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SAT0059
PLASMA ADIPONECTIN ASSOCIATES WITH CLINICAL MARKERS OF DISEASE ACTIVITY AND CIRCULATING CHEMOKINES IN SUBJECTS WITH UNTREATED EARLY RHEUMATOID ARTHRITIS

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Background: Adiponectin is an adipokine that circulates in blood in three main forms, low molecular weight trimers, middle molecular weight hexamers, and high molecular weight (HMW) multimers [1]. It is still unclear which form of adiponectin is the predominant one to mediate the protein functions. Total adiponectin levels are elevated in both serum and synovial fluid of patients with rheumatoid arthritis (RA) [2], and total circulating adiponectin levels associate with inflammatory markers in a population at high risk for future RA [3]. However, the association of circulating adiponectin with markers of disease activity in subjects with RA is still matter of debate.

Objectives: The aim of the study was to determine whether total and/or HMW adiponectin levels associate with markers of disease activity and/or plasma chemokine levels in a cohort of subjects with untreated early RA.

Methods: The cohort consisted of 70 untreated subjects with newly diagnosed RA. Clinical disease activity markers, including DAS28, CDAI, CRP and ESR, were assessed and data on patient history were recovered from clinical files. The plasma levels of 15 chemokines were measured with LEG-NDplex™ Human Proinflammatory Chemokine Panel or ELISA, and total and HMW adiponectin plasma levels were determined with ELISA. Multivariate factor analysis was used to examine the association between total and HMW adiponectin plasma levels with clinical disease activity markers and plasma chemokine levels. The multivariate models were used to select potentially associated markers and chemokines, which were then tested with linear regression.

Results: Both total and HMW adiponectin levels were associated with several clinical markers of disease activity (CRP, ESR, DAS28-ESR). Total adiponectin levels were also associated with DAS28-CRP. Furthermore, a positive association was found between total adiponectin levels and the pro-inflammatory chemokines CXCL10, CXCL9, and CCL2, whereas HMW adiponectin levels only associated with CXCL9.

Conclusion: This study shows for the first time that both total and HMW adiponectin levels are associated with several markers of disease activity as well as pro-inflammatory chemokines in a well-characterized cohort of subjects with untreated early RA. Those findings indicate adiponectin as a potential disease marker in subjects with RA.

Table 1. Clinical parameters

Characteristic	no=70
Women, no (%)	47 (69)
Age, yr	55 (42-64)
BMI	25 (23-28)
CRP, mg/L	9 (4-31)
ESR, mm/hour	24 (12-38)
SJC28	9 (5-12)
TJC28	9 (4-13)
DAS28-CRP	5 (4-6)
DAS28-ESR	5 (5-6)
ACPA+, no (%)	57 (81%)
RF+, no (%)	48 (69%)
CDAI	28 (22-38)
Symptom Duration, months	5 (3-8)
Smoking, no (%)	8 (11%)

Data shown as median (interquartile range), unless otherwise noted.
Abbreviations: BMI, Body-mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SJC28, swollen joint counts of 28; TJC28 tender joint counts of 28; DAS28, disease activity score in 28 joints; ACPA, Anti-citrullinated protein antibody; RF, Rheumatoid factor; CDAI, Clinical Disease Activity Index.

Results are adjusted for sex, age and BMI
Figure 1. Linear regression analysis of total and HMW adiponectin with CRPResults are adjusted for sex, age and BMI

Results are adjusted for sex, age and BMI
Figure 2. Linear regression analysis of total and HMW adiponectin with CXCL10Results are adjusted for sex, age and BMI

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SAT0060
OVERLAPPING SJOGREN'S SYNDROME REDUCES THE PROBABILITY OF REACHING TARGET IN RHEUMATOID ARTHRITIS PATIENTS: A PROPENSITY SCORE MATCHED REAL-WORLD COHORT FROM 2009 TO 2019

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Background: Overlapping Sjogren's syndrome (SS) is not uncommon in rheumatoid arthritis (RA), and considered as a probable detrimental factor of RA. But data on the impact of overlapping SS on RA therapeutic response is limited.

