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THU0071

THE COMBINATION OF RHEUMATOID FACTORS WITH ANTIBODY SYSTEMS TARGETING CITRULLINATED, CARBAMYLATED AND PEPTIDYL ARGININE DEIMINASE AUTOANTIGENS DISTINGUISHES RHEUMATOID ARTHRITIS

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Background: Novel antibody systems including anti-Carbamylated Protein Antibody (anti-CarP IgG) and anti-Peptidyl Arginine Deiminase Antibody (anti-PAD4 IgG) are emerging as independent diagnostic and prognostic biomarkers for Rheumatoid Arthritis (RA) (ref. 1-3). As such, these antibody systems may add value to rheumatoid factor (IgM) and anti-citrullinated peptide antibody (ACPA IgG), the hallmark antibodies in RA.

Objectives: We evaluated the diagnostic performance of Rheumatoid Factor (RF) with antibody systems targeting citrullinated, carbamylated and PAD4 autoantigens in RA.

Methods: The cohort consisted of 638 consenting subjects with RA (fulfilling the 1987 or 2010 ACR classification criteria, mean age: 59.8±0.5 years [SEM], 80% female) and a control group of 775 subjects (mean age: 44.7±0.5 years, 85% females, including Systemic Lupus Erythematosus [n=369], primary Sjogren's Syndrome [n=64], Primary Fibromyalgia [n=85], other connective tissue diseases [n=63], and a group of normal healthy donors [n=194]). Autoantibodies titers from serum were measured using fluoroenzyme immunoassays (anti-RF [IgM] and anti-CCP [IgG]; Phadia Upsala, Sweden), ELISA (anti-CarP [IgG], research use only [RUO], Inova Diagnostics, San Diego) and bead-based AptivaTM technology (anti-PAD4 [IgG], RUO, Inova Diagnostics) in a clinical laboratory accredited by the College of American Pathologists. For each positive antibody (above each cutoff) a score of 1 was assigned and the cumulative presence of the 4 antibodies was determined [range 0-4]. The ability of the biomarkers to distinguish RA from controls was calculated using sensitivity, specificity and interval likelihood ratio (LR). Positive Predictive Value (PPV) was estimated at 10% pre-test probability. Statistics consisted of Mann-Whitney and Chi-square tests.

Results: In this cohort anti-CarP IgG (>20 Units) yielded 33.5% sensitivity and 77.9% specificity. Anti-PAD4 (>1000 Units) yielded 35.0% sensitivity and 95.0% specificity. RF IgM (>5 Units/ml) and anti-CCP (>10 Units/ml) were 67.4% and 66.5% sensitive, respectively (87.5% and 97.0% specific, respectively). RA presented 5-fold higher 4-antibody system scores (2.02 ±0.05) than controls (0.42±0.02); (p<0.01). Scores greater than 2 yielded 42% sensitivity and 98.8% specificity. A total of 82 subjects presented with the full-house 4 antibodies (score = 4) while 81 of them had RA (99.9% specific). Interval LR and PV for each of the 4-antibody score are presented in the Table. There was no difference in the 4-antibody score between RA who fulfilled the 1987 ACR or 2010 ACR criteria (1.99±0.07 vs 2.08±0.09; p=0.40). In the subset of subjects newly diagnosed (less than one year), the average 4-antibody system score for RA (n=33) was 1.72±0.22 (36.3% with score greater than 2) and 0.58±0.12 for other diseases (0% with score greater than 2, 100% specific); (p<0.01).

Conclusion: This cumulative combination of antibody systems targeting citrullinated, carbamylated, PAD4 and Fc autoantigens (RF IgM) is highly specific for RA. It may be useful in diagnosing and classifying RA even in symptomatic patients who present early in the course of disease.

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Table 1: Combination of Rf IgM, anti-CCP (IgG), anti-CarP (IgG) and anti-PAD4 (IgG)

Score	RA (% N)	CTL (% N)	Likelihood Ratio [CI 95%]	Pre-test Probability	Post-test Probability	Change
0	20.5% (131/638)	65.8% (510/775)	0.31 [0.27 to 0.37]	10%	3.4%	-6.6%
1	11.6% (74/638)	27.2% (211/775)	0.43 [0.33 to 0.54]	10%	4.5%	-5.5%
2	25.5% (163/638)	5.8% (45/775)	4.40 [3.22 to 6.02]	10%	32.8%	22.8%
3	29.6% (189/638)	1.0% (8/775)	28.70 [14.26 to 57.77]	10%	76.1%	66.1%
4	12.7% (81/638)	0.1% (1/775)	98.39 [13.73 to 705.04]	10%	91.6%	81.6%

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THU0072

ULTRASOUND PREDICTS IMMINENT PROGRESSION TO ARTHRITIS IN ANTI-CCP POSITIVE AT-RISK INDIVIDUALS

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Background: Ultrasound (US) Power Doppler (PD) signal is predictive for the development of inflammatory arthritis (IA) in anti-cyclic citrullinated protein antibodies positive (CCP+) individuals with musculoskeletal (MSK) symptoms but no clinical synovitis (CS) [1]. Our previous data showed a late increase in the overall US inflammation before arthritis development, suggesting that a sub-clinical phase of synovitis could be detected [2]. This abstract describes the prediction of PD abnormalities in the months following US scan.

Objectives: 1. Presence of PD in one joint is predictive of imminent progression to IA in the next 3 months.

2. A rise in the number of joints with presence of PD increases the odds of progression to IA.

Methods: In a single-centre prospective observational cohort between June 2008 and December 2018, 307 CCP+ patients with a new MSK symptom but no synovitis were followed until CS occurred. Clinical and US findings were analysed. Following our previous study, we compared progression in the 3, 12 or >12 months after a US scan. 38 joints were included in the analysis (MTPs, hands, wrists, elbows, ankles and knees). Patients with palindromic rheumatism were excluded.

Results: Data from 96 CCP+ at-risk patients who developed CS (progressors) are compared to 211 CCP+ patients who did not (non-progressors). Age and gender are similar, the mean follow-up of the non-progressors is higher, with significantly more smokers and high titre CCP in the progressors group (Table1).

Overall, progressors have more joints with PD than non-progressors (Figure1). Patients with PD in one joint are more likely to develop CS in the following 3 months compared to those without PD (OR 7.52) and this remain significant when only the hands and wrists are included