

Conclusions: Anti-CCP+ individuals with non-specific MSK symptoms (in particular, a high risk group), exhibit increased aortic stiffness. This suggests presence of CV abnormalities prior to development of RA and implies a role of autoantibody-mediated development of atherosclerosis. These findings warrant further investigation in larger scale studies.

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THU0102 CLINICAL DISEASE ACTIVITY MEASURES ARE IMPORTANT DRIVERS OF MAJOR CHANGE IN MEDICAL TREATMENT IN US VETERANS ENROLLED IN THE VETERANS AFFAIRS RHEUMATOID ARTHRITIS (VARA) REGISTRY

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Background: Current guidelines encourage the measurement of rheumatoid arthritis (RA) disease activity and directing therapy to achieve a low disease state or remission (treat-to-target). Many RA patients with documented moderate to severe disease activity remain on their current therapy without change.

Objectives: This study investigated Veterans Affairs (VA) clinical data to identify patient factors associated with a major change in RA therapy and to determine the relative importance of these different factors.

Methods: US Veterans enrolled in the VARA registry were included if they had: 1) high/moderate disease activity (DAS28 \geq 3.2) at index date, 2) 18 months of VA data prior to the index date and 3) two or more other DAS28 measured during the preceding 18 months separated by at least three months. A major change was reported if within 7 days before to 90 days after the index date there was either: 1) initiation or escalation of DMARDs, 2) initiation or increase dose of prednisone and/or 3) \geq 2 joint injections.

Baseline DAS28 was estimated during the observation period prior to the index date using an area under the curve calculation and compared to the DAS28 at the index date. Patients were categorized as have a worsening or improvement of disease if the DAS28 at index date was 0.6 higher or lower than the average DAS28 during the observation period respectively. Other patients were categorized as no change in DAS28.

Analyses of clinical variables including components of the DAS28 and patient and physician reported measures were compared in patients with and patients without a major change in therapy.

Results: Of 941 patients who met study criteria, only 388/941 (41.2%) had a major change of therapy. Patients with worsening DAS28 were more likely to have a major change 183/369 (49.5%) than no DAS28 change 170/454 (37.4%) and improved DAS28 35/118 (29.6%) ($P < 0.001$). Clinical variables were strongly associated with changes in therapy among patients with worsening disease activity and not as strongly associated with change in therapy in those with no change disease activity. Clinical variables were not significantly associated with major change in patients with disease improvement, though that group had the smallest sample size. Ten representative clinical variables with the highest association with major change are included below.

Demographic elements	Comparison of Patients with Major Change to Patients without Major Change					
	DAS28 worsening (n=369)		DAS28 no change (n=454)		DAS28 improved (n=118)	
Major Change at Index Date - Number (%)	183/369 (49.5%)		170/454 (37.4%)		35/118 (29.6%)	
Age at RA Disease Onset - Mean (SD)	52 (413.7)		51 (413.7)		50 (512.9)	
Age at Index Date - Mean (SD)	65 (8210.6)		65 (8111.0)		64 (8010.8)	
Male - Number (%)	328 (88.9%)		410 (90.3%)		99 (84.0%)	
Clinical Variables from VARA registry	RR (CI 95)	p-value	RR (CI 95)	p-value	RR (CI 95)	p-value
DAS28 Score at Index Date	1.25 (1.11 - 1.42)	<0.001	1.30 (1.12 - 1.51)	0.001	1.23 (0.82 - 1.82)	0.318
Baseline DAS28 Score during 18 months observation period	1.20 (1.05 - 1.37)	0.009	1.27 (1.09 - 1.47)	0.002	1.27 (0.86 - 1.87)	0.319
Swollen Joint Count	1.03 (1.00 - 1.04)	0.031	1.05 (1.01 - 1.08)	0.006	1.06 (0.99 - 1.12)	0.070
Tender Joint Count	1.02 (1.00 - 1.04)	0.027	1.01 (0.98 - 1.03)	0.530	0.98 (0.91 - 1.07)	0.671
Modified Health Assessment Questionnaire (MD HAQ)	1.08 (0.87 - 1.37)	0.051	1.03 (0.81 - 1.31)	0.743	0.90 (0.50 - 1.61)	0.722
Pain Score	1.07 (1.01 - 1.13)	0.028	1.04 (0.99 - 1.10)	0.145	0.93 (0.83 - 1.05)	0.257
Patient Global Assessment	1.01 (1.00 - 1.01)	0.093	1.01 (1.00 - 1.02)	0.014	1.00 (0.98 - 1.01)	0.560
Physician Global Assessment	1.00 (0.99 - 1.01)	0.474	1.01 (1.00 - 1.02)	0.002	1.01 (0.99 - 1.02)	0.402
Erythrocyte Sedimentation Rate	1.01 (1.00 - 1.01)	0.073	1.00 (1.00 - 1.01)	0.882	1.00 (0.99 - 1.02)	0.630
C-reactive Protein	1.04 (1.00 - 1.08)	0.058	1.04 (1.00 - 1.17)	0.990	1.08 (0.92 - 1.26)	0.344