Objectives: Our current study aimed to identify the effect in a real-world cohort from 2009 to 2019.

Methods: The medical records of RA patients who attended the outpatient department of our medical center from 2009 to 2019 were reviewed, and the disease activity based on DAS28-ESR, DAS28-CRP, SDAI and CDAI at each follow-up point were collected. To correct confounders which may affect the therapeutic response between those RA patients with SS (RA-SS) and without (RA-noSS), we compared both the propensity score-matched and unmatched cohorts using the Cox proportional hazards model.

Results: Among the 1099 RA patients, 129 (11.7%) overlapped with SS validated by positive anti-SSA or pathological minor salivary gland biopsy (MSGb). After propensity score matching based on their baseline characteristics, 126 of 129 RA-SS and 126 of 970 RA-noSS patients were statistically extracted. Overlapping SS was associated with a 29%, 26%, 18%, 22% lower probability of reaching remission in RA patients based on DAS28-ESR, DAS28-CRP, SDAI, CDAI, respectively, which trend kept true for reaching low disease activity (LDA) either. Although overlapping SS had the most significant impact on ESR (HR 0.69, 95%CI 0.61-0.79), other components assessing RA disease activity were also in jeopardy. When stratified by age, RA duration, RF and ACPA status, baseline DAS28-CRP, the trend remained.

Conclusion: Overlapping SS is associated with a lower probability of reaching target in RA patients, and should be regarded as one of the poor prognostic factors in the management of RA.

Table Hazard Ratios for Reaching Remission/Low disease activity and Individual Components in RA patients Associated with Overlapping SS

	Unmatched cohort (n=1099)	Matched cohort (n=252)	Trimmed cohort (n=242)
Remission Based on Composite Disease Activity Score			
DAS28-ESR	0.68 (0.62, 0.75)	0.71 (0.62, 0.82)	0.74 (0.64, 0.85)
DAS28-CRP	0.80 (0.74, 0.87)	0.74 (0.66, 0.83)	0.74 (0.66, 0.83)
SDAI	0.82 (0.74, 0.91)	0.82 (0.70, 0.94)	0.83 (0.72, 0.97)
CDAI	0.77 (0.70, 0.86)	0.78 (0.67, 0.91)	0.78 (0.67, 0.91)
Boolean	0.83 (0.75, 0.92)	0.80 (0.69, 0.93)	0.82 (0.70, 0.95)
Remission/LDA Based on Composite Disease Activity Score			
DAS28-ESR	0.76 (0.70, 0.82)	0.73 (0.65, 0.82)	0.74 (0.66, 0.83)
DAS28-CRP	0.80 (0.74, 0.86)	0.76 (0.68, 0.84)	0.75 (0.68, 0.84)
SDAI	0.79 (0.73, 0.85)	0.74 (0.66, 0.82)	0.74 (0.66, 0.82)
CDAI	0.78 (0.73, 0.84)	0.74 (0.66, 0.82)	0.74 (0.66, 0.82)
Individual Components of Disease Activity Score			
28SJC≤1	0.83 (0.77, 0.89)	0.77 (0.69, 0.85)	0.76 (0.68, 0.84)
28TJC≤1	0.81 (0.75, 0.87)	0.79 (0.70, 0.88)	0.78 (0.70, 0.88)
PGA≤1	0.81 (0.74, 0.89)	0.82 (0.71, 0.94)	0.82 (0.72, 0.95)
PrGA≤1	0.81 (0.74, 0.88)	0.78 (0.69, 0.88)	0.79 (0.70, 0.89)
ESR≤ULN	0.66 (0.61, 0.73)	0.69 (0.61, 0.79)	0.74 (0.65, 0.84)
CRP≤1mg/dL	0.84 (0.78, 0.90)	0.76 (0.68, 0.84)	0.77 (0.69, 0.85)

