Table 1. Multiple regression models

	Model 1 n= 865		Model 2 n= 1, 251	
ERS-RA score	Coefficient	95% CI, p	Coefficient	95% CI, p
hs-CRP, every 10 mg/L increment	0.005	0.000 to 0.100, 0.043	0.005	0.000 to 0.011, 0.035
b/tsDMARD use	-0.002	-0.005 to 0.001, 0.199	-0.000	-0.002 to 0.002, 0.963
csDMARD use	0.002	-0.003 to 0.007, 0.394	0.002	-0.002 to 0.006, 0.371
Prob >F, model with only CRP	0.03		0.03	
Prob >F, full model	0.07		0.08	

A multiple linear regression (ENTER method) was performed for the dependent variable ERS-RA score using a listwise deletion analysis (Model 1) and a multiple imputation analysis (Model 2).

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POS0215

DIRECT AND CONDITIONAL EFFECTS OF EPICARDIAL ADIPOSE TISSUE VOLUME ON CORONARY PLAQUE PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: Epicardial adipose tissue volume (EATv) predicts coronary atherosclerosis presence, progression and cardiovascular event risk in general patients^{1,2}. Our group recently reported that EATv associated with greater sub-clinical coronary plaque burden, non-calcified plaque presence and vulnerable plaque characteristics in patients with rheumatoid arthritis (RA). The relationship was stronger in RA patients with lower disease duration, no traditional cardiac risk factors, and who were not obese.

Objectives: To evaluate the predictive value of EATv on long-term coronary atherosclerosis development, and moderators of the association between EATv and plaque formation.

Methods: This single-center observational cohort study included 100 patients without symptoms or diagnosis of cardiovascular disease who underwent computed tomography angiography for evaluation of EATv and coronary atherosclerosis at baseline and repeat assessments 6.9±0.3 years later to evaluate plaque progression. New plaque formation in segments without plaque at baseline was the main outcome. Robust multivariable logistic regression evaluated the effect of high versus low EATv (based on median) on likelihood of new plaque formation, accounting for clustering of segments within patients. Potential moderator effects of prespecified predictors were also assessed.

Results: High EATv (>107 cm³) predicted new plaque formation in segments without baseline plaque (OR 2.77 [95% CI 1.43-5.37], p= 0.003); however, significance was lost in the multivariable model. Importantly, high EATv associated with formation of higher-risk non- and partially calcified plaque after adjusting for Framingham D'Agostino risk score, obesity, segment location, time-averaged CRP, duration of bDMARD and statin treatment and cumulative prednisone dose (adjusted OR 2.57 [95% CI 1.02-6.48], p= 0.045). RA duration (<10 versus >10 years), cardiac risk factor burden (≤1 versus >1), presence of mixed/calcified plaque in other coronary segments at baseline, and statin exposure (≤1 versus >1 year, based on median) moderated the effect of EATv on all new plaque formation (all p for interaction ≤ 0.021). Specifically, high EATv predicted new plaque formation in patients with RA duration <10 years (adjusted OR 5.75 [95% CI 1.77-18.67]), those with ≤1 cardiac risk factors (adjusted OR 3.40 [95% CI 1.46-7.90]), those without calcification at baseline (adjusted OR 2.65 [95% CI 1.11-6.31]) and those with statin treatment <1 year (adjusted OR 3.33 [95% CI 1.13-9.77]). This was not the case for patients with RA >10 years, ≥ 2 cardiac risk factors, calcification at baseline and statin treatment >1 year (figure 1).

Conclusion: High baseline EATv independently predicted future higher-risk non-calcified and mixed coronary plaque in RA. Moreover, it conditionally promoted new plaque formation overall in patients with earlier disease, low cardiac risk factor burden, who had little or no atherosclerosis at baseline and who had limited exposure to statin therapy. These findings indicate the need for a larger prospective evaluation of the role of EATv as a biomarker of coronary atherosclerosis development in RA.

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*All models adjusted for proximal segment location, time-averaged CRP, cumulative prednisone dose, and total methotrexate dose.
†Additionally adjusted for Framingham risk score, body mass index, and statin duration.
‡Additionally adjusted for age, gender, body mass index, and statin duration.
§Additionally adjusted for Framingham risk score and statin duration.
¶Additionally adjusted for Framingham risk score and body mass index.