Conclusions: More than half of the patients with moderate disease activity did not have a major change in therapy. The likelihood of a major change in therapy increased with worsening disease activity. The clinical variables assessed were more strongly associated with change in therapy in patients with worsening of disease. Clinical disease activity measures are highly associated with the decision to initiate major changes. Future work will investigate the potential added value of administrative variables. This work emphasizes the need for methods to systematically collect and utilize clinical disease activity measurements, particularly longitudinally, to improve the treat-to-target strategy.

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THU0103 ANTI-RA33 AUTOANTIBODIES ARE ASSOCIATED WITH THERAPEUTIC RESPONSES TO METHOTREXATE AND ANTI-TNF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Besides the determination of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), anti-RA33 antibodies (which are directed to the nuclear antigen hnRNP-A2) could be of additional diagnostic and/or prognostic value in patients with rheumatoid arthritis (RA) because they are also found in RF/ACPA negative patients (1, 2).

Objectives: So far, published data on anti-RA33 antibodies refer only to the IgG isotype. It was therefore the aim of this study to measure the prevalence of anti-RA33 IgG, IgM and IgA antibodies in patients with RA and to determine their potential prognostic value regarding prediction of response to treatment.

Methods: A total of 255 patients were tested for the presence of IgG, IgM and IgA anti-RA33 antibodies by a newly developed EIA[®] (Thermo Fisher Scientific). All patients had initially been treated with conventional synthetic drugs (mostly methotrexate) and were subsequently treated with at least one TNF inhibitor. Therapeutic responses to MTX and TNF blocking biologicals were calculated in an inception cohort (n=104) who had started their DMARD therapy at our clinic. To define therapeutic responses the simplified disease activity index (SDAI)50 and American College of Rheumatology (ACR)20 responses were calculated.

Results: Among the 255 patients, 11% tested positive for anti-RA33 IgG antibodies, 15% for IgM antibodies and 6% for IgA antibodies. Altogether, 62 patients (24%) had at least one type of anti-RA33 antibody: 24 patients were RF-negative, 26 were ACPA-negative and 18 were RF/ACPA double negative. Thus, in 32 patients (13%), anti-RA33 was the only antibody specificity. Regarding response to anti-TNF therapy (Figure 1A), in the group of patients testing positive for anti-RA33 antibodies of any isotype (with or without concomitant RF and/or ACPA) the percentage of SDAI50 responders (24%) was significantly lower ($p=0.0117$) than in anti-RA33 negative (but RF/ACPA positive) patients (42% responders) and similar to the group of completely seronegative patients (21% responders). In contrast, regarding responses to MTX (Figure 1B) the percentage of SDAI50 responders was significantly higher ($p < 0.0001$) among anti-RA33 positive patients (with or without RF and/or ACPA) (59% responders) compared to anti-RA33 negative (but RF/ACPA positive) patients (37% responders) and seronegative patients (24% responders).

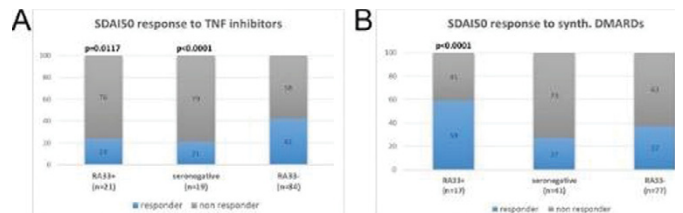


Figure 1: Percentages of (A) anti-TNF or (B) synthetic DMARD SDAI50 responder versus non responder in patients with anti-RA33 antibodies (IgG, IgM or IgA), seronegative patients (RA33-RF-ACPA-) compared to RA33 negative patients.

Conclusions: In agreement with previous findings (1,2) anti-RA33 antibodies reduced the diagnostic gap left by ACPA and RF and thus the percentage of seronegative patients by 13%. Importantly, the presence of anti-RA33 antibodies was associated with a favourable response to MTX on the one hand and with a diminished response to TNF inhibitors on the other hand. Therefore, these antibodies appear to have some prognostic value for prediction of therapeutic responses and could become helpful tools in therapeutic decision making.

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