

# Evaluation of the relationship between Orthopedic Foundation for Animals' hip joint scores and PennHIP distraction index values in dogs

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**Objective**—To compare 2 screening methods for detecting evidence of hip dysplasia (Orthopedic Foundation for Animals [OFA] and PennHIP) in dogs.

**Design**—Diagnostic test evaluation study.

**Animals**—439 dogs  $\geq$  24 months of age that received routine hip joint screening from June 1987 through July 2008.

**Procedures**—Dogs were sedated, and PennHIP radiography was performed (hip joint-extended [HE], compression, and distraction radiographic views). The HE radiographic view was submitted for OFA evaluation. A copy of the HE radiographic view plus the compression and distraction radiographic views were submitted for routine PennHIP evaluation, including quantification of hip joint laxity via the distraction index (DI).

**Results**—14% (60/439) of dogs had hip joints scored as excellent by OFA standards; however, 52% (31/60) of those had a DI  $\geq$  0.30 (range, 0.14 to 0.61). Eighty-two percent of (183/223) dogs with OFA-rated good hip joints had a DI  $\geq$  0.30 (range, 0.10 to 0.77), and 94% (79/84) of dogs with OFA-rated fair hip joints had a DI  $\geq$  0.30 (range, 0.14 to 0.77). Of all dogs with fair to excellent hip joints by OFA standards, 80% (293/367) had a DI  $\geq$  0.30. All dogs with OFA-rated borderline hip joints or mild, moderate, or severe hip dysplasia had a DI  $\geq$  0.30 (range, 0.30 to 0.83).

**Conclusion and Clinical Relevance**—Dogs judged as phenotypically normal by the OFA harbored clinically important passive hip joint laxity as determined via distraction radiography. Results suggested that OFA scoring of HE radiographs underestimated susceptibility to osteoarthritis in dogs, which may impede progress in reducing or eliminating hip dysplasia through breeding. (*J Am Vet Med Assoc* 2010;237:532–541)

The integrity of screening tests is paramount to the success of selective breeding to lower the incidence of hip dysplasia in dogs. Despite hip joint-screening programs designed to reduce the frequency of the disease, hip dysplasia continues to have a high prevalence worldwide, and no studies have shown a significant reduction in disease frequency through mass selection (selecting breeding candidates on the basis of their individual phenotypes and not on that of relatives).<sup>1–5</sup> Attending the long history of hip dysplasia in dogs, there has been much debate and controversy regarding whether radiographic evaluations can accurately and precisely identify dogs susceptible to the disease.<sup>1,6–10</sup> Ideally, a radiographic test for a polygenic disease should be based on a continuous metric having high heritability. The test requires optimal diagnostic accuracy and precision, per-

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## ABBREVIATIONS

DI	Distraction index
FCI	Fédération Cynologique Internationale
HE	Hip joint-extended
OA-HD	Osteoarthritis attributable to hip dysplasia
OFA	Orthopedic Foundation for Animals

mitting disease detection at the earliest possible age. Another essential requirement is the ability to use the test results to apply selection pressure to improve hip joint quality. When breeding dogs to improve hip joint quality, selection pressure is applied, for example, by mating 2 dogs with hip joints that are considerably better than average. Breeding 2 dogs with hip joints rated excellent would represent the maximum selection pressure that could be applied through use of the OFA scoring system. The frequency of hip dysplasia in the offspring of such a pairing would ideally represent the lower limit of hip dysplasia incidence achievable in the breed (ie, the best outcome one could achieve through mass selection and applying the maximum selection pressure). Many studies<sup>11–19</sup> have shown that mating dogs with normal (excellent, good, or fair) hip joints by OFA standards will not produce all normal offspring. Rather, 18.8% to 72.7% of the offspring would have hip dysplasia by 2 years of age.

To achieve genetic control of hip dysplasia, an accurate test must minimize false-negative diagnoses (dogs falsely judged hip-dysplasia free). False-negative diagnoses are more harmful to the gene pool than false-positive diagnoses, since the former encourages the breeding of dogs that carry genes coding for hip dysplasia. Particularly for a late-onset disease such as hip dysplasia, dogs remaining in the gene pool must not only be free of obvious signs of hip dysplasia at the time of evaluation (2 years of age for the OFA) but ideally should not be susceptible to the osteoarthritis that can develop with hip dysplasia later in life.