Figure 1. Moderators of influence of EATv on new coronary plaque formation

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POS0216

GREATER HIGH-DENSITY LIPOPROTEIN LEVELS OVER TIME ARE LINKED TO DECREASED CORONARY PLAQUE FORMATION AND REGRESSION AND STABILIZATION OF HIGH-RISK LESIONS IN RHEUMATOID ARTHRITIS

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Background: The relationship between serum lipoproteins and cardiovascular disease risk in rheumatoid arthritis (RA) is complex¹. Their levels and function may vary based on disease activity and medication use. Beneficial effects on high-density lipoprotein (HDL-C) levels, structure and behavior, in response to treatment have been described. However, the impact of HDL-C levels over time on coronary atherosclerosis progression in RA is unknown.

Objectives: We here evaluated the influence of HDL-C levels over time on long-term coronary plaque formation and progression in patients with RA.

Methods: One hundred one RA patients without symptoms or history of cardiovascular disease who participated in a computed tomography angiography study of coronary atherosclerosis had repeat assessments after 6.9±0.3 years to evaluate plaque progression. Clinical, laboratory and medication data were recorded at baseline and regular outpatient follow-up visits thereafter. Time-averaged HDL-C was calculated for each patient using available consecutive HDL measurements between baseline and follow-up. Robust logistic regression assessed the association between time-averaged HDL-C and likelihood of new plaque formation in segments without plaque at baseline, and transition of prevalent mixed plaque to calcified plaque. Robust multinomial logistic regression evaluated the effect of time-averaged HDL-C on likelihood of new non-calcified, mixed or calcified plaque formation in segments without plaque (compared to remaining without plaque), and non-calcified plaque regression or transition to mixed or calcified plaque at follow-up (compared to remaining non-calcified). All models accounted for clustering of coronary segments within patients and adjusted for Framingham D'Agostino risk score, proximal segment location, time-averaged CRP, cumulative prednisone dose, bDMARD duration, statin duration, waist-to-height ratio, and time-averaged triglycerides.

Results: Participants were mostly female (n=87, 86.1%), with a mean ± standard deviation (SD) age of 51.5±10.3 years and time-averaged HDL-C of 51.7±13.9. Ninety-seven new plaques formed in segments without plaque at baseline; 20 were noncalcified, 21 were mixed, and 56 were calcified. Time-averaged HDL-C

had no effect on new total plaque formation (adjusted odds ratio-OR 0.88 [95% CI 0.64-1.21]). However, each 1-SD increase in time-averaged HDL-C associated with a 44% reduced likelihood of new non-calcified plaque formation at follow-up (adjusted OR 0.56 [95% CI 0.35-0.92], Figure 1). In contrast, there was no effect of time-averaged HDL-C on new mixed or calcified plaque formation. Of 98 non-calcified plaques at baseline, 42 did not change at follow-up, 32 regressed (disappeared), 16 transitioned to mixed and 8 to calcified plaques. Each SD increase in time-averaged HDL-C yielded a 2.2-fold greater likelihood of non-calcified plaque regression (adjusted OR 2.21 [95% CI 1.02-4.83]). Sixteen of 52 mixed plaques present at baseline transitioned to more stable calcified lesions, and time-averaged HDL-C (per 1-SD increment) predicted a 3.5-fold increased likelihood of transition of mixed to fully calcified plaque (adjusted OR 3.56 [95% CI 1.25-10.17]).

Conclusion: Higher HDL-C over time predicted regression of existing and decreased formation of new higher-risk non-calcified plaque. It also associated with transition of vulnerable mixed plaque to more stable fully calcified plaque. These effects were independent of RA treatment duration, prednisone dose and statin exposure.

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*Adjusted for Framingham D'Agostino cardiac risk score, proximal segment location, time-averaged CRP, biologic DMARD treatment duration, statin treatment duration, cumulative prednisone dose, waist-to-height ratio, and time-averaged triglycerides.

Figure 1. Impact of HDL-C over time on coronary plaque progression in RA

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POS0217 PULSE WAVE VELOCITY ELEVATION ABOVE INDIVIDUAL REFERENCE VALUES AND AORTIC-BRACHIAL STIFFNESS MISMATCH AS EARLY MARKERS OF ARTERIAL STIFFNESS INCREASE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Arterial stiffness (AS) is a known predictor of cardiovascular (CV) disease. The measurement of pulse wave velocity (PWV) is considered to be a gold standard of AS assessment but the recommended threshold of 10 m/s¹ may not take into account multiple factors influencing PWV. Use of the proposed individual reference values may help to identify patients with AS increase despite PWV level below this threshold². The impact of AS on CV outcomes may be mediated by the reversal of the aortic-brachial stiffness (AS gradient)³. One small study in patients with type 2 diabetes has shown that the aortic-brachial stiffness mismatch (hereafter AS mismatch) was an earlier marker of AS than PWV elevation⁴. Patients with rheumatoid arthritis (RA) have high CV risk and may benefit from early detection of AS increase. Both approaches have not been studied in RA previously

