hypermobility group (7.26±0.46) vs. the non-hypermobility group (7.42±0.64) (p=0.04). The ages of the 120 participants in the knee examined subgroup were similar (hypermobility 51.2±15.8 years, non-hypermobility 57.6±15.8 years, p=0.06). The hypermobility group showed consistently lower odds of hand OA (Table 1). The hypermobility group also showed a lower odds of knee OA. By logistic regression, hypermobility was associated with a decreased likelihood ratio of knee OA (p=0.012); however, after controlling for age, the strength of the association was borderline significant (p=0.05). The hypermobility group also demonstrated significantly fewer OA affected PIP joints by examination (Table 2).

Conclusions: This cross-sectional study agrees with our previous study in a separate cohort showing that hypermobility protects against OA of the PIP joints. We observed a similar trend for OA of the DIP joints. This study suggests that joint hypermobility might serve as a quantitative trait for identifying a protective gene for OA.

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SEARCH FOR POTENTIAL OA OUTCOME BIOMARKERS - "MULTIMARKER APPROACH"

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Purpose: Identification of a panel of biochemical markers to serve as surrogate biomarkers for measuring early efficacy of DMOAD therapies in OA clinical trials.

Methods: Urine, serum, and plasma cross-sectional samples were collected from healthy and OA human subjects with symptomatic OA; n = 22, subjects with no symptoms but radiographic signs of OA (ROA) in knee/hip joints (n = 30), or ROA in hand/spine joints (n = 18), and in subjects with no symptoms or radiographic signs of OA (n = 12)). The diagnosis of symptomatic OA (SOA) was based on a combination of pain or stiffness on most days of a month during the past year and the presence of radiographic OA as defined by Kellgren and Lawrence grades (KLG) 2 and 3. Samples were analyzed for the levels of cartilage, bone, and synovium matrix degradation and synthesis markers as well as for markers of inflammation. Collagen type I neoepitope (TINE), type II (TIINE), type III (TI-III), aggrecan neoepitope (Agg), and osteopontin peptides were measured in urine by in-house developed LC-MS/MS assays. In plasma, 3-nitrotyrosine (3-NT) and procollagen type II terminal propeptides (PIIINP) were measured by published Elisa assays. Plasma levels of prostaglandin PGE2 and 15-HETE were determined by LC-MS/MS methods. Individual marker data was analysed using one-way ANOVA and Bonferroni’s multiple comparison test. Both principal component analysis (PCA) and partial least squares (PLS) algorithms were applied to the entire set of data.

Results: The levels of CTX-II, TIINE, TIIINE, osteopontin, PIIINP, PGE2, 15-HETE, and 3-NT levels were significantly higher in symptomatic OA patients as compared to other groups (p-values < 0.05 - 0.001). In contrast, plasma levels of NPII and urinary levels of Agg were significantly lower in SOA patients as compared other groups (p-value < 0.001 for NPII, and < 0.05 for Agg). PNP and TINE levels were similar in all groups (p-value = 0.4). The ratio of CTX-II or TIINE to NPII enhanced the differences between SOA patients and other groups. Levels of Agg marker were higher in the ROA in knee/hip group as compared to no ROA or SOA groups (p value < 0.05). Unguided PCA analysis was able to differentiate SOA subjects from the subjects with ROA in knee/hip, hand/spine, and no ROA. Five markers including PIIINP, pPGE2, 15-HETE, TIINE, and NP2 contributed most to the separation. Application of PLS-DA model allowed for the separation of ROA in knee/hip group from the ROA in hand/spine and no ROA. The most important markers contributing to this separation were Agg, TIINE, PIIINP, PGE2, and 15-HETE.

Conclusions: Application of biomarkers reflecting joint matrix protein degradation and synthesis as well as inflammation may provide a means of distinguishing subjects with symptomatic OA from subjects showing only radiographic OA in knee/hip.

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CARTILAGE LONGEVITY: A PROGNOSTIC OA BIOMARKER COMBINING BIOCHEMICAL AND MRI-BASED CARTILAGE MARKERS

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Purpose: The study population selection criteria are essential for the study outcome - without a high risk of progression in the population it left untreated, no treatment will have any chance of demonstrating an effect. The fundamental differences between biochemical and MRI-based biomarkers suggest that combinations may be appropriate. The purpose of this study was to evaluate whether an aggregate prognostic biomarker targeting cartilage longevity provided better performance than the individual markers.

Methods: A randomized population of 159 subjects was prospectively selected with age 56.2±15.8, 48% female, and BMI 26.3±4.2. Radiographs were acquired in a semi-flexed load-bearing position using the SynaFlex. MRI scans were acquired on a 0.18T Esaote scanner (Turbo 3D T1: 40° FA, TR 50 ms, TE 16 ms, 0.7 x 0.7 x 0.8mm3, time 10 min). Radiographs and MRI were acquired at baseline (BL) and at follow-up (FU) after 21 months. Fasting morning urine samples were collected (second void) at BL. 288 left and right knees were used in the study at BL (after 25 knees were used for training of computer-based methods) and 245 knees at FU. The Kellgren and Lawrence (KLG) score was evaluated from the radiographs in the medial tibio-femoral compartment and cartilage volume, mean thickness, congruity (a measure of the surface curvature), surface smoothness, and homogeneity (the entropy of the cartilage intensity distribution) were quantified by a fully automatic, computer-based framework in the medial tibial (and femoral) compartments. Urinary levels of collagen type II C-telopeptide fragments (uCTX-II) were mea-