Radiographic diagnosis of hip dysplasia in dogs is based on evidence of osteoarthritis, hip joint subluxation (laxity), or both.<sup>20</sup> The most obvious radiographic manifestation of osteoarthritis includes one or more of the following features: femoral head periarticular osteophyte formation, subchondral sclerosis of the craniodorsal aspect of the acetabulum, osteophytes on the cranial or caudal aspect of the acetabular margin, or joint remodeling from chronic wear. However, degenerative changes take time to develop; therefore, hip joint subluxation (hip joint laxity), which appears early in life, has been adopted worldwide in hip joint-scoring schemes as an indicator of dogs that will ultimately develop OA-HD.<sup>4,8,21–23</sup> The association between hip joint laxity and the degenerative joint disease of hip dysplasia is empirical but so well accepted that subluxation has been added to the definition of hip dysplasia and is, in essence, a radiographic surrogate for hip dysplasia even when radiographic signs of degenerative changes are lacking.<sup>6,20,21,24–30</sup> Hip joint subluxation (laxity) has for decades been considered the initiating factor leading to hip joint osteoarthritis. It is assumed that the process of subluxation during weight bearing leads to abnormal force distribution across the joint, which interferes with the usual development of the acetabulum and femoral head.<sup>11,26,30</sup> Despite the long-term and widespread acceptance of this paradigm, we could identify no reports of studies in which the precise relationship (positive and negative predictive values) was examined between radiographic hip joint subluxation and the ultimate development of OA-HD.

The OFA grading system consists of the following 7 categories of hip joint classification: excellent, good, fair, borderline, mild, moderate, and severe hip dysplasia. This organization, in association with the American Kennel Club, has become a central registry for dogs evaluated for hip dysplasia and other genetic diseases in the United States. As with most hip joint registries worldwide, the OFA permits voluntary submission of films for evaluation and entry into the database for genetic diseases.

Historically, since 1966, the OFA has relied upon the subjective 7-point scoring system applied to ventrodorsal, HE pelvic radiographs of dogs  $\geq$  2 years of age to diagnose hip dysplasia via the relative degree of joint laxity (subluxation), and the severity of osteoarthritis. The optimal age for OFA hip joint evaluation derives from a study<sup>31</sup> that predicted the likelihood of development of hip dysplasia after 5 years of age was negligible. In that study, 95% of the German Shepherd Dogs that ultimately developed radiographic signs of hip dysplasia by 5 years

of age already had these signs at 2 years of age. Accordingly, 2 years of age was selected as a reasonable compromise for timing of hip joint screening in the United States. However, the most commonly used standard for hip joint screening worldwide is to evaluate dogs 1 year of age or older, even though 30% of 1-year-old dogs receive a false-negative diagnosis.<sup>31</sup>

The stress-radiographic method used by PennHIP requires that dogs be sedated or anesthetized and positioned in dorsal recumbency.<sup>6</sup> A standard ventrodorsal, HE radiographic projection is the first of 3 radiographic views. This radiograph is evaluated for evidence of osteoarthritis. Two additional radiographs (compression and distraction) are obtained with hip joints in the neutral position. The compression view shows the femoral heads fully seated in the acetabula,<sup>32</sup> and the distraction view shows the femoral heads displaced laterally by use of a custom distractor.

Calculation of the PennHIP DI involves measuring the relative displacement of the femoral head from the acetabulum on the stress (distraction) radiographic view of the pelvis, and the DI is used to quantify this displacement. The DI ranges from 0 to 1 or higher, with 0 representing full congruency of the hip joint and 1 or greater representing complete luxation. The DI, a measure of passive hip joint laxity, has been correlated with the risk of developing hip joint osteoarthritis in dogs.<sup>22,25,33</sup> Studies<sup>1,6,24,25,33,34</sup> have shown the high sensitivity of the DI for detecting passive hip joint laxity relative to other radiographic methods. The PennHIP DI in dogs as young as 16 weeks of age is significantly correlated with the DI later in life.<sup>22</sup> To avoid the recognized selection bias associated with databases involving voluntary film submission,<sup>35</sup> submission of films to the PennHIP database is mandatory. The purpose of the study reported here was to compare official OFA hip joint scores with measured hip joint laxity (DI) and osteoarthritis susceptibility as determined by use of the PennHIP method.

