Table 1. Demographics and clinical characteristics of the RA cohort. Biomarkers significantly associated with DAS28ESR were determined by Lasso regression. Values listed are per standard deviation of each biomarker.

	Overall (N=373)	Cluster 1 (N=116)	Cluster 2 (N=70)	Cluster 3 (N=14)	Cluster 4 (N=173)
Demographics:					
Age	54.8 ± 3.6	63.6 ± 9.7	50.8 ± 14.9	58.2 ± 15.8	50.3 ± 12.1
Female Sex	318 (85%)	101 (87%)	57 (81%)	11 (78%)	149 (86%)
Race: Hispanic/Latino	181 (49%)	22 (19%)	27 (39%)	5 (36%)	107 (62%)
Asian	123 (33%)	73 (63%)	8 (11%)	6 (43%)	36 (21%)
Black	35 (9%)	12 (10%)	8 (11%)	2 (14%)	13 (8%)
White & Other	34 (9%)	9 (7%)	7 (10%)	1 (7%)	17 (10%)
Clinical Characteristics:					
Rheumatoid Factor	315 (85%)	104 (90%)	56 (80%)	13 (93%)	142 (82%)
ACPA	297 (80%)	98 (85%)	54 (77%)	12 (86%)	133 (77%)
Disease Duration	7.8 ± 7.6	13.7 ± 9.7	5.4 ± 4.6	6.7 ± 5.7	4.9 ± 3.8
csDMARD	344 (92%)	108 (93%)	63 (90%)	13 (93%)	160 (93%)
Biologic DMARD	185 (50%)	45 (39%)	30 (43%)	4 (29%)	106 (61%)
Prednisone Dose	6.7 ± 3.8	6.0 ± 4.0	8.6 ± 4.9	5.8 ± 1.4	6.3 ± 2.8
Body Mass Index	28.2 ± 4.5	26.6 ± 3.8	28.7 ± 3.8	28.0 ± 6.2	29.1 ± 4.7
DAS28ESR	4.2 ± 1.1	4.2 ± 1.0	5.5 ± 0.8	3.9 ± 0.8	3.7 ± 0.9
Lasso Results:					
EGF	-0.16*	-0.41***	--	--	-0.20**
Leptin	0.15**	--	0.21*	--	0.21**
c-reactive protein	0.34**	0.51***	--	--	--
VCAM1	--	--	--	-0.73*	--
YKL40	--	0.26*	--	--	--

-EGF: epidermal growth factor; VCAM1: Vascular cell adhesion protein 1; YKL40: Chitinase-3-like protein 1. *p<0.05, **p<0.01, ***p<0.001

panel was obtained at each visit. The MBDA measures 12 serum biomarkers. Four patient clusters were identified by unsupervised K-prototype clustering after collapsing all observations into a cross sectional dataset. Plots were created to display longitudinal disease activity trajectories for each cluster. Lasso regression was applied to identify biomarkers associated with DAS28ESR.

Results: We identified 4 distinct clusters in our cohort (Table 1) with visually different disease activity trajectories (Fig. 1). Cluster 1 (n=116) was older (63.6±9.7), had the highest proportion of Asian participants (n=73, 63%) with the most study visits and longest disease duration. Cluster 2 (n=70) had the highest mean DAS28ESR (5.5±0.7), and the highest mean dose of prednisone (8.6±4.9mg/day). Cluster 3 had the lowest number of participants (n=14), study visits and lowest biologic use (28.6%). Cluster 4 was the largest cluster (n=173) with the shortest disease duration (4.9±3.8 years) and highest biologic use (61.3%). In the Lasso regressions, leptin was found to have significant positive associations with DAS28ESR in the whole group as well as Clusters 2 and 4. EGF had negative associations with DAS28ESR in the whole group, Cluster 1 and 4. CRP had positive associations with DAS28ESR in the whole group and Cluster 1. YKL40 and VCAM1 were found to have significant associations in Clusters 1 and 3, respectively.

Conclusion: We identified 4 unique clusters of RA patients in a racially and ethnically diverse longitudinal cohort with different disease activity trajectories and biomarkers associated with disease activity. Although additional work is needed to explore longitudinal outcomes in each cluster, the application of machine learning methods may identify unique combinations of patient and disease characteristics influencing RA clinical outcomes.

Figure 1. DAS28ESR trajectory plots with 95% CIs for the whole cohort and by cluster.

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ASSOCIATION OF ANTI-CITRULLINATED PROTEIN ANTIBODIES OF IgA SUBCLASSES WITH SUSTAINED REMISSION AND FLARE IN RHEUMATOID ARTHRITIS

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Background: Understanding key mechanisms of flare development and sustained remission is one of the acute goals in modern rheumatology. Anti-citrullinated protein antibodies (ACPA) are the most abundant and specific autoantibodies in rheumatoid arthritis (RA) patients. However, the impact of ACPA of IgA isotype is poorly defined. IgA ACPA were previously shown to have a higher percentage of IgA2 in comparison to total IgA; and a correlation between IgA2% ACPA with the DAS28 score was observed in a previous study [1]. Of note, IgA1 and IgA2 were shown to exhibit different effector functions, with IgA2 being pro-inflammatory, which might be the background for its role in RA [1].

Objectives: We aimed to investigate, whether IgA ACPA could be used as a predictive factor for flare development in RA; and to look further into the changes in IgA ACPA levels in patients remaining in stable remission versus patients developing flare.

Methods: We analysed serum of 111 patients from a multicentre randomized controlled trial 'RETRO'. The study observational period was 12 months. Patients in the trial had to be in stable remission (DAS28-ESR<2.6) for a minimum of 6 months and were randomized into 3 different treatment arms: continuation of treatment, tapering by 50% or a gradual tapering until discontinuation [2]. IgA ACPA concentrations were measured with an enzyme-linked immunosorbent assay on CCP2-pre-coated plates.

Results: 60% of patients had IgG-ACPA. IgA ACPA levels were higher among the IgG-ACPA-positive patients (median 4.7 versus 2.24 µg/ml, p<0.0001). Baseline IgA1 and 2 ACPA levels were not different between patients who had a flare later on in the study period and those remaining in remission, showing no predictive value for flare development. However, the percentage of IgA2 in ACPA was correlating with the first registered DAS28 after flare (r=0.36, p=0.046). After the 12 months study period, IgA2 ACPA as well as IgA2% ACPA decreased significantly in patients who remained in stable remission by 17.5% (median, p<0.0001) and 13.6% (p=0.0006), respectively. By contrast, there was no significant change in IgA2 ACPA levels over time. Disease management strategies did not seem to influence IgA ACPA levels in a specific way, as baseline levels were similar between patients on biological and conventional DMARDs and changes in levels after 12 months did not depend on the assignment to either of the study arms.

Conclusion: Neither IgA1 nor IgA2 ACPA levels were predictive of flare development or associated with treatment strategies (though rituximab, JAK-inhibitors and abatacept were not amongst treatment options). However, in patients remaining in sustained remission after 1 year a decrease in IgA2 and IgA2% ACPA was observed and IgA2% ACPA was associated with DAS28 score registered after flare. This could be an indication towards ACPA of IgA2 isotype contributing to the severity of flare, alongside other factors, and its reduction being associated with a prolonged state of remission.

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