

# The clinical utility of anti-CCP antibodies in rheumatoid arthritis and psoriatic arthritis

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The most common chronic arthritis in rheumatology is rheumatoid arthritis (RA), which can affect between 0.5%-1% of the population (1). In addition to causing years of pain and disability, it also decreases life expectancy by an average of about a decade (2). The last 2 decades have witnessed early and intensive use of potent disease-modifying anti-rheumatic drugs, such as methotrexate and tumor necrosis factor inhibitors, leading to revolutionary changes in the disease outcome, such as reductions in the risk for serious joint damage and disability and probable increases in life expectancy.

It has now become clear that in order to be able to prevent disease progression and joint destruction, RA needs to be diagnosed early, which needs diagnostic markers that can reliably predict disease development and progression. However, early diagnosis of RA still remains difficult. There is no doubt that most attractive diagnostic markers for autoimmune diseases are autoantibodies. In this regard, rheumatoid factor (RF), an autoantibody directed against the Fc part of IgG, is a very important serological marker for the diagnosis of RA, which has been in use in everyday practice for years. However, RF is taken as a nonspecific marker of RA and may also be present in patients suffering from other diseases and even in healthy (especially elderly) persons. Therefore, during the last decade, much focus has been directed on the detection of autoantibodies with high specificity early in the rheumatic disease process and throughout the course of RA. Identification of citrullinated residues-epitopes recognized previously by the highly specific anti-perinuclear factor and anti-keratin antibody tests-resulted in the development of anti-CCP (cyclic citrullinated peptide) assays. Anti-cyclic citrullinated peptides are directed to antigens that contain arginyl converted to citrullyl residues by peptidylarginyl deiminase enzymes (3). Since the 1987 criteria for RA were not helpful in achieving the goal of early and effective intervention, new ACR/EULAR criteria for RA were developed in 2010 (4). The new criteria include anti-CCP testing, while its weight is similar to rheumatoid factor (RF).

In this issue of *European Journal of Rheumatology*, Eker et al. (5) present their work, aimed at identifying the role of anti-cyclic citrullinated peptide (anti-CCP) antibodies in angiogenesis among patients with RA and psoriatic arthritis (PsA) from Turkey.

Although the study hypothesized the contribution of anti-CCP antibodies to the pathogenesis of RA by means of angiogenesis, the results of this study did not show such a relationship, at least in the study population tested. Instead of discussing possible reasons behind this negative finding, I find it more constructive to discuss the practical issues that this study tells us.

It is known that the specificity and sensitivity of anti-CCP antibody for RA diagnosis may depend on the patient's race and ethnicity. Several studies conducted in various ethnic groups have examined the sensitivity and specificity of the anti-CCP test, while data regarding the diagnostic accuracy of these antibodies in Turkish patients with RA and PsA are rather scarce (6, 7).

The findings in the paper by Eker and colleagues yielded comparable results with regard to sensitivity (69%) of the anti-CCP test when matched with previous studies conducted in Turkey and in the other ethnic groups. There has been substantial discrepancy among the prevalence of anti-CCP antibody positivity in RF-negative RA patients reported in previous studies. This figure of the test is important, as it tells us the percentage of patients who can not be diagnosed if only the RF test is requested. There are reports showing the prevalence as low as 8% to as high as 60% in various RA cohorts (7). In the present study, Eker and colleagues found a rather low prevalence of anti-CCP test positivity (22%) in their study population of RF-negative RA patients. This finding is in line with previous studies conducted in Turkey, which reported a 20% prevalence of anti-CCP in their group of RF-negative RA patients (6, 7).



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The reported specificity for the anti-CCP test in the present study was 87.2%, which is a bit lower compared with previous studies (8). The reason for the lower specificity found in this study would be inclusion of patients with PsA as a control group (together with healthy controls), instead of constructing a more heterogeneous control group, with the inclusion of other forms of arthritis. Indeed, the percentage of anti-CCP-positive patients found in the present study is the highest in the literature (20.5%). Although concomitant RA was a concern in some cases, several authors suggested that in PsA, anti-CCP positivity might be related to polyarthritis and/or development of erosions. The finding of elevated VEGF levels in anti-CCP-positive PsA patients in the present study might also support this proposal.

Apart from the practical issues (usefulness of anti-CCP test), there are also some interesting points in the study of Eker and colleagues that await to be investigated in further studies, such as increased VEGF levels in the subgroup of PsA patients with positive anti-CCP, as well

as decreased frequency of diabetes mellitus in anti-CCP-positive RA patients.

The overall evidence obtained by the present study suggests that anti-CCP antibody is a significant serologic marker for RA in the Turkish population. With acceptable specificity (87%) and moderate sensitivity (69%), anti-CCP antibody tests play an important role in confirming the diagnosis of RA in a Turkish population.

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