graphic KOA severity. Furthermore, to look for patient and study characteristics that determine uCTX-II performance.

Methods: Medline and Embase databases were searched for studies into uCTX-II levels in adult subjects with radiographic KOA according to the Kellgren and Lawrence (K&L) classification system. uCTX-II levels were compared between subjects with KOA K&L ≥ 2 versus healthy control subjects and between subjects with KOA K&L 2 versus K&L 3–4 (i.e. moderate vs severe KOA). Controls were either selected based on lack of knee symptoms, based on K&L score, or were randomly selected from the general population. Differences between KOA subgroups were expressed as standardized mean differences (SMD). Subgroup analyses were performed to compare uCTX-II performance between genders, ethnicities, and large and small studies. Differences between subgroups were considered relevant when SMDs differed $>25\%$ between groups.

Results: 2035 Studies were screened for eligibility, of which ten studies were included. A moderate pooled SMD of 0.52 (confidence interval (CI): 0.40–0.65, $P < 0.0001$) was found for subjects with KOA K&L ≥ 2 versus controls, based on ten SMDs. For K&L3–4 versus K&L2 a moderate pooled SMD of 0.47 (CI: 0.32–0.63, $P < 0.0001$) was found, based on five SMDs. No indications for publication bias were identified using funnel plots. Subgroup analyses of the K&L ≥ 2 versus control comparison showed that uCTX-II performs better in women as compared to men and in Caucasian subjects as compared to other ethnicities. Study size did not influence the pooled SMD. Subgroup analysis was considered infeasible for the K&L 2 versus K&L 3–4 comparison due to a limited number of studies.

Figure 1: Forest plots for the comparisons of uCTX-II levels between subjects with radiographic KOA and controls and between subjects with KOA K&L3,4 and K&L2.

Conclusions: This is the first meta-analysis of uCTX-II performance in subjects with radiographic KOA. It appeared that uCTX-II levels can distinguish with moderate strength between radiographic KOA subjects and controls. Moreover, uCTX-II levels are consistently increased in severe versus moderate radiographic KOA. Female gender and Caucasian ethnicity were found to enhance uCTX-II performance in distinguishing radiographic KOA from controls. Yet, the number of studies was relatively small and criteria for KOA and control subjects differed between studies.

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SAT0499 IDENTIFICATION OF BIOCHEMICAL PHENOTYPES IN KNEE OSTEOARTHRITIS: LONGITUDINAL DATA FROM THE FNIH OA BIOMARKER CONSORTIUM

B. Jeremiassé¹, P.M. Welsing¹, C. Fellows², F.P. Lafeber¹, W.E. Van Spil¹.

¹Department of Rheumatology and Clinical Immunology, UMC Utrecht, Utrecht, Netherlands; ²School of Veterinary Medicine, University of Surrey, Guildford, United Kingdom

Background: It is hypothesized that patients with knee osteoarthritis (OA) can be classified into different phenotypes. Knowledge of these phenotypes may contribute to developing effective targeted treatment strategies.

Objectives: To identify different longitudinal phenotypes of knee OA using biochemical markers and to compare these phenotypes with regard to radiographic joint space loss (JSL) and/or pain progression.

Methods: Baseline, 1-year, and 2-year biochemical marker data from the FNIH OA Biomarker Consortium were used. This consortium is a nested case-control study of 600 subjects with one symptomatic index knee showing radiographic OA changes of Kellgren and Lawrence grade 1 to 3¹. Subjects were classified as either JSL progressors, pain progressors, JSL+pain progressors, or non-progressors according to predefined criteria (pain progression=persistent increase in WOMAC pain ≥ 9 points (0–100 scale) from baseline to 2, 3 or 4 years, JSL progression=decrease in JSW ≥ 0.7 mm from baseline to 2, 3 or 4 years). Biochemical markers included in the current analysis were sCTX-I, uCTX-I,

uβCTX-I, sNTX-I, uCTX-II, sCPII, sC2C, sC1,2C, sColl2–1 NO2, sCOMP, sHA, and sMMP (u=urinary, s=serum). First, using principal component analysis (PCA), the individual markers were reduced into a number of clusters of markers (components) that may represent common underlying domains. Second, a hierarchical cluster analysis (HCA) was performed to differentiate between longitudinal courses (phenotypes) of these marker clusters. The optimum number was determined from the additive value of each newly identified phenotype as compared to already identified phenotypes. Third, these longitudinal phenotypes were compared with regard to percentages of patients in each of the JSL and/or pain progression categories.

Results: PCA showed an optimal solution of three components. Looking at the markers that loaded maximally onto each of the components, they were interpreted as cluster of bone (sCTX-I, uαCTX-I, uβCTX-I, sNTX-I, uCTX-II), cartilage (sCPII, sC2C, sC1,2C, sColl2–1 NO2), and synovial (sCOMP, sHA, and sMMP) metabolism, respectively. HCA revealed an optimum of seven longitudinal phenotypes. Based on the relative predominance of the component(s) throughout follow-up, phenotypes were named “high bone”, “high cartilage”, “high synovium”, “low cartilage”, “low synovium”, “low bone, cartilage and synovium” and “low bone and high synovium” phenotype, respectively (Figure 1, dendrogram and heatmap). Phenotypes differed with regard to percentages of patients in JSL and/or pain progression categories (Figure 1, pie charts) as well as other demographic, clinical, and radiographic parameters (data not shown).

Figure 1: Heatmap depicting scores for the bone (bone), synovium (syno), and cartilage (cart) component for individual knee OA patients at baseline (0), 1 year (1), and 2 years (2). Patients were classified into seven phenotypes using HCA, represented by the dendrogram at the left side. Percentages of subjects in the pain, JSL, pain+JSL, and no progression subgroups in each of the phenotypes are represented in the pie charts at the right side.

Conclusions: Seven longitudinal phenotypes of knee OA could be identified based on biochemical markers representing bone, cartilage and synovial metabolism. These phenotypes showed relevant differences in other characteristics, such as JSL and/or pain progression.

References:

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SAT0500 SLEEP DISTURBANCE, KNEE INFLAMMATION, AND SYMPTOMS IN KNEE OSTEOARTHRITIS

C.K. Kwok¹, E. Ashbeck¹, A. Guermazi², F.W. Roemer^{2,3}, S. Parthasarathy⁴.

¹Univ. of Arizona Arthritis Center, Univ. of Arizona (UA), Tucson; ²Radiology, Boston Univ., Boston, United States; ³Radiology, Univ. of Erlangen-Nuremberg, Erlangen, Germany; ⁴UAHS Center for Sleep & Circadian Sciences, UA, Tucson, United States

Background: Sleep disturbance has been shown to contribute to systemic inflammation, as well as increased pain sensitization. The role of sleep disturbance in knee osteoarthritis (OA) has not been established. Sleep disturbance may be an aggravating contributor to and/or a consequence of knee OA symptoms, with inflammation serving as a potential mediator.

Objectives: To compare knee symptoms over nine years of follow-up by