Supplementary Material

Rheumatoid Arthritis, Cognitive Impairment, and Neuroimaging Biomarkers: Results from the Mayo Clinic Study of Aging

Supplementary Table 1. The association of RA activity markers with incident dementia in participants *without dementia* at Mayo Clinic Study of Aging baseline.

Comparison groups	N	Events	HR[1]	95%(CI)	p
RA duration, y	101	15	1.04	1.0, 1.1	0.07
RA seropositive versus RA seronegative[2]	83	8	3.2	0.6, 17.8	0.19
ESR at RA diagnosis, mm/h	71	7	0.98	0.9, 1.04	0.55
Large joint swelling[3] (versus not)	101	15	0.8	0.2, 2.4	0.65
RA with bDMARDS versus RA no-bDMARDS[4]	101	15	1.3	0.2, 6.7	0.77

RA, rheumatoid arthritis; ESR, erythrocyte sedimentation rate; bDMARD, biologic disease-modifying anti-rheumatic drug.

[1] Hazard Ratio (95% Confidence Interval) estimates retained from univariate Cox Proportional Hazards Models for Incident Dem-MR review adjusted for age, sex, education, and baseline cognitive status (CU/MCI);

[2] Positivity for either rheumatoid factor (RF) or anti-cyclic citrullinated peptide antibody (anti-CCP) at any time;

[3] Prior to MCSA baseline;

[4] Any bDMARD (including tumor necrosis factor alpha inhibitors).

Supplementary Table 2. Association between RA activity markers and comorbidities with change in cognitive global z-score.

Comparison groups	Global cognitive z-score		
	Coefficient[1]	SE	p
	Patient with RA, CU at baseline		
RA seropositive versus RA seronegative[2]	-0.05	0.17	0.75
Time	-0.07	0.01	<0.001
RA seropositive*time	0.06	0.01	<0.001
RA duration	0.01	0.007	0.08
Time	-0.06	0.01	<0.001
RA duration*time	0.002	0.0006	0.008
ESR at RA diagnosis	0.002	0.005	0.66
Time	-0.03	0.01	0.030
ESR at RA diagnosis*time	-0.0001	0.0004	0.82
Large joint swelling[3]	-0.05	0.15	0.759
Time	-0.03	0.01	0.001
Large joint swelling*time	0.01	0.01	0.350
RA with biologic DMARDs[3,4]	0.12	0.18	0.51
Time	-0.03	0.01	<0.001
RA with biologic DMARDs*time	0.05	0.02	0.012
TNFi[3]	0.12	0.18	0.51
Time	-0.03	0.01	<0.001
TNFi * time	0.05	0.02	0.012
History of hypertension	0.08	0.17	0.65
Time	-0.01	0.01	0.33
History of hypertension*time	-0.02	0.01	0.13
History of dyslipidemia	0.07	0.17	0.68
Time	-0.01	0.01	0.27
History of dyslipidemia*time	-0.03	0.01	0.047
History of atrial fibrillation	0.38	0.37	0.31
Time	-0.03	0.01	<0.001
History of atrial fibrillation * time	-0.08	0.07	0.21
History of coronary artery disease	-0.16	0.17	0.36
Time	-0.03	0.01	0.001
History of coronary artery disease * time	-0.0008	0.02	0.96

History of stroke	0.64	0.64	0.33
Time	-0.03	0.01	<0.001
History of stroke*time	0.22	0.28	0.42
History of heart failure	-0.15	0.26	0.57
Time	-0.03	0.01	<0.001
History of heart failure*time	0.02	0.04	0.56
History of diabetes	-0.07	0.19	0.71
Time	-0.02	0.01	0.016
History of diabetes*time	-0.06	0.02	0.002

RA, rheumatoid arthritis; ESR, erythrocyte sedimentation rate; DMARDs, disease-modifying anti-rheumatic drug; TNFi, tumor necrosis factor alpha inhibitors.

[1] Fixed model results from a linear mixed-effects model allowing for random individual intercepts and slopes; slope estimates represent an annualized change from baseline. Models were adjusted for age at baseline visit, sex, education, and whether the administration of the cognitive tests was the first time ever (i.e., test naïve).

[2] Positivity for either rheumatoid factor (RF) or anti-cyclic citrullinated peptide antibody (anti-CCP) at any time

[3] Prior to MCSA baseline.

[4] Any bDMARD (including TNFi)