and the sensitivity to change was moderate. The damage variables, bone erosion and bone proliferation, showed very limited change after 1 year of TNF-inhibitor therapy[17].

In a recent 48-week followup study of 41 patients with PsA initiating adalimumab therapy, MRI were acquired of the metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joints of the hand most clinically involved at baseline, and scored according to the PsAMRIS. In patients fulfilling the modified PsA Response Criteria at followup, a statistically significant improvement was seen for all inflammatory variables except periarticular inflammation. Bone damage showed very little change over time[3].

In a placebo-controlled trial, 22 patients with PsA were randomized to receive zoledronic acid, or placebo. Bone edema scored according to PsAMRIS decreased significantly in the zoledronic acid group, but not in the placebo group. No differences in MRI bone proliferation or bone erosion progression could be identified[19].

In another randomized controlled PsA trial[20], MRI

synovitis, bone edema, and bone erosion scored according to the OMERACT RAMRIS (the RA equivalent of PsAMRIS, using similar definitions of pathologies)[21] were exploratory endpoints in a comparison of abatacept (ABA) and placebo. Synovitis and bone edema decreased in the ABA-treated patients whereas it increased slightly in the placebo group[20]. Although PsAMRIS was not used in the latter study, the studies suggested that the OMERACT scoring systems could be useful as sensitive and discriminative outcome measures in PsA clinical trials.

Recent Validation of the OMERACT PsAMRIS in a Randomized Placebo-controlled Trial

A recent posthoc analysis of the above ABA clinical trial[20] was presented at the OMERACT meeting in May 2014 and at the GRAPPA meeting in July 2014. Three readers from the OMERACT MRI in arthritis group applied the PsAMRIS to MRI from 40 patients (20 of the foot and 20 of the hand) initiating either ABA or placebo. In the ABA group, a statistically significant improvement in synovitis score was seen in the metatarsophalangeal joint of the foot and for the summed synovitis score of the hands and feet at 6 months followup. All remaining inflammatory variables in the ABA group, but not the placebo group, showed a numerical but statistically non-significant improvement in score. The bone damage variables showed no change over 6 months. Intrareader and interreader intraclass correlation coefficients were generally high for all or some readers, especially for the inflammatory variables. The responsiveness of the PsAMRIS was excellent for tenosynovitis (hand), synovitis (foot), and periarticular inflammation (hand and foot).

Further validation of the PsAMRIS in other MRI datasets from longitudinal randomized controlled trials would be highly relevant.

Research Agenda and Future Perspectives

The PsAMRIS, a scoring system of inflammation and damage in different joint structures in the hands and feet of patients with PsA, is now validated and ready for use, allowing the use of MRI as an outcome measure in clinical trials and longitudinal cohorts. Clarification of its performance, including discriminative power, in different PsA populations is a high research priority. Further, research is warranted in determining the optimal joint areas to be included, and in optimizing MRI acquisition techniques. Dynamic MRI are recommended in future longitudinal studies of PsA to obtain more data and clarify its future role. The same is true for other semiautomated quantitative methods[22,23] that could potentially be applied in PsA. Development and validation of methods for assessment of cartilage damage/joint space narrowing in the PsAMRIS method, as was recently done in the RA equivalent RAMRIS[24], should also be considered.

Currently, the varying pattern of involvement of axial and peripheral joints and entheses challenges the use of MRI in PsA clinical trials. Whole-body MRI may overcome this limitation. Therefore, the method seems extremely promising in PsA, and technical and methodological development and validation of different whole-body MRI assessment methods are highly relevant.

The OMERACT PsAMRIS is currently the method of choice for MRI assessment of patients with PsA in clinical trials. Several aspects require clarification before the full potential of the PsAMRIS in future trials of different PsA populations is determined. Newer methods of MRI outcome measures, particularly whole-body MRI, seem promising, but need further development and validation.

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