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.

Baseline characteristics of the study population.	csDMARDs (n=43)	TNFi (n=64)	P value
Age, median years (IQR)	58.6 (53.0, 66.0)	58.1 (49.3, 67.0)	0.839
Female sex	33 (76.7)	54 (84.4)	0.321
Obesity	5 (11.6)	7 (10.9)	0.999
Hypertension	19 (44.2)	30 (46.9)	0.784
Anti-hypertensive drug	17 (39.5)	28 (43.8)	0.784
Smoking status, ever	18 (42.9)	30 (46.9)	0.684
Dyslipidemia	30 (40.2)	34 (59.8)	0.085
Current statin use	13 (34.2)	10 (15.9)	0.033
Diabetes mellitus	3 (7.0)	3 (4.7)	0.676
Anti-diabetic medication	1 (2.3)	1 (1.5)	0.999
CVD risk factors, median (IQR)	2 (1, 3)	2 (1, 3)	0.199
RF and/or ACPA positive	28 (65.1)	33 (51.6)	0.165
Disease duration, median years (IQR)	14.1 (11.5)	15.4 (10.5)	0.538
Methotrexate	38 (88.4)	52 (81.3)	0.192
Leflunomide	5 (17.9)	12 (19.0)	0.999
Hydroxychloroquine	9 (31.0)	5 (7.8)	0.009
Prednisone > 5 mg daily	7 (7.7)	5 (5.5)	0.823
NSAIDs	6 (20.7)	22 (34.4)	0.227

ACPA, anti-citrullinated peptides antibodies; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; IQR, interquartile range; NSAIDs, non-steroidal anti-inflammatory drugs; RF, rheumatoid factor; TNFi, tumor necrosis factor inhibitors. All data reported as absolute numbers (percentage) otherwise specified. P-value refers to Chi-squared or Fisher test for categorical variables or ANOVA for continuous variables.

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POS0219

EFFECT OF LOW-DOSE METHOTREXATE ON ESTIMATED GLOMERULAR FILTRATION RATE AND KIDNEY ADVERSE EVENTS IN THE CARDIOVASCULAR INFLAMMATION REDUCTION TRIAL

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Background: Low-dose methotrexate (LD-MTX) is a common first-line treatment for systemic rheumatic diseases, and its use is contraindicated in advanced chronic kidney disease (CKD) because it is primarily excreted by the kidneys. Among patients with preserved kidney function, the safety of LD-MTX on estimated glomerular filtration rate (eGFR) and kidney adverse events (AEs) has not been established.

Objectives: To investigate the effect of LD-MTX on eGFR and kidney AEs using data from a randomized clinical trial.

Methods: We performed a secondary analysis for eGFR and kidney AEs using the randomized double-blind, placebo-controlled Cardiovascular Inflammation Reduction Trial. Adults with known cardiovascular disease and diabetes and/or metabolic syndrome were randomly allocated to oral LD-MTX (target dose 15-20 mg/week) or placebo. All participants took folic acid 1 mg six days/week. Exclusion criteria included systemic inflammatory disease and creatinine clearance <40 mL/min (by Cockcroft-Gault). eGFR was calculated using the CKD-EPI formula. Clinical kidney AEs were blindly adjudicated. The least-squares mean change of eGFR from baseline was calculated at each study visit; the difference in eGFR slopes between LD-MTX and placebo was compared using a modified intention-to-treat approach. We also compared rates of kidney AEs for LD-MTX versus placebo using Cox proportional hazards models.

Results: A total of 2,391 subjects were randomized to LD-MTX and 2,395 to placebo. At baseline, mean age was 66 years, 19% were female, mean eGFR was 80.0 mL/min/1.73 m², and 18% had stage 3 CKD or worse. Median follow-up duration was 23 months, and median LD-MTX dose was 16 mg/week. Those randomized to LD-MTX had less decline in eGFR over the entire follow-up compared to placebo (slope difference 1.12, 95%CI 0.59-1.65, $p<0.001$, Figure 1). Those with CKD stage 3 or worse on LD-MTX saw less eGFR decline than those with CKD stage 2 or better (slope difference among CKD stage 3 or worse: 2.46, 95%CI 1.10-3.82, $p<0.001$; p for interaction 0.02). The LD-MTX group had higher eGFR than placebo over the first 24 months of study follow-up ($p<0.05$ at each visit). On safety laboratory monitoring, there were 159 acute kidney injury AEs in the LD-MTX group and 187 in the placebo group (HR 0.83, 95%CI 0.67-1.02, Table 1). There were 37 clinical kidney AEs in the LD-MTX group and 42 in the placebo group (0.87, 95%CI 0.56-1.36). One subject began dialysis in the LD-MTX group compared to 3 in the placebo group.

Conclusion: These results demonstrate the kidney safety of LD-MTX among patients without advanced CKD at baseline. We observed a possible beneficial effect of LD-MTX on preserving kidney function, suggesting that inflammation may be involved in the pathogenesis of CKD in this population.

Figure. Least-squares mean change of estimated glomerular filtration rate (eGFR) from baseline to each follow-up visit according to random assignment of low-dose methotrexate (LD-MTX) or placebo in the Cardiovascular Inflammation Reduction Trial (n=4,786). eGFR was calculated using the CKD-EPI equation. A slope difference significantly above 0 denotes less decline in eGFR for the LD-MTX group.