Objectives: To evaluate the incidence of PWV elevation above individual reference values and the frequency of AS mismatch in RA

Methods: Study group included 85 patients (pts) with RA (females 77.6%, aged 59.7±14.3 years, HTN 65%, mean DAS-28(CRP) 3.7±1.1) and control group (40 pts matched by gender, age and risk factors). Parameters of AS were measured

by applanation tonometry. Individual PWV reference values were assessed². The AS gradient was calculated as carotid-femoral (cf)PWV/carotid-radial (cr)PWV ratio and its elevation ≥1 was considered as AS mismatch. p<0.05 was considered significant

Results: In pts with RA with and without history of HTN mean cfPWV was 10.3±3.1 and 7.3±1.5 m/s, respectively, mean AS gradient – 1.4±0.4 and 1.1±0.1 (p<0.001 for trend); in controls – 9.6±1.9 and 6.7±1.4 m/s and 1.3±0.3 and 0.99±0.2, respectively (p<0.001 for trend). cfPWV elevation ≥10 m/s was observed in 34.1% pts with RA and 32.5% of controls: 6.7 and 6.3% of normotensives and 49.1 and 50% of hypertensives, respectively (p>0.05). cfPWV elevation above individual reference values was observed in 41.2% RA pts and 27.5% of controls (p=0.03): in 40% and 6.3% of normotensives (p=0.02) and 41.8% and 41.7% of hypertensives, respectively. After adjustment by age, gender and systolic BP cfPWV elevation above individual reference values in normotensive RA pts was independently associated with BMI (beta=0.39, p=0.02) and dyslipidemia (beta=0.48, p=0.01). The frequency of AS mismatch in RA was significantly higher compared to the controls in both normotensive and hypertensive subgroups: 76.7% vs 43.8% (p=0.03) and 94.5% vs 79.2% (p=0.04), respectively. The same trend was observed in a subgroup with normal cfPWV: AS mismatch was present in RA and controls in 82.1% vs 51.9% (p=0.004) in pts with PWV ≤ 10 m/s and in 82% and 51.7% (p=0.04), respectively in pts with PWV below individual reference values.

Conclusion: Patients with RA are characterized by higher frequency of cfPWV elevation above individual reference values compared to controls irrespectively of history of HTN. This method may be more appropriate for AS evaluation than use of standard criteria in this population. AS mismatch in RA pts is highly prevalent and may be considered as an earlier marker of AS than cfPWV elevation. These findings may be used for early detection of vascular ageing in patients with RA.

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POS0218 TUMOR-NECROSIS FACTOR INHIBITORS IMPROVE AORTIC STIFFNESS IN PATIENTS WITH LONGSTANDING RHEUMATOID ARTHRITIS

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Background: Major cardiovascular disease (CVD) benefits of disease-modifying anti-rheumatic drugs (DMARDs) therapy occur in early RA patients with treat-to-target strategy. However, it is unknown whether long-term DMARDs treatment in established RA could be useful to improve CVD risk profile.

Objectives: The aim of this study was to comparatively describe aortic stiffness progression in patients with longstanding and established RA treated with tumor necrosis factor inhibitors (TNFi) or conventional synthetic DMARDs (csDMARDs).

Methods: Ultrasound aortic stiffness index (AoSI) has to be considered a proxy outcome measure in established RA patients. We measured AoSI in a group of RA patients on long-term treatment with TNFi or csDMARDs. Eligible participants were assessed at baseline and after 12 months; changes in serum lipids, glucose and arterial blood pressure were assessed. All patients were on stable medications during the entire follow-up.

Results: We included 107 (64 TNFi and 43 csDMARDs) RA patients. Most patients (74%) were in remission or low disease activity and had some CVD risk factors (45.8% hypertension, 59.8% dyslipidemia, 45.3% smoking; table 1). The two groups did not differ significantly for baseline AoSI (5.95±3.73% vs 6.08±4.20%, p=0.867). Follow-up AoSI was significantly increased from baseline in the csDMARDs group (+1.00%; p<0.0001) but not in the TNFi group (+0.15%, p=0.477). Patients on TNFi had significantly lower follow-up AoSI from baseline than the csDMARDs group (-1.02%, p<0.001; ANCOVA corrected for baseline AoSI, age and systolic blood pressure). Furthermore, follow-up AoSI was significantly lower in TNFi users with 1-2 or >2 CVD risk factors than in those without (figure 1).

Conclusion: Long-term treatment with TNFi was associated with reduced aortic stiffness in patients with established RA and several CVD risk factors.