## Materials and Methods

**Animals**—Dogs  $\geq$  24 months of age evaluated at the Matthew J. Ryan Veterinary Hospital, University of Pennsylvania for routine hip joint screening from June 1987 through July 2008 were eligible for inclusion in the study. To be included, dogs were required to have hip joint radiographs that were evaluated independently by the OFA in Columbia, Mo, and by PennHIP, in Malvern, Pa. As mentioned, voluntary film submission of the OFA is associated with selection bias, meaning dogs with dysplastic hip joints are less likely to receive an official OFA evaluation than are dogs with healthy hip joints.<sup>35</sup> Therefore, this sample did not reflect the total number of dogs that underwent hip joint evaluation at the hospital during the study period.

Standard ventrodorsal, HE radiography as well as compression-distraction radiography was performed for each dog. For both radiographic procedures, dogs were sedated by use of various common sedation protocols. Owners wishing to submit their dogs' radiographs to the OFA were provided with exact copies of the HE radiographs.

The compression, distraction, and HE radiographs for each dog were submitted in accordance with standard procedure directly to the PennHIP Analysis Center for measurement of hip joint laxity (DI). For each dog, the hip joint with the higher DI (greater laxity) was used for statistical comparison. The DI of the opposite hip joint was used for statistical analysis in situations of unilateral cavitation or severe osteoarthritis. Bony remodeling, as occurs in severe osteoarthritis, distorts the measurement of the DI. Because no laxity score can be provided for hip joints with severe osteoarthritis, dogs that had severe osteoarthritis bilaterally were excluded from the statistical analysis.

**Statistical methods**—Values are reported as mean  $\pm$  SD. Dogs were grouped by OFA score; mean DI was compared for the groups via 1-way ANOVA. Post hoc pairwise comparisons between each group were conducted by use of the Tukey least significant difference test. A linear contrast was computed post hoc to determine whether a linear association existed for the mean DI within each OFA score group. False-negative estimates and negative predictive values were calculated for the OFA diagnoses. The Student *t* test was used to determine the comparability of the DIs of the 4 most common breeds within the sample of dogs (German Shepherd Dogs, Golden Retrievers,

Labrador Retrievers, and Rottweilers) to the DIs of respective breeds in the larger PennHIP database. Statistical analysis was performed with commercially available statistical software.<sup>a,b</sup> For all analyses, significance was set at  $P < 0.05$ . Data for dogs for which a DI could not be calculated from either hip joint were excluded from analysis. Data for dogs designated as borderline were excluded from the false-negative and negative predictive value calculations because borderline is a nondiagnostic category according to the OFA scoring system.

## Results

**Animals**—Routine hip joint screening was performed on 1,357 dogs  $\geq$  24 months of age from June 1987 through July 2008. Of these, 439 (32%) dogs representing 66 breeds received official hip joint evaluation by both the OFA and PennHIP and were included in the study (Table 1). The 4 most common breeds were German Shepherd Dog, Labrador Retriever, Golden Retriever, and Rottweiler. Mean  $\pm$  SD age was  $32.7 \pm 12.3$  months. The distribution of OFA scores among the 439 dogs was as follows: excellent, 60 (13.7%); good, 223 (50.8%); fair, 84 (19.1%); borderline (nondiagnostic designation), 7 (1.6%); mild hip dysplasia, 38 (8.7%); moderate hip dysplasia, 25 (5.7%); and severe hip dys-

Table 1—Number of dogs  $\geq$  2 years of age of various breeds that underwent routine hip joint screening, including both OFA and PennHIP evaluation, at a veterinary teaching hospital from June 1987 through July 2008.

