Sex Differences in Knee Cartilage Pressure Distribution Under Functional Loading Conditions: Implications for Knee Osteoarthritis Risk

Ata M. Kiapour, Ph.D.¹, Carmen E. Quatman, M.D./Ph.D.², Samuel C. Wordeman, B.S.², Vijay K. Goel, Ph.D.³, Timothy E. Hewett, Ph.D.², Constantine K. Demetropoulos, PhD⁴.
¹Boston Children's Hospital, Harvard Medical School, Boston, MA, USA, ²The Ohio State University, Columbus, OH, USA, ³University of Toledo, Toledo, OH, USA, ⁴Johns Hopkins University, Laurel, MD, USA.


Introduction: Osteoarthritis (OA) is a major public health problem due to its high prevalence, costs, and levels of pain and disability. Efforts are underway to identify causal mechanisms for the development of OA. While risk factors such as age, obesity, anatomy, injury and genetic profiles have been identified, the sex differences that may affect OA onset are unclear [1]. The study of sex disparities in knee OA has gained substantial momentum as a hot topic for research especially following the Institute of Medicine report in 2001 (Exploring the Biological Contributions to Human Health: Does Sex Matter?) and the 2004 combined AAOS and NIH workshop on "The Influence of Sex and Gender on Musculoskeletal Health." The prevalence, incidence, and severity of osteoarthritis (OA) are different in women than in men, with higher OA prevalence and incidence rates, along with more severe knee OA, in females than males [2]. Despite the well-described effect of sex on the prevalence of knee OA, the mechanisms through which sex affects the cartilage loading, and thus the risk of knee OA, is not well studied. Hence, this study aimed to characterize the role of sex on the knee cartilage pressure distribution under a wide range of physiologic loading conditions experienced by the knee joint during daily activities. We hypothesized that females, compared to males, would have greater magnitudes of peak pressure and shorter center of pressure excursion across the medial compartment of the tibiofemoral joint.

Methods: 16 fresh frozen cadaveric limbs (45±7 yrs, 8 females and 8 males) were sectioned at the mid-femoral shaft and potted with the quadriceps and hamstrings tendons isolated and clamped to simulate muscle forces. Specimens were tested using a custom designed passive 6-DOF of freedom Force Couple Testing System (FCTS). This system utilizes servo-electric actuators to drive a cable-pulley system that generates an unconstrained pure moment through knee range of flexion. A K-Scan sensor (Tekscan Inc, Boston, MA) was used to map tibiofemoral articular pressure distribution. This system allows for the bicondylar tracking of pressure distribution with high resolution (0.1 MPa and 0.1 mm). With the anterior horn of the medial and lateral meniscus dissected from the tibial plateau, the laminated and calibrated sensor was arthroscopically placed into the medial and lateral compartments below the menisci. Care was taken to avoid crinkling of the sensors, while sensors were sutured to the knee capsule to avoid relative translations. Simulated muscle forces (400 N quadriceps and 200 N hamstrings) were used as a baseline. The following loading conditions were applied to each specimen in addition to the baseline, while the specimens were cycled from 0° to 60° of flexion: ±5, ±10 and ±15 Nm of pure abduction, and ±5, ±10 and ±15 Nm of pure internal rotation moments. Data were collected at 100 Hz over four cycles of flexion-extension, and data from the third cycle were used for analysis. The effect of
sex on cartilage pressure distribution was investigated using a multivariate analysis of covariance (MANCOVA) with an a priori level of \( \alpha=0.05 \).

**Results:** Compared to males, females showed greater peak medial compartment pressure under knee adduction and internal tibial rotation moments (Fig 1). These differences were significant for all magnitudes of applied adduction and internal rotation moments \( (p<0.0005 \text{ for all comparisons}) \) except for 5 Nm of knee adduction \( (p=0.282) \). For both sexes, increased knee flexion resulted in a significant decrease in peak cartilage pressure across the medial compartment under knee adduction and internal tibial rotation moments \( (p<0.05 \text{ for all comparisons}; \ Fig \ 1) \). An applied 15 Nm of knee adduction moment resulted in significant increase in peak medial compartment pressure compared to the baseline for both males and females \( (p<0.0005; \ Fig \ 2) \). The changes in maximum peak pressure across the medial compartment due to the applied 15 Nm adduction moment were 3.7±4.9 MPa (132% increase) and 6.1±2.8 MPa (189% increase) in males and females, respectively. The increased peak pressure across the medial compartment due to the applied 15 Nm of knee adduction was significantly greater in females than males throughout the knee range of flexion \( (p<0.1 \text{ for all comparisons}) \). Females also demonstrated significantly shorter center of pressure excursion across the medial compartment compared to their male counterparts under baseline and 5-15 Nm knee adduction moments \( (p<0.05 \text{ for all comparisons}) \). Females showed a significantly longer lateral compartment center of pressure excursion compared to males under all modes of loading \( (p<0.0005 \text{ for all comparisons}) \).

**Discussion:** To our knowledge, this is the first time that sex has been demonstrated to significantly alter the cartilage pressure distribution in human knee under unconstrained functional loading conditions. Females showed significantly greater peak pressures and shorter excursion across the medial compartment compared to the males under identical knee adduction and internal tibial rotation moments. Compared to males, females knees were also more sensitive to knee adduction moment with regard to increased medial cartilage peak pressure. The significantly greater cartilage pressure in females may be due in part to the thinner cartilage than males [3]. Also, the shorter excursion path in females may be a result of greater medial tibial plateau depth (concavity) and a smaller medial meniscus in females than males [4]. This greater concavity and smaller meniscus may act to lock the medial femoral condyle in place and limit its translation across the tibia. The observed combination of higher pressure and shorter excursion likely leads to an increased pressure distribution over a more focused area in the medial cartilage, which likely leads to an increased risk of cartilage wear and degradation, and subsequent OA, in females compared to males. Despite the sex differences in peak pressure across the medial compartment, no significant differences in peak lateral cartilage pressure were observed between males and females. However, females showed a significantly longer excursion path in the lateral compartment than their male counterparts. This is in agreement with previous studies that reported higher rotational knee laxity in females than males [5].

Together, these current findings support our tested hypothesis that significant differences in tibiofemoral joint pressure distribution would be observed between males and females. Given that the medial compartment is the most common site of knee OA, the present findings highlight sex variations in medial compartment pressure distribution as an important potential mechanistic contributor to the higher incidence and severity of knee OA in females than males.

**Significance:** The results demonstrate a significant need for further studies to better characterize the pathomechanistic role of sex on risk of knee OA. This may in turn lead to improved prevention and
rehabilitation strategies designed to decrease the risk and severity of knee OA in particular among women.

Fig 1: Sex-specific differences in peak medial compartment pressure under knee adduction moments (KAM) and internal tibial rotation moments (ITR).

Fig 2: Increased peak pressure across the medial compartment under applied 15Nm of knee adduction moment compared to the baseline.
Fig 3: Sex differences in increased peak pressure across the medial compartment under 15 Nm knee adduction moment compared to the baseline.

ORS 2015 Annual Meeting
Paper No: 0037