from 2015 to 2017. We fitted linear mixed models for Rheumatoid Arthritis Disease Activity Index (RADAI), Fatigue visual analog scale (VAS), and Pain VAS scores separately without/with adjusting for age, sex, sociodemographic factors, body mass index, RA duration, physical function (Modified Health Assessment Questionnaire [mHAQ]), smoking, depression and other comorbidities at baseline. Models include the outcome at three years (2015-2017) as the dependent variables, an indicator variable representing the year of measurement (2015-17), PA level at baseline, their interactions, and baseline characteristics as covariates. Models include random effects for subjects to account for correlations among within-subject repeated measures. Missing values were imputed using multiple imputation methods. The analyses were conducted using R 3.5.

Results: Of the 169 patients who responded to the 2015 survey, 29.6%, 42.0%, and 28.4% had low, medium, and high levels of PA in 2015, respectively. There were no significant differences in RADAI ($p=0.67$), Fatigue ($p=0.78$), and Pain ($p=0.98$) at baseline (Figure 1). The low PA group experienced significant worsening of disease activity outcomes over time, including yearly increases of 0.31 in RADAI ($p=0.007$), 0.41 in Fatigue ($p=0.007$), and 0.43 in Pain ($p=0.007$). Those in the medium and high PA groups at baseline experienced either a decrease or no change in their disease activity outcomes over time. The interaction terms for PA level and year show that the low PA group had significantly different time trends for RADAI, Fatigue, and Pain compared to the medium and high PA groups (all p values <0.05). The results remain robust after adjusting for age, sex, and other covariates.

Figure 1. Time Trends for Mean RADAI, Fatigue, and Pain by Baseline Physical Activity Level

Table 1. Linear Mixed Model without/with Adjusting for Baseline Characteristics

Model Covariates	RADAI		Fatigue		Pain	
	Coef. [95% CI]	p	Coef. [95% CI]	p	Coef. [95% CI]	p
A. Unadjusted Linear Mixed Model						
Physical Activity (PA)						
Low	ref		ref		ref	
Medium	-0.24 [-0.99, 0.52]	0.542	-0.24 [-1.26, 0.77]	0.638	0.08 [-0.87, 1.04]	0.865
High	-0.39 [-1.22, 0.44]	0.357	-0.33 [-1.44, 0.78]	0.558	-0.13 [-1.17, 0.92]	0.811
Year (Low PA Group)	0.31 [0.07, 0.54]	0.012	0.41 [0.1, 0.72]	0.009	0.43 [0.11, 0.75]	0.009
Physical Activity*Year						
Medium*Year	-0.36 [-0.67, -0.05]	0.025	-0.44 [-0.84, -0.03]	0.036	-0.5 [-0.92, -0.08]	0.021
High*Year	-0.35 [-0.69, -0.01]	0.048	-0.68 [-1.12, -0.24]	0.003	-0.54 [-1.01, -0.08]	0.021
B. Adjusted Linear Mixed Model						
Physical Activity (PA)						
Low	ref		ref		ref	
Medium	0.54 [-0.22, 1.29]	0.162	0.25 [-0.55, 1.06]	0.537	0.54 [-0.22, 1.29]	0.162
High	0.94 [0.11, 1.77]	0.027	0.74 [-0.15, 1.63]	0.105	0.94 [0.11, 1.77]	0.027
Year (Low PA Group)	0.44 [0.12, 0.77]	0.007	0.43 [0.12, 0.74]	0.007	0.44 [0.12, 0.77]	0.007
Physical Activity*Year						
Medium*Year	-0.51 [-0.94, -0.08]	0.019	-0.46 [-0.86, -0.05]	0.028	-0.51 [-0.94, -0.08]	0.019
High*Year	-0.56 [-1.03, -0.1]	0.017	-0.7 [-1.14, -0.26]	0.002	-0.56 [-1.03, -0.1]	0.017

* The difference in trends for RA disease activity outcomes between the Medium and Low PA groups.
** The difference in trends for RA disease activity outcomes between High and Low PA groups.