Breed	No. of dogs	Breed	No. of dogs
Afghan Hound	2	Giant Schnauzer	4
Airedale Terrier	6	Golden Retriever	62
Akbash Dog	2	Gordon Setter	12
Akita	12	Great Pyrenees	6
American Bulldog	3	Greater Swiss Mountain Dog	2
American Cocker Spaniel	1	Havanese	4
American Foxhound	1	Irish Setter	5
American Water Spaniel	2	Irish Water Spaniel	1
Anatolian Shepherd	1	Kerry Blue Terrier	1
Appenzeller	1	Komondor	5
Australian Shepherd	8	Kuvasz	1
Belgian Sheepdog	2	Labrador Retriever	40
Bichon Frise	1	Leonberger	4
Bloodhound	1	Miniature Poodle	1
Border Collie	5	Newfoundland	3
Bouvier des Flandres	1	Norwegian Elkhound	5
Briard	4	Old English Sheepdog	1
Brittany	6	Otterhound	1
Bull Terrier	1	Pembroke Welsh Corgi	1
Bullmastiff	4	Portuguese Water Dog	10
Cardigan Welsh Corgi	1	Puli	2
Cavalier King Charles Spaniel	1	Rhodesian Ridgeback	9
Chesapeake Bay Retriever	7	Rottweiler	63
Curly-Coated Retriever	5	Samoyed	2
Doberman Pinscher	2	Shetland Sheepdog	1
English Cocker Spaniel	1	Siberian Husky	1
English Mastiff	7	Spanish Water Dog	1
English Setter	7	Spinone Italiano	2
Fila Brasileiro	2	Standard Poodle	4
Flat-Coated Retriever	10	Standard Schnauzer	1
German Shepherd Dog	35	Vizsla	19
German Shorthaired Pointer	1	Weimaraner	16
German Wirehaired Pointer	2	Welsh Springer Spaniel	4

plasia, 2 (0.5%). Thus, in total, scores for 367 (83.6%) dogs were considered normal (excellent, good, or fair) and scores for 65 (14.8%) were considered dysplastic.

Distraction indices were calculated for 438 dogs in the sample. For 1 dog with bilateral severe osteoarthritis (and an OFA rating of severe hip dysplasia), the DI could not be accurately calculated for either hip joint; therefore, data for this dog were not included in the statistical analysis. Unilateral cavitation was evident in 12 dogs (5

right hip joints, 7 left hip joints), and unilateral severe osteoarthritis was diagnosed in 1 dog. For those dogs only, a DI was calculated for the opposite hip joint, which was then used for statistical analysis. For the 438 dogs with a DI, the mean value was  $0.435 \pm 0.139$ . Thirty-one (52%) OFA-rated excellent dogs had DIs  $\geq 0.30$  (range, 0.14 to 0.61), 183 (82%) OFA-rated good dogs had a DI  $\geq 0.30$  (range, 0.10 to 0.77), and 79 (94%) OFA-rated fair dogs had a DI  $\geq 0.30$  (range, 0.14 to 0.77).

