



simply independent disorders with shared risk factors. Coronary artery calcification (CAC) is considered a late stage pathognomonic feature of coronary atherosclerosis. CD40L, VCAM-1, and VEG-f are serum biomarkers that reflect initial inflammatory stages of vascular wall damage in the ischemic cascade. In the vascular endothelium, VEG-f is a protein that stimulates angiogenesis, CD-40L and VCAM-1 are molecules that initiate coagulation and immune responses. We therefore investigated the association between these markers of early and late atherosclerosis and presence and progression of knee OA, a possible cardiometabolic phenotype of OA, in a large population-based cohort study.

**Methods:** The analyses on prevalence of knee OA were performed in 3,465 participants from the prospective population-based Rotterdam Study (mean age 73.1 years, 61% women). Data on coronary artery calcification (CAC) were available for 1,669 participants and plasma levels of CD40L, VCAM-1, and VEG-f in 975. For the analyses on progression of knee OA, data on CAC was available for 979 participants (17% progressors), and 246 participants (20% progressors) had plasma levels of CD40L, VCAM-1, and VEG-f. We scored radiographs of the knee with the Kellgren-Lawrence (K&L) score for osteoarthritis (knee OA present with a K&L graded score greater or equal to 2) at baseline and follow-up (average follow-up time 4.5 years ( $\pm 0.5$ )). Overall progression of knee OA was defined as the combination of the incidence and the progression of existing OA at baseline and was considered present if the K&L score increased 1 grade between baseline and follow-up visit. After stratification by gender, multivariate logistic regression models with generalized estimated equations on knee level were used to calculate odds ratios (95% confidence intervals) for prevalence and progression of knee OA per each SD increase in marker levels.

**Results:** Within the study population, 18% had radiographic knee OA, 11% of the men, 23% of the women. CAC and VEG-f were not associated with prevalent knee OA. Among women, CD40L (adjusted odds ratio (aOR) 1.31 (1.12 to 1.56)) and VCAM-1 (aOR 1.31 (1.08 to 1.59)) were associated with prevalent knee OA (table). No associations with progression were found in women. In men, too few progressors were available to assess associations.

**Table. Markers of atherosclerosis in relation to prevalent knee OA, stratified by gender**

	Knee OA (Women) OR (95% CI)*	Knee OA (Men) OR (95% CI)*
Coronary artery calcification	1.11 (0.95–1.30)	1.11 (0.86–1.43)
CD40L	1.32 (1.12–1.56)**	1.05 (0.80–1.37)
VCAM-1	1.31 (1.08–1.59)**	1.08 (0.82–1.42)
VEG-f	1.08 (0.93–1.24)	1.07 (0.90–1.28)

**Conclusions:** In this population-based study, coronary artery calcification and VEG-f were not associated with presence or progression of knee OA. However, plasma levels of CD40L and VCAM-1 were higher in women with knee OA and not in men. This might reflect an association between early atherosclerosis and knee OA through low-grade systemic inflammation in women.

#### 509 MECHANISMS INVOLVED IN INHIBITION OF INFLAMMATION IN THP-1 CELLS BY THE HEXADECYLAMIDE DERIVATIVE OF HYALURONIC ACID.

F. Oliviero †, A. Scanu †, R. Ramonda †, P. Frallonardo †, P. Sfriso †, J. Dayer ‡, L. Punzi †. † *Rheumatology Unit, Univ. of Padova, Padova, Italy;* ‡ *Faculty of Med., Geneva, Switzerland*

**Purpose:** Intra-articular injections of hyaluronic acid are widely used in the treatment of inflammatory and degenerative joint diseases. The immune regulation exerted by hyaluronic acid is modulated by its interaction with different receptors including CD44 and the toll-like receptors 2 and 4. A novel hexadecylamide derivative of hyaluronic acid (HA), HYADD®4, has recently been tested in animal models of osteoarthritis, showing both anti-inflammatory and anabolic effects. The purpose of this study is to investigate the possible mechanisms involved on the effect of unmodified and hexadecylamide derivative

#### 508 MARKERS OF ATHEROSCLEROSIS IN RELATION TO PRESENCE AND PROGRESSION OF KNEE OSTEOARTHRITIS: THE ROTTERDAM STUDY

T.A. Hoeven, M. Kavousi, M.A. Ikram, J.B. van Meurs, P.J. Bindels, A. Hofman, O.H. Franco, S.M. Bierma-Zeinstra. *Erasmus Univ. Med. Ctr., Rotterdam, Netherlands*

**Purpose:** Several observational studies have found an association between subclinical measures of atherosclerosis and osteoarthritis (OA) of the hands and knees, predominantly among women. Different mechanisms have been suggested to explain the potential relation between atherosclerosis and OA; systemic low-grade inflammation caused by visceral adipose tissue is particularly mentioned and may consequently highlight a route to improve prevention and treatment of atherosclerosis and OA. However, the reported associations between subclinical measures of atherosclerosis and OA were modest in effect size, derived mainly from cross-sectional studies and generally attenuated after adjustment for cardiovascular risk factors. Furthermore, previous results were inconsistent for the different imaging markers of atherosclerosis. In previous work, we found no relation between peripheral measurements of atherosclerosis (including carotid intima-media-thickness or carotid plaque) and progression of knee, hand, or hip OA in a large sample of a prospective cohort study. Hence, it remains unclear whether atherosclerosis and OA are related or whether they are