collagen degradation. These results strongly support the use of both assays as discriminating biomarkers for the diagnosis and severity of OC injury in equine joints.

Methods: SF was taken from 2 groups of TB racehorses: (1) rested horses (n = 40) and (2) OC injured horses: racehorses that had arthroscopic surgery for removal of OC fragments resulting from racing injury (n = 44). From group 1 horses, SF was obtained from 20 metacarpophalangeal joints (MCP), 10 middle carpal joints (MCJ), and 10 radiocarpal joints (RCJ) (n = 40). SF samples from group 2 horses were from 16 MCP, 6 metatarsophalangeal joints (MTP), 12 MCJ, and 10 RCJ (n = 44). SF samples were assayed using a commercially available ELISA (HMGB1, Shino-Test Corp.). Differences between groups were determined by an unpaired t-test for the metacarpo/metatarsophalangeal (MP) and carpal joints. Positive and negative predictive value of SF HMGB1 for identifying OC injury was determined by Fisher's exact test. P < 0.05 was considered significant.

Results: SF HMGB1 concentrations in OC injured MP and carpal joints were significantly higher than in normal joints (P < 0.0001; Figure 1). SF HMGB1 concentrations ≥ 11 ng/mL for MP joints and ≥ 10 ng/mL for carpal joints were arbitrarily chosen to determine predictive value for discriminating OC injured horses from normal horses. This yielded a positive predictive value of 89% and a negative predictive value of 68% for MP joints, and positive predictive value of 90% and negative predictive value of 81% for the carpus.

Conclusions: OC injury caused a significant increase in SF HMGB1 concentrations in MP and carpal joints compared to normal joints. The assay yielded good positive and negative predictive values. Based on these findings, SF HMGB1 analysis may be useful for evaluation of joint injury.

Figure 1 Scatter plot of SF HMGB1 concentrations for MP and carpal joints in normal and OC injured TB racehorses. The short horizontal solid lines represent the mean value for each group. ***P < 0.0001.

OSTEOCHONDRAL INJURY INCREASES HIGH MOBILITY GROUP BOX CHROMOSOMAL PROTEIN 1 (HMGB1) IN SYNOVIAL FLUID OF THOROUGHBRED RACEHORSES


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Purpose: Type II collagen is a major component of articular cartilage and is highly specific for this tissue. CP II (cleaved C-propeptide of type II collagen) has been directly correlated with type II collagen synthesis. CTX II (crosslinked C-telopeptide fragments of type II collagen) has been used to assess collagen degradation. The objectives of the current study were to evaluate the effects of osteochondral (OC) injury on type II collagen synthesis (CP II), degradation (CTX II), and the ratio of synthesis to degradation (CPII:CTXII) in synovial fluid (SF) of horses.

Methods: SF was taken from the metacarlo-/metatarsophalangeal or carpal joints of 2 groups of Thoroughbred racehorses: (1) normal rested horses (n = 32) and (2) OC injured horses: racehorses that had arthroscopic surgery for removal of OC fragments resulting from racing injury. From group 1 horses, SF was obtained from 12 metacarpophalangeal joints (MCP), 10 middle carpal joints (MCJ), and 10 radiocarpal joints (RCJ) (n = 32). SF samples from group 2 horses were from 16 MCP, 5 metatarsophalangeal
joints (MTP), 10 MCJ, and 10 RCJ (n=41). CP II concentrations were measured by a commercially available ELISA (CP II, IBEX Technologies, Inc), previously validated for equine use. CTX II concentrations were measured by an ELISA (Pre-Clinical CartilLaps®, IDS Nordic A/S) previously validated for use in equine SF. Differences between groups and joints for CP II concentrations, CTX II concentrations, and the ratio (CP II:CTX II) were evaluated using the Kruskall-Wallis one-way analysis of variance (CPII, CTXII concentrations, and the ratio (CP II:CTX II)) were evaluated using the Kruskall-Wallis one-way analysis of variance with Dunn's multiple comparison test. P < 0.05 was considered significant.

