The Effects of Gender and Female Sex Hormones on Post-traumatic Osteoarthritis

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**Background:** After the age of 50, the incidence of osteoarthritis (OA) in females begins to rise. The etiology is associated with the onset of menopause and the cessation of the cartilage-protective effects of estrogen. Secondarily, women are 2-8 times more likely to sustain a knee joint injury during sports than their male counterparts. Therefore, the cartilage-protective effects of estrogen in the setting of prior joint injury deserve investigation. We developed a post-joint injury animal model to study the effects estrogen and joint injury. The hypothesis was that estrogen-deficient female rats with a simulated meniscal tear would develop the most severe OA than estrogen-intact female rats.

**Methods:** 50 three-month-old Lewis rats were obtained (40 female and 10 male). Ovariectomies were performed on 20 of the female rats. Two weeks following the ovariectomy, a destabilization of the medial meniscus (DMM) was performed on ten ovariectomized rats and ten rats with their ovaries intact. The remaining 20 females had sham operations. The rats were sacrificed at 8 weeks. Urine was collected from the rats at 2 week intervals to be tested for CTX II (a by-product of cartilage breakdown). The males were divided into two groups of 5; 5 with a DMM and 5 with a sham injury. Following sacrifice, the knees were removed and embedded with paraffin for sectioning and staining. Two blinded observers scored the slides according to OARSI guidelines.

**Results:** Estradiol levels were used to confirm ovariectomy. Two ovariectomized rats with elevated estradiol were removed from further analyses. In females, DMM resulted in an increase in cartilage degradation in the injured limb compared to the uninjured limb. DMM-induced cartilage degradation was not more pronounced in the ovariectomized group. Furthermore, ovariectomized rats did not have increased cartilage degradation compared to non-ovariectomized counterparts. In males, DMM resulted in an increase in cartilage degradation in the injured limb compared to the uninjured limb. CTX-II analysis yielded no definitive results.

**Discussion:** DMM induced cartilage degradation in both genders at a time course of 8 weeks. The combination of ovariectomy and DMM did not yield statistically more OA than DMM alone. In previous studies, ovariectomy alone caused cartilage breakdown, however this was not seen in this study partly because of the short time course and species utilized.

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**Key words:** Osteoarthritis; estrogen; Post-traumatic Osteoarthritis