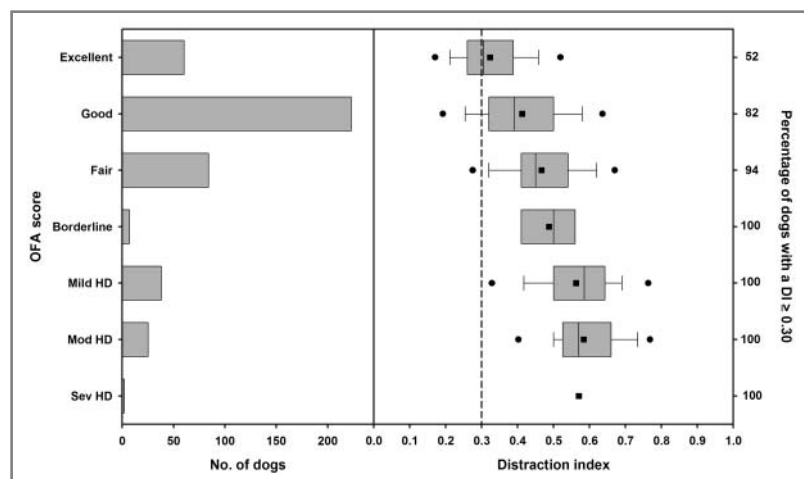


Figure 1—Distribution of OFA scores (left) and associated box-and-whisker plots of DIs (right) for 439 dogs  $\geq 2$  years of age of various breeds that underwent routine hip joint screening at a veterinary teaching hospital from June 1987 through July 2008. In the box plots, the vertical line within each box represents the median, the square in the center represents the mean, the vertical edges of each box represent the 25th (left) and 75th (right) percentiles, and the whiskers represent the 10th (left) and 90th (right) percentiles. Circles represent the 5th and 95th percentiles. The vertical line at a DI of 0.3 indicates the cutoff used to designate osteoarthritis-nonsusceptible ( $< 0.30$ ) and osteoarthritis-susceptible ( $\geq 0.30$ ) dogs. HD = Hip dysplasia. Mod = Moderate. Sev = Severe.

**Comparisons of OFA and PennHIP scores**—Of the 367 dogs judged phenotypically normal by the OFA method, 293 (80%) had a DI  $\geq 0.30$ . All dogs judged by the OFA to be borderline or to have mild, moderate, or severe hip dysplasia had a DI  $\geq 0.30$  (range, 0.30 to 0.83; Figure 1). Within each 0.10 DI interval, respective OFA hip joint scores were tabulated (Table 2). Tighter hip joints as indicated by a DI  $< 0.30$  were always associated with passing OFA scores (excellent, good, or fair); however, passing OFA hip joint scores were only associated with tight hip joints, free of osteoarthritis susceptibility (DI  $< 0.30$ ) 18% of the time.

A significant association was found between OFA scoring category and corresponding mean DI (ANOVA;  $P < 0.001$ ): dogs with a better OFA score when averaged had tighter hip joints as indicated by the DI. Linear contrast analysis revealed a significant ( $P < 0.001$ ), strong linear association between the mean DI within each OFA score group (severe HD group excluded, which consisted of only 2 dogs). Tukey multiple

Table 2—Distribution of OFA scores within each DI interval for 438 dogs  $\geq 2$  years of age that underwent routine hip joint screening, including both OFA and PennHIP evaluation, at a veterinary teaching hospital from June 1987 through July 2008.

DI	Excellent	Good	Fair	Borderline	Mild HD	Moderate HD	Severe HD
0.10–0.19	4	11	1	0	0	0	0
0.20–0.29	25	29	4	0	0	0	0
0.30–0.39	19	73	12	1	3	1	0
0.40–0.49	7	47	34	2	4	0	0
0.50–0.59	4	43	23	3	13	15	1
0.60–0.69	1	13	7	1	16	6	0
0.70–0.79	0	7	3	0	1	3	0
0.80–0.89	0	0	0	0	1	0	0

HD = Hip dysplasia.

Table 3—Values of  $P$  for Tukey least squares difference comparisons of mean DIs between pairs of OFA categories for 438 dogs  $\geq 2$  years of age that underwent routine hip joint screening, including both OFA and PennHIP evaluation, at a veterinary teaching hospital from June 1987 through July 2008.

OFA category	Excellent	Good	Fair	Borderline	Mild HD	Moderate HD
Excellent	—	—	—	—	—	—
Good	$< 0.001$	—	—	—	—	—
Fair	$< 0.001$	$< 0.001$	—	—	—	—
Borderline	$< 0.001$	0.107	0.662	—	—	—
Mild HD	$< 0.001$	$< 0.001$	$< 0.001$	0.128	—	—
Moderate HD	$< 0.001$	$< 0.001$	$< 0.001$	0.062	0.499	—

HD = Hip dysplasia.  
 — = Not applicable.  
 A value of  $P < 0.05$  was considered significant.



Table 4—Comparison of hip joint laxity scores (DIs) for 4 breeds of dogs that underwent routine hip joint screening (both OFA and PennHIP methods) at a veterinary teaching hospital (study dogs) with DIs for all dogs of those breeds in the PennHIP database.

