Prevalence of Femoral Arthritis of the Hip and Knee Joints in Portuguese Water Dogs from "The Georgie Project": Implications for Genetic Analyses

John G. Skedros[1], J. Hunter Marshall[1], Weston Smith[1], Quinn Smith[1], Meredith G. Luczak[1], Kevin Chase[2]
[1]University of Utah Department of Orthopaedic Surgery and [2]Department of Biology, Salt Lake City, UT
Email of corresponding author: jskedrosmd@uosmd.com

Disclosures: The authors have nothing to disclose.

INTRODUCTION: Osteoarthritis (OA) in canines is defined as the degenerative deformation of the articular surface of joints and is characteristically different from inflammatory arthritis such as septic arthritis [1]. In humans OA has been shown to be more prevalent and more severe in the female population [2, 3]. Conversely in canines, males have shown to suffer from OA more frequently than females [4]. Genetic predisposition is one of the major risk factors for developing OA in canines, and the canine could be a useful translational model for identifying genetic markers for the pathogenesis of OA in humans [5,6]. Canines generally suffer from secondary OA of as a result of trauma, joint laxity, and/or developmental abnormalities [6]. Clinical evaluation of hip and femoral condylar OA has been quantified radiographically in canines by previous investigators [7,8]. In this study we sought to examine the prevalence of femoral OA of the femoral head and condyles according to sex in our large sample of Portuguese Water Dogs (PWDs) from "The Georgie Project," and to describe a method of quantifying femoral arthritis on canine cadavers via direct observation of dissected bones. Additionally we devised a symmetrical method for scoring overall OA of the femur by incorporating the severity of OA of the femoral head and condyles.

MATERIALS AND METHOD: PWD carcasses were obtained from animals that had been autopsied for various organ pathologies in our prior studies from "The Georgie Project" [9,10]. With IACUC approval we examined the right femora (total sample= 415, males= 145, females= 207, unknown sex= 63) from the remaining skeletally mature animals that had been donated for these studies by the animal owners. Age range: 2-16 years old. The right femur from each dog was examined for the presence of femoral head and condylar arthritis. Femoral head OA was quantified on an increasing scale of 0-5 using methods modified from Dennis [7]. Dennis quantified femoral head OA on radiographs, whereas in our sample of dissected femora we were able to directly examine abnormalities (see **Table 1** for numerical assignments given to Dennis' OA grades). Condylar arthritis was also quantified according to a similar modification of radiographic-based methods by Innes et al. [11] on a scale of 0-3. All bones were independently scored by two trained observers followed by an orthopaedic surgeon. There was less than 1% disagreement among the observers. In efforts to quantify the overall average of femoral arthritis we created a bipolar OA score that was representative of the average femoral and condylar arthritis score (here "bipolar" refers to the two ends of the femur). To do this we first reduced the scale of femoral head OA from 0-5 to 0-3 so condylar OA and femoral OA were symmetrically scored, and the scores were combined as shown in **Table 2**. Chi-square analyses were performed using the statistical software program NCSS 2020. For circumstances where expected values in a given cell were <5 we applied the Fisher's exact test.

RESULTS: Chi-squared analyses of the prevalence of femoral head OA, condylar OA, and bipolar OA showed that OA was significantly associated with sex, and that males were more likely to have head OA ($p < 0.01$), condylar OA ($p < 0.01$), and bipolar OA than females ($p < 0.01$). We grouped our sample according to young (<8 years old) and old (≥8 years old) to test the significance of age and OA prevalence. The Fisher's exact test showed that arthritis prevalence was independent of age group for femoral head OA ($p > 0.05$), condylar OA ($p > 0.05$), and bipolar OA ($p > 0.05$). Unpaired t-tests showed that the mean body weight between PWDs with bipolar OA, femoral OA, and condylar OA and those without were not significantly different ($p > 0.5$, $p = 0.3$, and $p > 0.5$ respectively).

