

Anti-CCP: a truly helpful rheumatoid arthritis test?

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Clinical question

For adult rheumatoid arthritis (RA), what is the diagnostic usefulness of anticyclic citrullinated protein antibodies (anti-CCP)?

Bottom line

With a specificity of about 96% and a positive likelihood ratio of about 14, anti-CCP assists with the diagnosis of RA. It is present in only a quarter to half of patients before or at diagnosis, so a negative result does not rule out RA. It can also predict aggressive joint erosion.

Evidence

- In 7 systematic reviews¹⁻⁷ of anti-CCP in adult RA, with 27 to 151 observational studies, pooled results revealed the following:
 - Sensitivity and specificity^{2-4,7} were 53% to 71% and 95% to 96%, respectively.
 - Positive likelihood ratios were 12.5 to 15.9 and negative likelihood ratios were 0.36 to 0.42.^{3,4}
 - Focusing on higher-level studies with undifferentiated arthritis, the sensitivity was generally lower (about 54%) but the specificity was similar.⁴
- A positive anti-CCP result means RA is likely but a negative result does not rule out RA.
- Concerns include the following (although study quality did not seem to affect findings⁷):
 - Few studies were well designed, ie, had cohorts of patients with early stage, undifferentiated RA with long-term follow-up by blinded study personnel.⁴
 - There was heterogeneity in control populations,⁴ study designs,⁴ test cutoffs,^{2,6} and laboratory standards.^{2,6}

Context

- A positive anti-CCP result also predicts joint erosion in RA (odds ratio 4.4; 95% CI 3.6 to 5.3).⁸
- Anti-CCP is present in 23% of patients with early stage RA, in about 50% of patients at diagnosis, and in about 53% to 70% of patients 2 years after diagnosis.²
- Anti-CCP occurs in 1.5% or less of healthy populations and in 10% or less of those with other rheumatic disease, except palindromic rheumatism, in which the occurrence is similar to RA.² Values might be higher in those with erosive joint disease.⁹
- Rheumatoid factor has a similar sensitivity but worse specificity.³ Specificities of anti-CCP and rheumatoid factor are 95% and 85%, respectively.
 - Positive likelihood ratios are 12.5 and 4.9, respectively.
 - A positive anti-CCP result is more reliable than a positive rheumatoid factor result for diagnosing RA.

- Diagnostic criteria for RA include joint involvement, acute-phase reactants, and the serology markers anti-CCP and rheumatoid factor.¹⁰

Implementation

Some clinical features might be particularly helpful when considering RA. First, confirm a history of joint pain with morning stiffness of longer than 1 hour that improves with activity. Second, demonstrate joint tenderness at the metacarpophalangeal joints on hyperextension or stressing the wrists at full flexion or by squeezing the forefoot. Try it on yourself to see how hard to press—it should not hurt! If these maneuvers are painful, the patient could have RA. Check for anti-CCP—a positive anti-CCP result makes RA very likely but a negative result is of little help. Handouts for newly diagnosed patients are available.¹¹ 🌿

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Competing interests

Dr Shojania has consulted for and has stock options with Augurex.

The opinions expressed in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

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