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REVIEWED
By Chris Tighe at 1:36 pm, Nov 02, 2018

Test ID: CCP
Cyclic Citrullinated Peptide Antibodies, IgG, Serum

Useful For

Evaluating patients suspected of having rheumatoid arthritis (RA)

Differentiating RA from other connective tissue diseases that may present with arthritis

Testing Algorithm

See Connective Tissue Disease Cascade (CTDC) in Special Instructions.

Clinical Information

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic joint inflammation that ultimately leads to joint destruction. RA affects approximately 1% of the world's population. The diagnosis of RA is established primarily on clinical criteria and serologic findings. Historically, rheumatoid factor (RF), which is an antibody specific for the Fc portion of human IgG, has been considered a marker for RA. RF is, in fact, one of the diagnostic criteria for RA that was established by the American College of Rheumatology.(1) Although 50% to 90% of patients with RA are RF-positive, the specificity of the RF test is known to be relatively poor. RF is found in many patients with other autoimmune diseases, infectious diseases and some healthy individuals. Consequently, a search for better diagnostic markers, with improved specificity for RA, ensued. Antiperinuclear factor (APF) and antikeratin antibodies (AKA), identified by immunofluorescence, were found to have a specificity of close to 90% for RA, but testing for these autoantibodies has never become popular. It was subsequently determined that APF and AKA react with the same antigen, specifically a citrullinated form of filaggrin (citrulline is an unusual amino acid formed by posttranslational modification of arginine residues by the enzyme peptidyl arginine deaminase).(2) Recombinant filaggrin fragments, after enzymatic deamination in vitro, react with autoantibodies in RA sera. Synthetic cyclic citrullinated peptide (CCP) variants also react with anti-filaggrin autoantibodies and serve as the substrate for detecting anti-CCP antibodies serologically. Most studies of anti-CCP antibodies demonstrated that these autoantibodies have much improved specificity for RA compared to RF.(3)

See Connective Tissue Diseases Cascade (CTDC) in Special Instructions.

Reference Values

<20.0 U (negative)

20.0-39.9 U (weak positive)

40.0-59.9 U (positive)

> or =60.0 U (strong positive)

Reference values apply to all ages.

Interpretation

A positive result for cyclic citrullinated peptide (CCP) antibodies indicates a high likelihood of rheumatoid arthritis (RA).

A Mayo prospective clinical evaluation of the CCP antibody test showed a diagnostic sensitivity for RA of 78% with fewer than 5% false positive

results in healthy controls (see Cautions). CCP antibodies have also been reported in approximately 40% of seronegative RA patients, and, like rheumatoid factor (RF), a positive CCP antibody result indicates an increased likelihood of erosive disease in patients with RA.

High levels of CCP antibodies may be useful to identify patients with aggressive disease, but further studies are needed to document this association. The level of CCP antibodies may also correlate with disease activity in RA, but further studies are needed to document this clinical application.

Cautions

Positive results for cyclic citrullinated peptide (CCP) antibodies may occur in some patients with systemic lupus erythematosus or other autoimmune, connective tissue diseases. In the Mayo study mentioned above, the false-positive rate in this subgroup was approximately 10%.

Antirheumatic therapy should not be initiated based solely on a positive test for CCP antibodies, and changes in treatment should not be based upon the levels of CCP antibodies.

Clinical Reference

1. Banal F, Dougados M, Combescure C, Gossec L: Sensitivity and specificity of the American College of Rheumatology 1987 criteria for the diagnosis of rheumatoid arthritis according to disease duration: a systemic literature review and meta-analysis. Ann Rheum Dis 2009 July;68:1184-1191

2. Schellekens GA, Visser H, De Jong BA, et al: The diagnostic properties of rheumatoid arthritis antibodies recognizing a cyclic citrullinated peptide. Arthritis Rheum 2000 Jan;43(1):155-163

3. Visser H, le Cessie S, Vos, K, et al: How to diagnose rheumatoid arthritis early: a prediction model for persistent (erosive) arthritis. Arthritis Rheum 2002 Feb;46(2):357-365

Special Instructions

- **Connective Tissue Disease Cascade (CTDC)**