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IGA RF IS ASSOCIATED WITH HIGH AGE OF RHEUMATOID ARTHRITIS ONSET

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Background: IgM RF and anti-CCP2 have been shown to associate with young age at RA diagnosis [1, 2]. By contrast, little is known about the association between other RF isotypes and age at onset, or sex.

Objectives: To examine the association between individual RA autoantibodies, sex and age at RA onset.

Methods: Anti-CCP2, IgA-, IgG- and IgM-RF were analysed centrally in baseline sera from 1600 Epidemiological Investigations in RA (EIRA) patients aged 18-70 years and classified according to the 1987 ACR criteria within one year of first symptoms. Cut-offs for RF isotypes were determined at the 98th percentile based on the EIRA RA-free controls, close to the 98.4% anti-CCP2 specificity.

Results: Anti-CCP2, IgA-, IgG- and IgM RF were found in 1020 (64%), 692 (43%), 529 (33%), and 916 (57%), of the patients, respectively. Mean (median) age at diagnosis among men was 54 (57) year, higher than 51 (54) years among women (p<0.0001). The figure shows the autoantibody distribution in relation to sex and age tertiles. In univariate analysis, anti-CCP2 and IgM RF were both associated with lower age at RA diagnosis (table). When occurrence of all four autoantibodies were compared simultaneously as independent variables and with age at diagnosis as dependent variable in multiple regression, a strong association between IgA RF and higher age at RA diagnosis appeared, and the association between IgM RF and low age at RA diagnosis weakened (table). IgA RF and IgG RF associated with male sex, but IgM RF with female sex. No sex-difference was seen for anti-CCP2 (table). When the multiple regression was adjusted for sex, the association between IgM RF and age disappeared, whereas the strong associations between IgA RF and high age and between anti-CCP2 and low age at diagnosis persisted (table).

Conclusion: On average, IgA RF positive (vs. negative) RA patients are almost four years older at the time of diagnosis; the opposite was found for anti-CCP2 and IgM RF. Whereas sex-differences explain the age-association for IgM RF, this is not the case for anti-CCP2 and for IgA RF.

REFERENCES

- [1] Diaz FJ, et al. Joint Bone Spine 2011;78:175.
- [2] Jacobsen S. Clin Rheumatol 2004;23:121.

	Anti-CCP2 Pos/ Neg	P	IgA RF Pos/ Neg	P	IgG RF Pos/ Neg	P	IgM RF Pos/ Neg	P
N	1020/ 580		692/ 908		529/ 1071		916/ 684	
Age (mean) univariate	51/54	<0.0001	53/52	0.08	52/52	0.98	51/53	0.0042
Age (least squares mean multivariate)	51/55	<0.0001	55/51	<0.0001	53/53	0.7170	52/54	0.0401
Age multivariate (corr. sex)	52/55	<0.0001	55/52	<0.0001	54/53	0.9378	53/54	0.1128
Females n(%)	727/ 400 (71)/ (69)	0.3315	462/ 665 (67)/ (73)	0.0050	350/ 777 (66)/ (73)	0.0089	665/ 462 (73)/ (68)	0.0287

Figure. Distribution of individual autoantibodies in relation to sex and age tertiles.

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