DISCUSSION: Body weight was not a significant factor of OA prevalence in our sample, which was not expected because high BMI has been associated as a risk factor for OA in canines [5]. Unfortunately, in our sample we were unable to calculate BMI because we did not have the height of dog at the withers, however high BMI is associated with high body mass. Our results in the PWD breed support conclusions made by previous investigators that, unlike humans, male canines tend to have a higher prevalence of OA [4]. However, severity of arthritis was independent of sex. The sex-related differences of arthritis prevalence suggest a there may be significant genetic implications in the heritability of risk factors for developing OA. Previously our associated lab has reported that, "One QTL identified by the SSR marker, FH2320 on CFA 3[…] is associated with OA [of the acetabulum]" [10]. We are hopeful to further understand the genetic factors involved in the development of both proximal and distal femoral OA (i.e., bipolar arthritis), and the sex-related OA prevalence disparity in the PWD.

SIGNIFICANCE/CLINICAL RELEVANCE: Sex was significantly associated with the prevalence of arthritis in our large sample of purebred Portuguese Water Dogs where males were more likely to present with arthritis, but sex was not associated with the severity of arthritis. "Bipolar arthritis" of the femur in canines warrants further study to see if there are important genetic influences.

REFERENCES: [1] Ajmal and Hayward (1970) J Small Ani Pract 11:197-; [2] Boyan et al. (2013) Biol Sex Differences 4:4-; [3] O'Connor (2007) JAAOS 15:S22-; [4] Anderson et al. (2018) Sci Reports 8:5641; [5] Anderson et al. (2020) Front Vet Sci 7:220-; [6] Gregory et al. (2012) Arthritis: 764621; [7] Dennis (2012) (BVA) In Practice; [8] Wessely et al. (2017) Vet Comp Orthop Traum 30:377-; [9] Chase et al. (2002) PNAS 99:9930-; [10] Chase et al. (2011) Age 33:461-; [11] Innes et al. (2004) Vet Radiol Ultrasound 45:143-.

Table 1

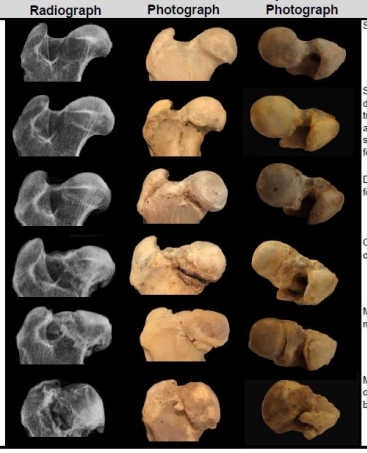
Score	Radiograph	A-P View Photograph	Superior View Photograph	Description: Femoral head and neck exostoses	Description: Femoral head recontouring
0				Smooth, rounded profile	Nil
1				Slight exostosis in 'ring form' and/or dense vertical line adjacent to the trochanteric fossa ('Morgan line'), and/or slight exostosis visible on the skyline and/or density on the medial femoral head	Femoral head does not fit in a circle due to exostosis or bone loss, and/or some bone loss and/or femoral head/neck ring of exostosis
2				Distinct exostosis in 'ring form'	Obvious bone loss and distinct exostosis giving a slight conical appearance
3				Obvious complete collar of exostosis	Gross remodelling. There is obvious bone loss and exostosis gives a mushroom-like appearance
4				Massive exostosis giving a mushroom-like appearance	Very gross remodelling with marked bone loss and much new bone
5				Massive exostosis and infill of the trochanteric fossa and below the femoral head	Femoral head is improperly shaped due to maldevelopment of the femoral head center

Table 2

(Head OA : Cond OA)	Bipolar Scale	Description
[1:1]	1	Mild
[2:1, 1:2]	2	Mild-Moderate
[3:1, 2:2, 1:3]	3	Moderate
[3:2, 2:3]	4	Moderate-Severe
[3:3]	5	Severe