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SAT0061 **ROLE OF SHARED EPITOPE IN THE PROGNOSIS OF RHEUMATOID ARTHRITIS IN RELATION TO ACPA POSITIVITY**

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Background: The mechanistic association of HLA-DRB1 alleles that code a "shared epitope" (SE) with rheumatoid arthritis (RA) is not yet clear. Previous data has suggested the carriage of SE is associated with the production of cyclic citrullinated peptide antibodies (anti-CCP)¹ and severe RA²⁻⁴. The interrelationship among SE, anti-citrullinated protein antibody (ACPA) positivity and disease outcomes is not fully understood.

Objectives: To assess the RA prognosis associated with the carriage of SE, in relation to ACPA positivity.

Methods: Pts enrolled in a large RA registry, Brigham and Women's Hospital RA Sequential Study between March 2003 to June 2018, with known SE and ACPA status were included in the analysis. HLA-DRB1 SE status was determined by allele-specific polymerase chain reaction and DNA sequencing for most of the subjects and by GWAS-based imputation for the rest. Disease activity (DA) was measured at baseline (BL) and 1-year follow-up by DAS28(CRP), CDAI and SDAI. Pts were stratified by SE+ (1 or 2 SE alleles) and SE- (0 alleles) and ACPA status. We analyzed the relationship of SE with ACPA positivity and change in DA by a linear regression model separately. A mediation analysis was used to examine the mediating effect of ACPA on association between SE and change in DA.

Results: Out of 926 pts included in the analysis, 65.1% were SE+, of whom 75.6% were ACPA+. In comparison, 51.7% were ACPA+ in SE- pts. SE+ pts were similar with SE- pts in age, gender, BMI and smoking status, but had longer disease duration, were more likely to be rheumatoid factor positive,

have erosive disease and higher comorbidity burden irrespective of ACPA status. The differences were more pronounced if the pts were also ACPA+. Adjusting for BL differences, pts with SE 1 and 2 alleles (vs 0) had an odd ratio of 1.97 (95% CI:1.36-2.84; p=0.0003) and 3.82 (95% CI: 2.44-5.98; p<.0001) to be ACPA+, respectively. The regression analysis suggests that SE+ (vs SE-) pts had an average increase in DAS28 (CRP) of 0.22 (p=0.033), CDAI of 2.07 (p=0.045) and SDAI of 2.43 (p=0.029) over a year (Fig 1). Using a mediation analysis, the direct effect of SE+ account for 78.8% to 81.0% of total effect in the increase in DAS28 (CRP), CDAI and SDAI, and the indirect effect mediated by ACPA account for 19.0% to 21.2% (Table 1).

Figure 1. Linear Regression Model for SE Association with Change in Disease Activity

*Estimates, p-values are shown as data labels on the graphs; Change in disease activity (DA) = (follow-up DA - baseline DA); The above model is adjusted for age, gender, CCI, baseline DA, baseline biologic use, SE status and smoking status

Table 1. Mediation Analysis for SE and ACPA Association with Change in DA

Parameter	Change in DAS28 CRP (N=666)		Change in CDAI (N=653)		Change in SDAI (N=629)	
	Estimate	P-value	Estimate	P-value	Estimate	P-value
Total Effect of SE on DA change	0.22	0.034	2.05	0.047	2.40	0.030
Direct effect of SE on DA change excluding mediation of ACPA	0.17	0.101	1.57	0.140	1.89	0.098
Indirect effect of SE on DA change due to ACPA mediation and interaction	0.04	0.183	0.48	0.133	0.51	0.143

The model is adjusted with other covariates: Age, Gender, Charlson comorbidity score; baseline biologic use, Smoking status, baseline DA, Interaction term (ACPA*SE)

Conclusion: SE is strongly related to ACPA and a greater burden of disease in RA pts. In pts receiving standard treatments including biologics, SE is predictive of a greater increase in DA, which is partially mediated by the presence of ACPA.

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