Results: Concentrations of CP II were significantly elevated in SF from the carpal joints of horses with OC injury compared to normal (P < 0.05) (Fig 1A). Concentrations of CP II were significantly elevated in the carpal joints compared to MCP/MP joints in horses with OC injury (P < 0.001). Concentrations of CTX II were significantly elevated in SF from all joints of horses with OC injury compared to normal (P < 0.001) (Fig 1B). There was no significant difference in concentrations of CTX II or CP II between joints in the normal horses. Concentrations of the CP II:CTX II ratio were significantly decreased in SF from all joints of horses with OC injury compared to normal (P < 0.05) (Fig 1C). There was no significant difference in the CP II:CTX II between joints in either group.

Conclusions: Although OC injury caused an increase in type II collagen synthesis in carpal joints, this increase was not seen in MCP/MP joints. Our results clearly show that the increased type II collagen degradation resulting from injury was of greater magnitude than the synthetic response to injury. The inevitable outcome of this metabolic imbalance would be a net loss of type II collagen from the injured cartilage.

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Biomechanics & Gait

[119] BASELINE ARTICULAR CONTACT STRESS IS PREDICTIVE OF INCIDENT SYMPTOMATIC KNEE OSTEOARTHRITIS IN THE MOST STUDY


Purpose: The prevalence of symptomatic knee osteoarthritis (OA) is between 9 and 21% among people age 65 years and older. There is no reliable way to identify this group prior to onset of symptoms. A biomechanical framework might help an epidemiological model predict incident symptomatic knee OA. Discrete element analysis (DEA) is a practical means to estimate contact stress based upon bony articular geometry. Identification of a contact stress threshold, predictive of incident symptomatic knee OA, would enable design of therapies targeted at mechanisms for the association with biomechanical risk factors. The hypothesis tested in this study was that contact stress estimates from baseline knee MRI predict the development of incident symptomatic knee OA by 15-month follow-up.

Methods: This nested case-control study was conducted within the NIH-funded Multicenter Knee Osteoarthritis (MOST) Study cohort of 3026 older adults, age 50–79 years, with or at risk for developing symptomatic knee OA. Thirty cases were randomly selected among MOST subjects at one clinical site who had incident symptomatic knee OA at their 15-month follow-up visit (OA cases), and 30 control subjects (controls), matched by date of MRI, were also selected. At baseline and 15-month follow-up all subjects underwent weight-bearing, fixed-flexion knee radiographs and were surveyed for symptoms. Symptomatic knee OA at the 15-month follow-up visit was defined as frequent knee symptoms and KL Grade of 2 or greater. No eligible knees had this combination at baseline. Investigators were blinded to OA case/control status. For each subject, the articular bony geometry was segmented on the baseline knee MRI (1T Coronal STIR), and the articular surfaces were discretized with a triangulated mesh. Surfaces were registered using radiographs to obtain loaded knee alignment. A distributed array of linear springs, modeling articular cartilage, was distributed between the joint surfaces. Contact stresses were determined from the deformations of the modeled system of springs. Peak contact stress was compared between each OA case and matched control using a two-sided paired t-Test. The areas engaged at discrete contact stress ranges were plotted, normalized to the total articular contact area. Linear mixed model analysis for repeated measures was utilized to examine the association of the logit transformation of the percent area engagement with articular contact stress, OA case/control status, and their interaction.

Results: There were no significant differences between the OA case and control groups with respect to age, sex, body mass index, height or lower limb alignment. However, the peak articular contact stress was 0.54±0.77 MPa (mean±SD) higher in incident OA cases in comparison with control knees (p=0.0007). The level of contact stress at which the OA case subjects continued to have articular surface engagement was significantly higher than that for the control subjects (p<0.0001). Above a threshold of 3.2 MPa, the interaction between OA case-control status and contact stress was significant, demonstrating an association between contact stress over this level and development of incident symptomatic knee OA.