Diagnostic Accuracies of Anti-cyclic Citrullinated Peptide Antibody and Rheumatoid Factor in Korean Patients with Rheumatoid Arthritis: A Meta-analysis

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= Abstract =

한국인 류마티스관절염 환자에서 항CCP항체와 류마티스인자의 진단정확성에 대한 메타분석연구

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목적: 한국인 류마티스관절염 환자에서 항CCP항체와 류마티스인자의 민감도와 특이도, 진단정확성에 대해 연구하였다.

방법: 문헌검색은 Medline과 Koreamed, 대한류마티스학회지를 이용하였고 논문들의 참고문헌도 조사하였다. Random-effects 모델을 이용하여 메타분석을 시행하였으며 항CCP항체와 류마티스인자의 민감도, 특이도, positive와 negative likelihood ratios (PLR, NLR), diagnostic odds ratio (DOR)와 summary receiver-operating characteristic curve (SROC 커브)를 구하였다.

결과: 항CCP항체와 류마티스인자의 민감도와 특이도를 연구한 7개의 논문의 류마티스관절염 환자 1,041명과 대조군 970명이 메타분석에 포함되었다. 항CCP항체의 민감도와 특이도, PLR, NLR, DOR은 76.7% (95% confidence interval [CI] 74.0∼79.2), 95.1% (93.8∼96.3), 14.837 (11.567∼19.031), 0.244 (0.202∼0.294)과 59.235 (43.806∼80.097)이었고 류마티스인자의 수치는 78.2% (0.756∼0.807), 80.5% (78.1∼82.6), 3.687 (3.027∼4.492), 0.298 (0.218∼0.406)과 12.915 (8.427∼19.771)이었다. 항CCP항체의 area under the curve (AUC)와 Q* index는 0.9453과 0.8842이었고 류마티스인자
Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic inflammation of the synovial joints that leads to disability and loss of quality of life (1). The early diagnosis of RA is important, because joint damage can be prevented and prognosis can be improved by early treatment (2). Currently, RA is diagnosed using the classification criteria of the American College of Rheumatology (ACR) (3), but these criteria are unsuitable for the early diagnosis of RA (4).

Rheumatoid factor (RF) is an antibody directed against the Fc portion of IgG, which has been used as a diagnostic marker for RA. Although RF is the only serological test in the ACR criteria, it is nonspecific and may be present in healthy individuals or in those with other autoimmune diseases (5). The most specific RA autoantibody system known is directed against citrullinated antigens (6). However, several new antibodies have been studied in RA, such as, the antibodies of filaggrin, keratin, and fibrin, but not all have been successfully incorporated into routine clinical practice despite their high specificities, because their detections are technically demanding (7). The epitopes of their antigens are arginyl residues citrullinated by peptidyl arginine deiminase (8). To improve RA diagnostic sensitivity, assays based on cyclic citrullinated peptide (CCP) were developed to detect anti-CCP antibody, which appears to be useful for diagnosing RA (9). Although previous meta-analyses have shown that anti-CCP antibody has similar sensitivity to and higher specificity than RF for diagnosing RA (10,11), it remains unclear if the diagnostic values of these antibodies are dependent on ethnicity.

To assess the diagnostic accuracies of anti-CCP antibody and RF for the diagnosis of RA in a Korean population, we performed this meta-analysis using published data, on the sensitivities and specificities of anti-CCP antibody and RF for the diagnosis of RA in Koreans.

MATERIALS AND METHODS

1. Identification of eligible studies and data extraction

We performed an exhaustive search for studies that examined anti-CCP antibody, RF, or both for the diagnosis of RA in Koreans. This analysis concerned Korean patients with RA, control populations of healthy subjects, and patients with other rheumatic diseases. We searched Medline and Koreamed and the Journal of Korean Rheumatism Association to identify suitable articles in which anti-CCP antibody and/or RF were determined in Korean RA patients and controls. Furthermore, all cited references in these studies were reviewed to identify additional works not indexed by electronic databases. The following key words and subject terms were searched: ‘anti-cyclic citrullinated peptide’, ‘CCP’, ‘rheumatoid factor’, ‘RF’, ‘rheumatoid arthritis’, ‘RA’, ‘Korea’, and ‘Korean’. We included studies that provided sufficient data to allow sensitivity and specificity for a diagnosis of RA to be calculated.