Table 1. Multivariate linear regression model exploring the effect of Heijde-modified Sharp Score on selected HR-pQCT (distal radius) parameters, adjusted for age and sex.

		R^2	Effect	p-value
HSS total (n=146)	Tt. BMD (mg HA/cm^3)	0.129	-0.052	0.519
	Ct. BMD (mg HA/cm^3)	0.138	0.060	0.642
	Ct. Th (mm)	0.096	0.001	0.084
	Tb. BMD (mg HA/cm^3)	0.284	-0.173	<0.001
	Tb. N (1/mm)	0.319	-0.003	<0.001
HSS of the hands (n=145)	Tt. BMD (mg HA/cm^3)	0.124	-0.073	0.522
	Ct. BMD (mg HA/cm^3)	0.132	0.046	0.801
	Ct. Th (mm)	0.087	0.001	0.122
	Tb. BMD (mg HA/cm^3)	0.279	-0.242	0.001
	Tb. N (1/mm)	0.324	-0.005	<0.001
HSS of the wrists (n=146)	Tt. BMD (mg HA/cm^3)	0.127	-0.121	0.614
	Ct. BMD (mg HA/cm^3)	0.136	-0.029	0.939
	Ct. Th (mm)	0.089	0.001	0.158
	Tb. BMD (mg HA/cm^3)	0.273	-0.467	0.003
	Tb. N (1/mm)	0.311	-0.010	<0.001

HR-pQCT: high resolution peripheral quantitative computed tomography,HSS: Heijde-modified Sharp Score, Tt.: total, Ct.: cortical, Tb.: trabecular, BMD: bone mineral density, HA: hydroxyapatite, Th.: Thickness, N: number

Conclusion: Among patients with RA, the correlation between axial and peripheral bone is strongest between trabecular bone parameters of the radius and aBMD at the hip, which suggests that prediction of hip fractures is maintained. However, the degree of erosive disease negatively impacts the trabecular bone parameters. This may potentially interfere with the hip fracture prediction abilities of HR-pQCT in patients with high degree of erosive disease.

REFERENCES:

[1] L. Dirven, M. van den Broek, J. H. van Groenendael et al. Prevalence of vertebral fractures in a disease activity steered cohort of patients with early active rheumatoid arthritis. BMC Musculoskeletal Disorders 2012;13: 125.

[2] van der Heijde D. How to read radiographs according to the Sharp/van der Heijde method. The Journal of rheumatology. 2000;27(1):261-3.

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POS0596 SERUM CHOLESTEROL LOADING CAPACITY ON MACROPHAGES IS LINKED TO OXIDIZED LOW-DENSITY LIPOPROTEIN AND REGULATED BY SEROPOSITIVITY AND C-REACTIVE PROTEIN IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Excessive cholesterol accumulation in macrophages underlies foam cell formation, initiation and progression of atherosclerosis. LDL oxidation and unregulated uptake of oxidized LDL by macrophages are critical in foam cell development. Cholesterol loading capacity (CLC) is the ability of serum to deliver cholesterol to cells and is related to foam cell formation. Rheumatoid arthritis (RA) serum increased cholesterol content in macrophages and promoted foam cell formation significantly more than control serum[1]. Although inflammation, LDL oxidation and antibodies to oxidized LDL (anti-oxLDL) may be higher in RA, their relationships and their individual and synergistic contributions to CLC in RA are unknown.

Objectives: To explore determinants and moderators of serum CLC in patients with RA. We also investigated whether oxidized LDL influences CLC directly or indirectly through anti-oxLDL IgG and proprotein convertase subtilisin/Kexin type-9 (PCSK9), independently or conditionally on RA-related autoantibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) or level of inflammation.

Methods: In an observational study of 104 patients, CLC was measured fluorimetrically as intracellular cholesterol content in human THP-1-derived macrophages after incubation with patient serum. Oxidized LDL was measured as oxidized phospholipids on apoB100 particles (oxPL-apoB100). Anti-oxLDL, PCSK9 and C-reactive protein (CRP) were also quantified. Associations of oxPL-apoB100, anti-oxLDL IgG and PCSK9 with CLC were examined with multivariable linear regression. A two-stage dual moderated mediation model explored whether an indirect association of oxPL-apoB100 with CLC through parallel mediators anti-oxLDL IgG and PCSK9 varied as a function of moderators CRP and RF/ACPA positivity.

Results: OxPL-apoB100, anti-oxLDL IgG and PCSK9 positively associated with CLC (all adjusted p<0.020). In the final dual moderated mediation model oxPL-apoB100 was directly linked to CLC only in dual seropositive patients (unstandardized b [95% bootstrap confidence interval]=2.08 [0.38-3.79], Figure 1). An indirect effect of oxPL-apoB100 on CLC through anti-oxLDL IgG was present and increased along with level of CRP (index of moderated mediation=0.55 [0.05-1.17]). CRP also moderated the other indirect effect of oxPL-apoB100 on CLC through PCSK9, but only in dual seropositive patients (conditional indirect effect=0.64 [0.13-1.30]).

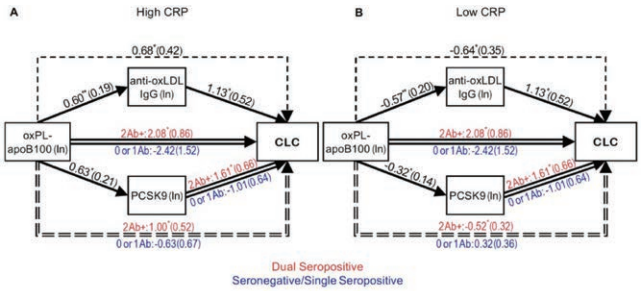

Figure 1. Determinants of CLC in RA. Unstandardized regression coefficients (standard errors) for paths of the dual moderated mediation model at **(A)** high (+1 SD above the mean) and **(B)** low (-1 SD below the mean) levels of the moderator CRP. ASCVD score, statin use, LDL-C, anti-oxLDL IgM, obesity, and age at diagnosis were included as covariates. Double lines are paths moderated by RF/ACPA seropositivity. Single dashed lines are the indirect effect of oxPL-apoB100 on CLC through anti-oxLDL IgG. Double dashed lines are the indirect effect of oxPL-apoB100 on CLC through PCSK9.
*p<0.05, **p<0.01

Conclusion: Oxidized LDL can directly influence CLC in dual seropositive RA patients, regardless of CRP. This suggests that targeting LDL oxidation in addition to inflammation may enable a more comprehensive reduction of atherosclerotic risk in these patients. Depending on CRP level, oxidized LDL also affected CLC indirectly via anti-oxLDL IgG and via PCSK9 in dual seropositive patients. If externally validated, our findings may have clinical implications for cardiovascular risk stratification and prevention.

REFERENCES:

[1] Voloshyna I *et al.* Plasma from rheumatoid arthritis patients promotes pro-atherogenic cholesterol transport gene expression in THP-1 human macrophages. *Exp Biol Med (Maywood)* 2013;238:1192–7.

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POS0597 PREDICTORS OF PERCEIVED RISK IN FIRST DEGREE RELATIVES OF RHEUMATOID ARTHRITIS PATIENTS

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