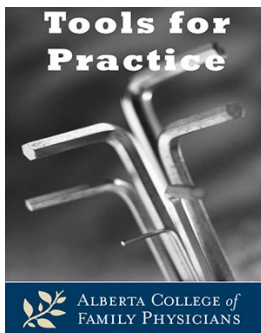


Tools for Practice is proudly sponsored by the Alberta College of Family Physicians (ACFP). ACFP is a provincial, professional voluntary organization, representing more than 4,000 family physicians, family medicine residents and medical students in Alberta. Established over fifty years ago, the ACFP strives for excellence in family practice through advocacy, continuing medical education and primary care research. www.acfp.ca

Love Tools for Practice? Wish there was a conference just like them? There is! For more information, visit [the Conference webpage](#). Registration is available now!

September 14, 2015



Anti-CCP: A truly helpful Rheumatoid Arthritis lab test?

Clinical Question: For Adult Rheumatoid Arthritis (RA), what is the diagnostic utility of Anti-Cyclic Citrullinated Protein antibodies (Anti-CCP)?

Bottom-line: Anti-CCP, with ~96% specificity and ~14 positive likelihood ratio, is good for assisting with the diagnosis of RA. Anti-CCP is present in only ¼ to ½ of patients before or at diagnosis, so a negative test does NOT rule out RA. It can also predict more aggressive joint erosion.

Evidence:

- Seven systematic reviews¹⁻⁷ of Anti-CCP in adult RA, with 27-151 observational studies. Pooled results:
 - Sensitivity and specificity^{2-4,7} were 53%-71% and 95-96%, respectively.
 - Likelihood ratios:^{3,4} Positive likelihood ratio 12.5-15.9 and negative 0.36-0.42.
 - Focusing on higher-level studies (diagnostic cohort) with an undifferentiated arthritis presentation: sensitivity generally lower (~54%) but specificity similar.⁴
- Interpretation: Positive Anti-CCP means RA likely but a negative does NOT rule out RA.
- Concerns (although study quality did not seem to impact findings⁷):
 - Minority of studies well-designed: Cohorts of early, undifferentiated patients with prolonged follow-up by blinded study personnel.⁴
 - Significant heterogeneity: Different control population,⁴ study designs,⁴ test cut-offs,^{2,6} and laboratory standardizations.^{2,6}

Context:

- Positive Anti-CCP also predicts joint erosion in RA, Odds Ratio 4.4 (95% Confidence Interval 3.6-5.3).⁸
- How common is Anti-CCP:
 - In RA patients?²
 - 23% early in symptoms.

- ~50% at diagnosis.
- ~53-70% at two years after diagnosis.
- Other populations?²
 - ≤1.5% in healthy populations.
 - ≤10% in other rheumatic disease (from lupus to psoriatic arthritis), except palindromic which is similar to RA.
 - Perhaps higher in some if erosive joint disease present.⁹
- Rheumatoid Factor has a similar sensitivity but worse specificity.³
 - Specificity: Anti-CCP=95% and Rheumatoid Factor=85%.
 - Positive likelihood ratios are 12.5 versus 4.9, respectively.
 - Interpretation: Positive Anti-CCP > positive Rheumatoid Factor for making an RA diagnosis.
- In Juvenile RA, Anti-CCP has a similar specificity (99%) but considerably worse sensitivity (10%): Anti-CCP is commonly negative, which does not rule out RA.¹⁰
- RA diagnostic criteria: As well as joint involvement and acute phase reactants (ESR or C-Reactive Protein), Anti-CCP and Rheumatoid Factor are RA serology markers.¹¹
 - Note: Anti-CCP is sometimes called ACPA (Anti-Citrullinated Protein Antibody).

Authors:

Emélie Braschi PhD MD, G Michael Allan MD CCFP

Disclosure:

Authors do not have any conflicts to disclose

References:

1. Riedemann JP, Muñoz S, Kavanaugh A. Clin Exp Rheumatol. 2005; 23(5 Suppl 39):S69-76.
2. Avouac J, Gossec L, Dougados M. Ann Rheum Dis. 2006; 65:845-51.
3. Nishimura K, Sugiyama D, Kogata Y, *et al.* Ann Intern Med. 2007; 146:797-808.
4. Whiting PF, Smidt N, Sterne JA, *et al.* Ann Intern Med. 2010; 152:456-64; W155-66.
5. Schoels M, Bombardier C, Aletaha D. J Rheumatol Suppl. 2011; 87:20-5.
6. Taylor P, Gartemann J, Hsieh J, *et al.* Autoimmune Dis. 2011;2011:815038.
7. Zintzaras E, Papathanasiou AA, Ziogas DC, *et al.* BMC Musculoskelet Disord. 2012; 13:113.
8. Jilani AA, Mackworth-Young CG. Int J Rheumatol. 2015; 2015:728610.
9. Budhram A, Chu R, Rusta-Sallehy S, *et al.* Lupus. 2014; 23(11):1156-63.
10. Wang Y, Pei F, Wang X, *et al.* J Immunol Res. 2015; 2015:915276.
11. Aletaha D, Neogi T, Silman AJ, *et al.* Arthritis Rheum. 2010; 62:2569-81.

Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practicing family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity.

The ACFP has supported the publishing and distribution of the Tools for Practice library since 2009. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at <http://bit.ly/signupfortfp>. Archived articles are available at no extra cost on the [ACFP website](#).

You can now earn credits on Tools for Practice! In August 2014, the ACFP launched [GoMainpro, an online accreditation tool](#) to help facilitate MAINPRO® accreditation for the ACFP's Tools for Practice library which has been accredited for Mainpro-M1 credits by the College of Family Physicians of Canada (CFPC). The combination of the CFPC's Direct Entry Program and GoMainpro's tracking and reporting features provide an easy and convenient way to earn Mainpro-M1 credits.

This communication reflects the opinion of the authors and does not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.