Conclusion: Across RADAI, Fatigue VAS, and Pain VAS scores, RA patients with a low PA level demonstrated a significant increase in disease activity over the span of three years. The trends for both the high and medium PA groups differ significantly from that of the low PA group, showing small, overall decreases in disease activity over time. These results add to the accumulating evidence that physical activity may reduce disease activity and is an essential aspect of RA management.

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SAT0098 ANTIBODIES AGAINST CITRULLINATED ANTIGENS ARE ASSOCIATED WITH TREATMENT RESPONSE IN ACPA-NEGATIVE RHEUMATOID ARTHRITIS PATIENTS

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Background: RA patients who are ACPA-positive (ACPA+) are known to have worse prognosis. Less is known regarding predictors of treatment outcomes in ACPA-negative (ACPA-) patients.

Objectives: We investigated whether autoantibodies captured on a custom array were associated with response to therapy in ACPA- RA patients.

Methods: RA patients were recruited to either the Biologics in RA Genetics and Genomics Study Syndicate (BRAGGSS, starting adalimumab, established disease) or the RA Medication Study (RAMS, starting methotrexate, early disease). Serum samples were collected at pre-treatment and 3/6 months in BRAGGSS/RAMS, respectively. Treatment groups were pooled for analysis. ACPA was measured using a commercially available ELISA (Axis-Shield Diagnostics Ltd, Dundee, UK). Pre-treatment RA and healthy blood donor control (HC) serum samples were incubated on a bead-based assay (Luminex FlexMap 3D) containing 376 human protein antigens associated with autoimmune disease (39 in citrullinated (cit) form) to detect autoantibodies. Median fluorescence intensity (MFI) values were calculated for each autoantibody for RA and HC, then normalised and log2-transformed. The 95th percentile for each autoantibody in HC was used to determine whether an RA sample was positive/negative for that autoantibody. Proteins with $<10\%$ frequency in RA patients were excluded from analysis. Linear regression was used to determine autoantibodies differing in MFI between RA and HC; p-values were adjusted using the Benjamini-Hochberg correction. Significant autoantibodies (adjusted $p<0.05$) were tested for associations with treatment outcomes in RA patients only using: (i) linear regression for improvement in DAS28; (ii) logistic regression for good/poor vs all EULAR response. All regression was adjusted for age, gender, disease duration and baseline DAS28. Subanalysis was carried out in a subset of ACPA+ patients.

Results: 168 patients with RA were included in analysis (mean age 59.6 years, mean disease duration 14.3 years, 126 (75%) female patients, 90 (53.6%) ACPA+ patients). 34 autoantibodies were differentially expressed in RA patients, only one of which (TNF ligand superfamily member 13, TNFSF13) was lower than in HC. 29/34 autoantigens were in cit-form. In multivariate models of all differentially expressed autoantibodies, heterogeneous nuclear ribonucleoprotein A1 (HNRNPA1) was significantly associated with EULAR response (coefficient (coef) 0.7, 95% CI 0.1-1.3), and cit-vimentin (VIM) was significantly associated with poor EULAR response (OR_{adj} 4.2, 95% CI 1.1-18.3) and reduced odds of good EULAR response (OR_{adj} 0.2, 95% CI 0.1-0.8). ACPA remained the best predictor of treatment response. In a subanalysis of the 78 ACPA patients, cit-cleavage and polyadenylation specificity factor subunit 6 (CPSF6) was significantly associated with worse DAS28 (coef (-1.8), 95% CI (-3.6)-(-0.1)). cit-DnaJ homolog subfamily B member 1 (DNAJB1) was significantly associated with DAS28 improvement (coef 2.2, 95% CI 0.6-3.8). No autoantibody was associated with EULAR response.

Conclusion: A subset of ACPA patients have ACPA fine specificities not seen by a commercial assay. Larger ACPA profiling may provide additional information on treatment response. This requires validation with larger sample sizes and replication in an independent cohort.

REFERENCE

[1] Ann Rheum Dis 2013;72:844. 2. Arthritis Res Ther 2016;18:235.

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