Progression of Osteoarthritis Post-Destabilization in a Female Rat Model

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Background: Treatment of osteoarthritis is predominantly limited to symptom management rather than prevention of this degenerative joint disease. Osteoarthritis affects articular cartilage and subchondral bone of synovial joints. Although after age 50 osteoarthritis is more prevalent in women, most preclinical studies use male animals. To address this gap, we aimed to develop a female rat model of posttraumatic osteoarthritis.

Hypothesis: A destabilizing or impact injury to the knee joint in female rats will induce more severe osteoarthritis than in uninjured rats.

Methods: To induce osteoarthritis, the knee joint was injured using an established drop-tower model. A 90, 120, or 160g metal rod was dropped onto the flexed knee of anesthetized rats. Rats were then sacrificed at 2, 4, 6, 8, 12, or 20 weeks post-injury. Both the contralateral and ipsilateral knees were removed from each subject to be histologically processed and scored by two blinded observers based on grade and stage of osteoarthritis. Additionally, urine was collected at baseline and at time of sacrifice. Blood was collected only at time of sacrifice. CTX-II assays were performed on both urine and serum samples. An assay was performed to detect estradiol levels after extraction from serum samples.

Results: The greatest weight that delivered an impact without frequently fracturing the femur was 160 g. Rats impacted with 120 g scored worse than uninjured control rats but the effect was not statistically significant. Further, impact force did not correlate with score. CTX-II levels in serum and urine did not change during the study. Estradiol did not correlate with score of CTX-II levels.

Conclusions: A drop tower device and standardization of scoring were developed to induce osteoarthritis and to grade it consistently. We did not observe a correlation between serum estradiol at sacrifice and histological or CTX-II outcome, supporting the use of female rats as subjects of osteoarthritis studies. However, we also did not observe osteoarthritis at any timepoint after impact injury in this model. We are currently investigating surgical destabilization of the medial meniscus as an alternative method to drive progression of osteoarthritis in female rats.

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