TIME DEPENDENT DIFFERENCE IN SYNOVIAL FLUID AND SERUM TYPE II COLLAGEN BIOMARKER C2C AFTER KNEE INJURY – A CROSS-SECTIONAL STUDY

N. Kumahashi1, P. Sward1, L.S. Lohmander2, R. Frobell1, A. Struglics3, Shimane Univ., Izumo, Japan; 1Lund Univ., Lund, Sweden; 2Res. Unit for Musculoskeletal Function, Physiotherapy and Dept. of Orthopaedics and Traumatology, Univ. of Southern Denmark, Odense, Denmark

Purpose: The aim of this cross-sectional study was to analyze the time dependent release of cartilage type II collagen degradative C2C neo-epitope into synovial fluid (SF) after knee injury and to correlate it with serum (SE) C2C, SF- ARGS-aggrecan, SF- cartilage oligomeric matrix protein (COMP), SF- sulfated glycosaminoglycan (sGAG), SF- osteocalcin (OCL), SF- secreted protein acid and rich in cysteine (SPARC), SF- osteopontin (OPN), SF- pro-inflammatory cytokines (IL-1β, IL-6, IL-8, TNF-α) and with structural bone and cartilage injuries as visualized by magnetic resonance imaging (MRI).

Methods: At 0-32 days (n=148, acute phase) or more than 2 years (n=41, chronic phase) after a severe knee injury, 189 patients (29% women, median age 22 years). SF- sGAG was analyzed by the Alcian blue method. SF-COMP (BioVendor), and SF- and SE-C2C (IBEX) biomarkers were analyzed using ELISA according to the manufacturers. SF- ARGS was measured with an electrochemiluminescence (ELCL; from MSD) in-house immunoassay using an anti-aggrecan antibody (AHP0022; Invitrogen) for capture, and a monoclonal anti-ARGS for detection. SF- OCL, OPN, SPARC, IL-1β, IL-6, IL-8 and TNF-α were measured by ELCL multiplex assays according to manufacturer (MSD). We evaluated: (1) the correlation between SE- and SF-C2C concentrations and other cartilage and bone markers and cytokines; (2) the relationship between SF-C2C concentrations in the acute phase and the presence and severity of osteochondral fracture, and anterior cruciate ligament, meniscus and cartilage injuries by 1.5 Tesla magnetic resonance imaging (MRI). Statistical analyses were performed using One way-ANOVA for comparison of SF-C2C concentrations depending on time between injury and SF aspiration, ANCOVA in MRI comparisons and Pearson partial correlation for correlation analysis when adjusted for days after injury, age and sex, respectively. In the correlation analysis, biomarkers with skew distribution were log transformed before analysis.

Results: The mean C2C concentration in SF was significantly increased compared to the reference group 1 day after injury (P<0.034, Fig.1) and stayed elevated up to a chronic phase (P=0.014, Fig. 1). SF collected between 4-7 days and 8-32 days after injury had significantly higher C2C levels compared to those collected the same day as the injury (P=0.02 and 0.002, respectively, Fig.1). The SF-C2C concentrations were significantly associated with SE-C2C levels in the acute phase (P<0.001, r=0.611). The acute phase SF-C2C levels were significantly associated with SF levels of ARGS-aggrecan, sGAG, OCL, OPN and inversely associated with IL-8 (Table 1). No correlations were found between the acute phase SF-C2C levels and MRI findings.

Conclusion: The SF-C2C concentration was significantly elevated from day 1 after knee injury and stayed higher than reference levels more than 2 years after injury. The SF-C2C concentrations correlated significantly with SE-C2C in acute period. In the acute phase after injury, the SF-C2C concentration correlated with the aggrecan degradative fragment SF-ARGS, but showed no correlation with structural injuries as visualized on MRI.

KNEE INJURIES ARE ASSOCIATED WITH THE ONSET OF RAPID KNEE OSTEOARTHRITIS: DATA FROM THE OSTEOARTHRITIS INITIATIVE

J.B. Driban1, C.B. Eaton2, G.H. Lo3, M.F. Barbe4, R.J. Ward1, B. Lu5, T.E. McAlindon1, 1Tufts Med. Ctr., Boston, MA, USA; 2Alpert Med. Sch. of Brown Univ., Pawtucket, RI, USA; 3Harvard Hlth.Serices Res. and Dev. (HRS&D) Ctr. of Excellence Michael E. DeBakey VAMC, Houston, TX, USA; 4Baylor Coll. of Med., Houston, TX, USA; 5Temple Univ. Sch. of Med., Philadelphia, PA, USA; #Harvard Med. Sch., Boston, MA, USA; 1Brigham & Women’s Hosp., Boston, MA, USA

Purpose: While knee osteoarthritis (KOA) is typically a slowly progressive disorder, it has recently been appreciated that 5-17% of knees rapidly progress (e.g. from normal to end-stage structural damage within 4 years). Knee injuries are a strong risk factor for KOA and may distinguish knees with rapid KOA from traditional (non-rapid) KOA progression and knees with no KOA. We aimed to evaluate if recent knee injury was associated with rapid KOA.

Methods: In the Osteoarthritis Initiative (OAI) we only studied participants free of any knee OA on their baseline radiographs (Kellgren-Lawrence [KL] < 2). We compared three groups: 1) rapid KOA: at least one knee progressed to end-stage KOA (KL Grade 3 or 4) within 48 months, 2) non-rapid progression: at least one knee increased in radiographic score within 48 months (excluding those defined as rapid KOA), and 3) No KOA: no change in KL grade by 48-month follow-up. At baseline, participants were asked if their knees had ever been “injured badly enough to limit ability to walk for at least two days” and at each annual visit they were asked this question about injuries during the prior 12 months. Among individuals with no KOA we examined if either knee incurred an injury. We first evaluated the distribution of knee injuries among the three groups with Chi-square tests. We then used multinomial