no radiological evidence of OA (KL<2). The longitudinal data was analyzed using generalized least squares adjusted to JSN score and height with a covariance structure grouped by subject and using time as continuous covariate.
Results: From the 133 analyzed subjects, 18 subjects met the analysis criteria (KL<2). Table 1 shows the results of the quantitative analysis of change.
Conclusions: Our results show that a significant proportion (74% to 83%) of subjects with frequent knee pain and stiffness and KL scores lower than 2 had statistically significant changes in articular cartilage thickness at the WB regions. Based on these results subjects with OA symptoms but no radiographic evidence of OA may be staged and monitored for disease progression. The SRM of the mean on the order of 0.8 allows the design of clinical trials of reasonable size for this kind of population.

113

A DECREASE IN SERUM LEVEL OF MATRIX METALLOPROTEASES IS PREDICTIVE OF A DRUG'S DMOAD EFFECT ASSESSED BY QUANTITATIVE MRI IN KNEE OSTEOARTHRITIS PATIENTS

J.-P. Pelletier[1], J.-P. Raynauld[1], J. Caron[1], F. Mineau[1], F. Abram[2], M. Dorais[3], B. Haraoui[1], D. Choquette[1], J. Martel-Pelletier[1]
[1]Univ. of Montreal Hosp. Res. Ctr. (CRCHUM), Montreal, QC, Canada; [2]ArthroVision Inc., Montreal, QC, Canada; [3]StatSci. Inc., Montreal, QC, Canada

Purpose: To explore in a Phase III clinical trial in knee osteoarthritis (OA) patients, the impact of disease-modifying OA drug (DMOAD) treatment on biomarker levels.
Methods: 161 knee OA patients (according-to-protocol population) were selected from a two-year DMOAD trial studying the effect of licofelone (200 mg bid) versus naproxen (500 mg bid). MRI was done at baseline and two years. Patients underwent clinical evaluation using the WOMAC questionnaire. Seven OA biomarkers were measured at baseline and two years: MMP-1, MMP-3, IL-6, CRP, COMP, and CTX-I in serum, and CTX-II in urine.
Results: Over time an increase in all biomarker levels was found with the exception of IL-6, CRP, and CTX-II, which decreased. The increase in MMP-1 and MMP-3 was significantly less ($p<0.05$; $p<0.0001$) in the licofelone than the naproxen group. The MMP-1 level at baseline was a significant predictor (inverse correlation) of cartilage volume change for the medial compartment (univariate, p=0.043; multivariate regression analysis, p=0.038) and COMP, a positive predictor for the lateral compartment (univariate $p<0.0001$; multivariate $p<0.002$). IL-6 and CRP also presented a significant relation to the volume change for the medial compartment but only in the univariate model (p=0.038 and p=0.007, respectively). A significant association was observed in the univariate model between the change in the level of MMP-1 (p=0.034), MMP-3 (p=0.019), and cartilage loss (lateral compartment) over two years. Baseline levels of CTX-I correlated (p=0.02) with increase in bone marrow lesion size in the medial compartment. The CRP levels at baseline correlated positively with worsening of symptoms: WOMAC total index (p=0.0009), pain (p=0.002) and function (p=0.001).
Conclusions: This study demonstrated that higher baseline values of IL-6, CRP, and COMP were predictive of a greater risk of OA cartilage loss. However, over time a reduction in the MMP-1 and MMP-3 levels correlated best with a reduction in the loss of cartilage and the effect of drug treatment. The baseline CRP was found to be a good predictor of the symptomatic response to treatment.

114

THE MITOCHONDRIA-RELATED PHENOTYPE IN THE OSTEOARTHRITIS DISEASE

I. Rego-Perez[1], M. Fernandez-Moreno[1], M. Deberg[2], S. Pertega[3], C. Fernandez-Lopez[1], N. Oreiro[1], M. Acasuso[4], V. Bonome-Gonzalez[5], Y. Henrotin[2], F.J. Blanco[1]
[1]Osteoarticular and Aging Res. Lab. Rheumatology Div. INIBIC-Complejo Hosp. Univ. A Coruña, A Coruña, Spain; [2]Bone and Cartilage Res. Unit. Univ. of Liege, Liege, Belgium; [3]Epidemiology Unit. INIBIC-Complejo Hosp. Univ. A Coruña, A Coruña, Spain; [4]Centro de Salud San José - SERGAS, A Coruña, Spain; [5]Centro de Salud Matogrande - SERGAS, A Coruña, Spain

