Vascular endothelial function changes during treatment in patients with rheumatoid arthritis (RA).

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Rheumatoid Artrhitis (RA) patients have an increased risk for accelerated atherosclerosis. Endothelial dysfunction and arterial stiffness, assessed by measurement of carotid-femoral pulse wave velocity (PWV) and common carotid artery intima-medial thickness (CCA-IMT), respectively, are proven surrogate markers of premature and potentially reversible atherosclerosis. Disease modifying anti-rheumatic drugs (DMARDs), and particularly biologic treatments, because of their higher capacity for controlling inflammation, might improve these surrogate markers of atherosclerosis.

Objective: To assess the short-term effect (1 year) of treatment with conventional synthetic DMARDs, TNF-inhibitors, or Abatacept, on endothelial function and arterial stiffness in RA patients.

Patients and methods: Consecutive patients meeting 1987 ACR classification criteria for RA in whom their treating Rheumatologist prescribed a new DMARD or a change in DMARD (including biologics), were included. Patients with history of cardiovascular disease were excluded from the study. Common carotid artery (CCA) intima-medial thickness (IMT) and carotid plaques (CP) were measured in the right common carotid artery using high-resolution B mode ultrasound with a 10 MHz linear transducer. Carotid-femoral pulse wave velocity (PWV) was measured using a hand-held tonometry probe. Clinical evaluation included assessment of disease activity using the Disease Activity Score including 28 joint count (DAS28), the Argentinean validated HAQ-DI, blood pressure measurement, and 10-year risk for coronary events using the Framingham 2010 risk equation. All measurements were performed at baseline, and after one year of treatment. In patients switching or stopping treatment, measurements were completed within one month of treatment stop/change.

Results: Thirty-four patients were included. Baseline characteristics and follow up outcomes, according to treatment at the initiation of the study are shown in the table.

Variable	DMARDs (n=15)	TNFα inhibitors (n= 10)	ABATACEPT (n= 9)

Female, n (%)	11 (73)	9 (90)	8 (89)
Mean age, years (SD)	53.8 (14)	56.9 (12.4)	56.7 (6.6)
Mean Disease duration, years (SD)	7.4 (9.5)	18.5 (11.8)	13.7 (9.2)
Rheumatoid Factor positivity, n (%)	13 (87)	6 (60)	9 (100)
Previuos TNFα inhibitors, n (%)	0 (0)	1 (10)	7 (78)
DAS 28 , mean (SD)	4.4 (1.3)	4.9 (1.5)	4.9 (1.3)
Mean HAQ (SD)	0.9 (0.7)	1.6 (0.7)	1.4 (0.9)
Mean Systolic Blood Pressure, mmHg (SD)	131 (18.7)	142.6 (13.7)	129.4 (18.2)
Mean Framingham 2010 10 years, Cardiovascular Risk	5.7%	3.1%	2.4%
Mean PWV, m/sec (SD)	8.1 (2.4)	8.3 (1.5)	7.3 (1.2)
Mean CCA-IMT, mm (SD)	0.85 (0.3)	0.83 (0.2)	0.78 (0.2)
Carotid Plaques, n (%)	6 (40)	2 (20)	3 (33)
Mean time to follow up study, months (SD)	12.3 (2.4)	12.4 (0.7)	11.4 (2.9)
Patients stopping/Switching treatment, n (%)	8 (53)	7 (70)	5 (55)
Mean time to stop/switch treatment , months (SD)	8 (6)	8.5 (3)	8.4 (5)
Mean PWV, m/sec (SD) at follow up	8 (1.6)	7.95 (1.3)	8 (1.3)
Mean CCA-IMT, mm (SD) at follow up	0.87 (0.28)	0.88 (0.22)	0.8 (0.2)

After a mean follow up of 12.1 (SD: 2,2) months there was a significant reduction in DAS28 in all three treatment groups, [mean 4.7 (SD:1.3) vs 4 (SD: 1.2); p=0.0425], while there was no difference in HAQ [1.2 (SD:0.8) vs 1.1 (SD:0.7); p=0.3244], in any of them. All patients had normal baseline PWV, and there were no significant changes after one year in any of the treatment groups. In a similar way, there were no differences between baseline and follow up mean CCA-IMT. No patient developed new carotid plaques.

Conclusions: After one year of treatment, there were no significant changes in surrogate markers of atherosclerosis in long standing RA patients, with low basal cardiovascular risk. Parameters of endothelial dysfunction and arterial stiffness remained within normal values after one year of follow up.

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