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Rheumatoid Factors and Antibodies to Citrullinated Proteins in the Laboratory Diagnosis of Rheumatoid Arthritis

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Abstract: This study investigated the clinical significance of IgM and IgA rheumatoid factors (RF) and antibodies to citrullinated proteins (CCP, MCV, AKA) in rheumatoid arthritis (RA). 993 RA patients were compared to 616 controls. MCV showed the highest diagnostic sensitivity (83%), while CCP demonstrated the highest specificity (87%). CCP had the highest positive likelihood ratio (5.5). IgA RF and MCV exhibited the largest area under the curve (0.9) in ROC analysis. IgM RF levels correlated with joint damage and systemic manifestations, while CCP concentration correlated with disease activity. CCP and MCV demonstrated the best diagnostic efficacy for RA, with autoantibody levels correlating with disease severity and activity.

Keywords: Rheumatoid arthritis, Rheumatoid factor, Anti-citrullinated protein antibodies, Diagnostic sensitivity, Diagnostic specificity, Modified citrullinated vimentin, Cyclic citrullinated peptide, Biomarkers

Introduction/Purpose. The determination of rheumatoid factors (RF) and antibodies to citrullinated proteins (ACP) is crucial for diagnosing rheumatoid arthritis (RA) and differentiating it from other rheumatic diseases (RD). The aim of this study was to investigate the clinical significance of IgM and IgA rheumatoid factors (RF) and antibodies to citrullinated proteins: cyclic citrullinated peptide (CCP), modified citrullinated vimentin (MCV), and anti-keratin antibodies (AKA) in RA.

Materials and Methods. Participants: 993 patients with RA, with a median disease duration of 96 months (25th-75th percentile range: 36-192 months); 757 women and 239 men, age 51 years (25th-75th percentile range: 42-57 years); DAS28 score of 5.2 (25th-75th percentile range: 3.8-6.0).Comparison Group: 616 individuals, including 397 patients with various rheumatic diseases (RD) and 297 healthy donors, matched for sex and age with the RA patients.Testing Methods: IgM RF was measured using nephelometry, IgA RF and ACP were measured using enzyme-linked immunosorbent assay (ELISA) and indirect immunofluorescence (for AKA).

Results/Discussion. Diagnostic Sensitivity and Specificity:The highest diagnostic sensitivity was observed for MCV (83%).The highest diagnostic specificity was observed for CCP (87%).Likelihood Ratios:The highest positive likelihood ratio was for CCP (5.5).The lowest negative likelihood ratios were for IgA RF and MCV (0.2).Area Under the Curve (AUC; ROC Analysis):The largest AUC for RA was demonstrated by IgA RF and MCV (0.9).Correlations:The level of IgM RF correlated with the Sharp/van der Hejde joint damage index (r=0.3) and systemic manifestations (r=0.2).The concentration of CCP correlated with the disease activity score (DAS28) (r=0.2).

Conclusion. CCP and MCV show the best diagnostic efficacy for RA. The levels of autoantibodies (IgM RF, CCP) correlate with the extent of joint damage, systemic manifestations, and disease activity.