Purpose: Recent evidences led to the conclussion that mitochondria mediate in the pathogenesis of the osteoarthritis (OA). Biomarkers are a promising tool to detect patients with OA preferably in an early stage of the disease. In this work we aim to assess a mitochondria-related phenotype in patients with OA.
Methods: We analyzed the results from our previous determinations of serum levels of several OA-related biomarkers such as MMP-1, MMP-3, MMP-13, MPO, Coll2-1 Coll2-1NO_2, C2C, CPII, hyaluronic acid, YKL-40, COMP and cathepsin K, in 48 OA patients and 52 healthy controls carrying the haplogroups H and J, to perform logistic regression models and receiver operating characteristic (ROC) curves that permit us to predict diagnosis of OA. This models also included clinical variables such as gender, age and smoking status.
Results: The MMP-13 was the only biomarker significantly increased in OA patients, when compared with healthy controls, in both mtDNA haplogroups H and J ($p<0.001$). Type II collagen biomarkers such as Coll2-1, Coll2-1NO_2, Coll2 ratio, C2C, CPII and C2C:CPII ratio were significantly increased in OA patients that carry the mtDNA haplogroup H when compared with OA carriers of the mtDNA haplogroup J ($p<0.01$ in all cases). Two logistic regression models for diagnosis, adjusted for age, gender and smoking status, were constructed. For haplogroup H, the regression model obtained showed that the biomarkers significantly associated with OA were hyaluronic acid and C2C:CPII; the area under the curve (AUC) of the ROC curve for this model was 0.926 (95% CI=0.857-0.995) and the optimal probability cutoff for discriminate between OA and healthy controls was 0.269, with a sensitivity of 96%, a specificity of 78%, and a positive likelihood ratio of 4.3. For haplogroup J, the biomarkers significantly associated with OA were MMP-13, MMP-3 and C2C; the AUC for this model was 0.880 (95% CI=0.782-0.978), and the optimal probability cutoff for discriminate between OA patients and healthy controls was 0.271, with a sensitivity of 96%, a specificity of 68%, and a positive likelihood ratio of 3.
Conclusions: The MMP-13 appears to be a good candidate diagnosis biomarker for OA. Some of the OA-related biomarkers clearly show a different profile depending on the mtDNA haplogroup. This permitted us to perform two models of diagnosis of OA haplogroup-based.

115

ASSOCIATION BETWEEN ADIPOKINES AND PROGRESSION OF HAND OSTEOARTHRITIS

E. Yusuf, A. Ioan-Facsinay, J. Bijsterbosch, J.C. Kwekkeboom, P.E. Slagboom, T.W. Huizinga, M. Kloppenburg
Leiden Univ. Med. Ctr., Leiden, Netherlands

Purpose: Obesity is a major risk factor of osteoarthritis. The link between obesity and osteoarthritis (OA) may be explained by the increased joint stress accompanying obesity. However, it does not explain why being obese is also associated with osteoarthritis in non-weight-bearing joints, such as the hands. It is suggested that systemic products of fat with systemic metabolic activity may influence the onset and/or progression of osteoarthritis. We investigated here the association between three most common adipokines: leptin, adiponectin and resistin and the progression of hand osteoarthritis.
Methods: We selected patients with radiographic hand OA (HOA) from the GARP (Genetic ARthrosis and Progression) cohort. In this cohort, Caucasian sibs with predominantly symptomatic OA at multiple sites were included. We defined HOA as Kellgren and Lawrence score ≥ 2 in at least two from 20 hand joints (four proximal interphalangeal joints (PIP's), four distal interphalangeal joints (DIP's), one interphalangeal (IP-1) and one carpometacarpal (CMC-1) on each hand). Using the Osteoarthritis Research Society International atlas, the baseline and 6-years follow-up radiograph were assessed for the joint space narrowing (JSN, grade 0 to 3: 0 normal, 3: severe narrowing) of 20 joints (four DIP's, four PIP's, one IP-1 and one CMC-1) per patient. JSN reflects articular cartilage damage. The radiographs were assessed by two readers in consensus and the intra-class correlation coefficient for intra-reader reproducibility based on 25 randomly selected pairs of radiographs was high (0.87). Progression was defined as a change in JSN above the smallest detectable change (SDC) of 2, reflecting change above measurement error. Baseline serum adiponectin concentration was measured by Bio-Plex Pro Assay (Bio-Rad, USA). With logistic regression analysis odds ratios of hand osteoarthritis progression were computed and transformed to risk ratio (RRs). Adjustments for confounders as age, sex, body mass index (BMI) and family effect were made. We categorized all adipokines in tertiles.
Results: Of 248 included patietns, complete follow-up data were available