INPLASY PROTOCOL

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None declared.

Diagnostic value of anti-cyclic citrullinated peptide antibody combined with rheumatoid factor in rheumatoid arthritis in Asia: a meta-analysis

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Review question / Objective: **The objective of this meta-analysis is to explore the diagnostic value of combined detection of anti-cyclic citrullinated peptide antibody (anti-CCP) and rheumatoid factor (RF) for rheumatoid arthritis (RA) by a method of meta-analysis in the Asian population.**
Condition being studied: **Previous clinical diagnostic criteria for RA are mainly based on clinical manifestations (symptoms and signs), rheumatoid factor (RF) detection and imaging (X-ray) examination. In the early stage of RA, drug treatment for RA patients can effectively control the disease and alleviate the progression of the disease. In recent years, the detection of autoantibodies has provided an important basis for early diagnosis of disease and evaluation of disease activity. The significant autoantibodies include RF, anti-cyclic citrullinated peptide (anti-CCP), anti-Sa antibody, anti-keratin (AKA), anti-perinuclear factor (APF), anti-filaggrin antibody (AFA), anti-RA33/36, anti-RA54 antibody and anti-P68 antibody. At present, many scholars have conducted a lot of research to find indicators with high specificity and sensitivity for the diagnosis of RA, and index of disease activity.In order to objectively evaluate the clinical applicability of the combined detection of RF and anti-CCP in the diagnosis of RA, a meta-analysis is adopted in this study to systematically evaluate the published trials of the combined detection of RF and anti-CCP in the Asian population, thereby providing theoretical and clinical basis for the diagnosis of RA.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 August 2021 and was last updated on 27 August 2021 (registration number INPLASY202180106).

INTRODUCTION

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rheumatoid arthritis (RA) by a method of meta-analysis in the Asian population.

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METHODS

Search strategy: Two investigators independently collected relevant literature from Excerpta Medica Database (Embase), Medline, Cochrane Library, Chinese Science and Technology Periodicals Database, China National Knowledge Infrastructure (CNKI), China Wanfang Database, from January 1, 2000 to February 1, 2021, to evaluate the diagnostic value of RF and CCP antibody combined tests for RA in Asia. The retrieval strategies were as follows: ("anti-cyclic citrullinated peptide antibody" OR "anti-CCP") AND ("rheumatoid factor" OR "RF") AND ("rheumatoid arthritis" OR "RA"). Languages were not restricted.

Participant or population: Rheumatoid arthritis in Asia.

Intervention: Anti-cyclic citrullinated peptide antibody combined with rheumatoid factor.

Comparator: Non-rheumatoid arthritis in Asia.

Study designs to be included: Diagnostic test.

Eligibility criteria: (1) Study on the diagnosis of RA by combined detection of RF and CCP antibody; (2) The research paper contained the sensitivity and specificity of the combined detection of RF and CCP antibodies to RA, or provided the information that could calculate sensitivity and specificity. (3) The subjects were the Asian population.

Information sources: Relevant literature from Excerpta Medica Database (Embase), Medline, Cochrane Library, Chinese Science and Technology Periodicals Database, China National Knowledge Infrastructure (CNKI), China Wanfang Database.

Main outcome(s): A total of 24 published papers were included, of which 21 were combined in series and 8 were combined in parallel. The results of this meta-analysis showed that in the combination of tandem, the pooled sensitivity=0.64 (95%CI: 0.58~0.70), specificity=0.97 (95%CI: 0.95~0.98), +LR=19.70 (95%CI: 12.74~30.46), -LR=0.37 (95%CI: 0.31~0.43), DOR=53.43 (95%CI: 34.46~82.40), the area under the summary receiver operating characteristic (SROC) curve was 0.89; in parallel combination, pooled sensitivity=0.87 (95%CI: 0.80~0.92), pooled specificity= 0.76 (95%CI: 0.67~0.84), +LR=3.68 (95%CI: 2.62~5.17), -LR= 0.17 (95%CI: 0.11~0.26), DOR=21.56 (95%CI: 11.63~39.99), the area under the SROC curve was 0.89.

Quality assessment / Risk of bias analysis: The Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) was used to

assess the quality of all included studies. The checklist contained 11 standards, each of which is evaluated as "yes", "no", and "unclear". "Yes" was to satisfy this criterion; "No" meant not satisfied or not mentioned; "Unclear" was defined as partial satisfaction or insufficient information from the literature.

Strategy of data synthesis: Using Stata 15.0 statistical software, meta-analysis of diagnostic test accuracy was carried out. The pooled sensitivity, specificity, positive likelihood ratio (+LR), negative likelihood ratio (-LR) and diagnostic odds ratio (DOR) were calculated using a bivariate mixed model. The area under the curve (AUC) was calculated by using the summary receiver operating characteristic (SROC) curve, to analyze the diagnostic performance of the combined detection of RF and anti-CCP for RA. AUC was in the range of 0.5 to 0.7, indicating that the diagnostic value was low; AUC in the range of 0.7 to 0.9 indicated that the diagnostic value was moderate; AUC greater than 0.9 indicated that the diagnostic value was high. The overall sensitivity and specificity of the selected studies were summarized through a bivariate mixed model. Deeks' funnel plot was used to assess publication bias.

Subgroup analysis: Meta-regression and subgroup analysis were performed to explore the source of heterogeneity.

Sensitivity analysis: sensitivity analysis was conducted to verify the robustness of the conclusion.

Language: Languages were not restricted.

Country(ies) involved: China.

Keywords: Cycliccitrullinated peptide; Diagnosis; Meta-analysis; Rheumatoid arthritis.

Contributions of each author:
Author 1 - Xiaochun Yang.
Author 2 - Yue Cai.
Author 3 - Bin Xue.
Author 4 - Bo Zhang.

XY designed the study, conducted the analysis, drafted the manuscript. YC participated in the study design, and critically reviewed the manuscript. BX participated in the study design, participated in the analysis, and critically reviewed the manuscript. XY, YC, BX and BZ contributed to patient recruitment, critically reviewed the manuscript.