Usefulness of Magnetic Resonance Imaging of the Hand versus Anticyclic Citrullinated Peptide Antibody Testing to Confirm the Diagnosis of Clinically Suspected Early Rheumatoid Arthritis in the Absence of Rheumatoid Factor and Radiographic Erosions

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Objective: The diagnosis of rheumatoid arthritis (RA) is sometimes difficult to establish early in the disease process, particularly in the absence of its classic hallmarks. Our aim was to compare the practical usefulness of magnetic resonance imaging (MRI) of the hand versus anticyclic citrullinated peptide (anti-CCP) antibody testing to confirm the diagnosis of clinically suspected RA in the absence of rheumatoid factor (RF) and radiographic erosions.

Methods: We prospectively included patients with early inflammatory arthritis and strong clinical suspicion of RA, in whom initial complementary tests (RF and radiographs of hands, wrists, and feet) did not provide unequivocal confirmation of the diagnosis. In all patients, anti-CCP antibodies were assessed and contrast-enhanced MRI of the most affected hand was performed according to a specifically designed protocol. The MRI criterion for the diagnosis of RA was either the presence of synovitis with bone erosions or bone marrow edema, which is currently considered to be a forerunner of erosions.

Results: In the 40 patients (28 women), the mean age at diagnosis was 54 ± 6 years and the median duration of symptoms was 4 ± 2.6 months (range 1.5 to 12). Final diagnoses at 1-year follow-up were RA in 31 patients, undifferentiated arthritis in 7 (5 self-limiting), and psoriatic arthropathy (PsA) and antisynthetase syndrome in 1 patient each. Anti-CCP antibodies were positive only in 7 patients, all of whom were finally diagnosed with RA. The prevalence of anti-CCP positivity in our series of seronegative RA patients was thus 23% (7/31); in these patients the anti-CCP antibodies had a specificity of 100% (95% CI: 71.7 to 100) and sensitivity of 23% (95% CI: 9.6 to 41.1). Use of the MRI criterion led to the correct diagnosis in 100% of patients with RA and to false-positive results (1 with PsA and 1 with antisynthetase syndrome). The MRI criterion had a specificity of 78% (95% CI: 40.0 to 97.2) and sensitivity of 100% (95% CI: 90.8 to 100) for identification of seronegative RA.

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Conclusion: Although the tests are not mutually exclusive, in our experience MRI is more helpful than anti-CCP antibody determination in confirming the diagnosis of clinically suspected early RA in patients in whom the diagnosis cannot be confirmed using conventional methods.
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Abbreviations	
anti-CCP	Anticyclic citrullinated peptide antibodies
BME	Bone marrow edema
DMARD	Disease-modifying antirheumatic drugs
MRI	Magnetic resonance imaging
MCP	Metacarpophalangeal
NSAID	Nonsteroidal anti-inflammatory drugs
RA	Rheumatoid arthritis
RF	Rheumatoid factor
PIP	Proximal interphalangeal
PsA	Psoriatic arthropathy
US	Ultrasonography

Prompt diagnosis and appropriate therapy have been recognized as essential factors to improve clinical outcomes in early rheumatoid arthritis (RA). To prevent irreversible damage to joints, the diagnosis must be confirmed or ruled out within a few months of the onset of synovitis (1,2). However, the diagnosis of RA is difficult early in the disease process, as no specific tests are available. There is no single clinical manifestation, laboratory test, or imaging study result that allows a diagnosis of RA to made with certainty. As with other autoimmune rheumatic diseases, the diagnosis depends on the aggregation of characteristic symptoms, signs, laboratory data, and radiologic findings. The modified classification criteria of the American College of Rheumatology (ACR) are often used to diagnose RA, although they were developed for the classification of patients with RA for the purpose of epidemiologic studies and clinical trials, not primarily for clinical diagnosis (3). These criteria are primarily used for patients with established disease. They may not be satisfied early in the course of disease in patients who subsequently develop typical RA (4). For example, in the Norfolk Arthritis Register (NOAR)—a primary-care-based cohort of patients with recent-onset inflammatory polyarthritis of more than 4 weeks' duration—only 38% of patients satisfied the criteria when first seen, but this figure rose to 66% when applied cumulatively over 5 years (5). In practice, in the early months of RA, patients usually present with symmetrical peripheral polyarthritis and early morning stiffness rather than nodules, erosions, and rheumatoid factor (RF). Radiographs are not helpful in most cases for establishing early diagnosis, as fewer than 20 to 25% of patients have erosions initially; up to 30% of patients test negative for RF in serum, and other pathognomonic features such as rheumatoid nodules usually appear late in the disease process (1,2,6).

In the absence of the classic hallmarks of the disease, the use of other laboratory tests that could be an alternative to RF, such as anticyclic citrullinated peptide (anti-CCP) antibody testing, and the use of other, more sensitive imaging techniques for identifying bone erosions, such as magnetic resonance imaging (MRI) and ultrasonography (US), seem to be helpful for addressing this diagnostic problem. Anti-CCP antibodies have attracted attention as a useful marker for the diagnosis of RA, having high specificity. Several studies have shown that the sensitivity of anti-CCP antibodies is close to that of RF, but their specificity is higher, in the range of 90 to 96% (6-14). Anti-CCP antibodies can be detected very early in RA as well as during the preclinical phase in some patients and may be used as an indicator for the progression and prognosis of RA (6-14). Accordingly, anti-CCP antibody determination has been proposed as a clinically useful tool for distinguishing RA from other rheumatic diseases (7,8). MRI and US have demonstrated greater sensitivity for the detection of synovitis and erosions than clinical examination and conventional radiography (15). MRI also allows the detection of bone marrow edema (BME), which is closely related to the degree of synovitis and predicts subsequent radiographic erosion progression (16-23). BME may be found alone or surrounding bone erosions and is currently considered to be a "forerunner" of erosions (22,23). The use of MRI or US to estimate of the amount of synovial tissue or to detect erosions that cannot be appreciated on plain radiography is not yet a widely accepted surrogate marker of disease activity, nor do these techniques have an established role in the evaluation of patients with polyarthritis. However, if available and affordable, these studies may be considered as alternatives to plain film radiographs in selected clinical situations, including patients with early, unclassified arthritis, to assist in the differential diagnostic process (15).

We compared the practical usefulness of MRI of the hand versus anti-CCP antibody testing to confirm the diagnosis in a cohort of patients with early inflammatory arthritis and strong clinical suspicion of RA, in the absence of RF and radiographic erosions. We chose the hand because its joints are generally the earliest and most often affected area in patients with RA.