Breed	Data source	No. of dogs	Mean $\pm$ SD DI	Mean difference	P value
German Shepherd Dog	PennHIP database	1,382	0.4083 $\pm$ 0.1155	0.0820	< 0.001
	Study dogs	35	0.3263 $\pm$ 0.1156		
Golden Retriever	PennHIP database	2,839	0.5217 $\pm$ 0.1246	0.0199	0.212
	Study dogs	62	0.5018 $\pm$ 0.1123		
Labrador Retriever	PennHIP database	3,667	0.4663 $\pm$ 0.1331	-0.009	0.671
	Study dogs	40	0.4753 $\pm$ 0.1378		
Rottweiler	PennHIP database	647	0.4907 $\pm$ 0.1272	0.0426	0.011
	Study dogs	63	0.4481 $\pm$ 0.1194		

A value of  $P < 0.05$  was considered significant.

comparisons revealed significant differences in mean DI by OFA category (Table 3). The mean DI for OFA-rated excellent dogs was significantly smaller (tighter) than that of dogs classified as good, fair, borderline, mild hip dysplasia, and moderate hip dysplasia. The mean DI for OFA-rated good dogs was significantly different from mean DIs of the other diagnostic groups (ie, was looser than excellent and tighter than fair, mild hip dysplasia, and moderate hip dysplasia) but was not different from that of the nondiagnostic borderline group. The mean DI for OFA-rated fair dogs was significantly different from mean DIs for all diagnostic groups (ie, was looser than excellent and good and tighter than mild and moderate hip dysplasia) but was not different from that of borderline dogs. The mean DI for OFA-rated mild hip dysplasia dogs was significantly different (looser) from mean DIs for excellent, good, and fair groups but was not different from that of dogs with borderline or moderate hip dysplasia. In addition, the mean DI for OFA-rated moderate dysplastic dogs was significantly different (looser) from mean DIs for excellent, good, and fair groups but was not different from the DI for dogs with borderline or mild hip dysplasia.

Results for 431 dogs were grouped into 2 OFA categories (dysplastic and normal) and 2 DI categories (osteoarthritis-susceptible [DI  $\geq 0.30$ ] and osteoarthritis-nonsusceptible [DI  $< 0.30$ ]). In all, 64 dogs were classified as dysplastic and osteoarthritis-susceptible, 0 dogs were classified as dysplastic and osteoarthritis-nonsusceptible, 293 dogs were classified as normal and osteoarthritis-susceptible, and 74 dogs were classified as normal and osteoarthritis-nonsusceptible. Thus, the proportion of false-negative results was 82% (293/357) for the OFA diagnoses (7 borderline dogs and 1 severe bilateral dysplastic dog not included).

A negative predictive value of 20% (74/367) was calculated, meaning that 20% of the dogs were accurately diagnosed by the OFA as normal (ie, not susceptible to the OA-HD).

Mean hip joint laxity in the 4 most common breeds (German Shepherd Dog, Labrador Retriever, Golden Re-

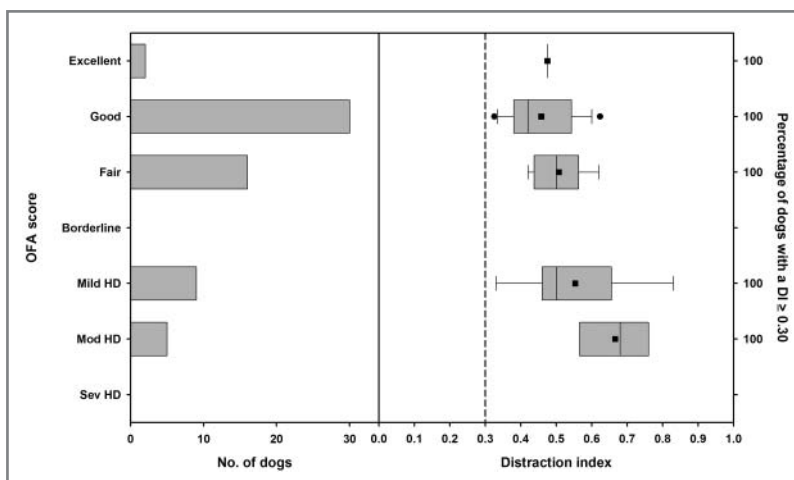


Figure 2—Distribution of OFA scores (left) and associated box-and-whisker plots of DIs (right) for 62 Golden Retrievers  $\geq 2$  years of age that underwent routine hip joint screening at a veterinary teaching hospital from June 1987 through July 2008. See Figure 1 for key.

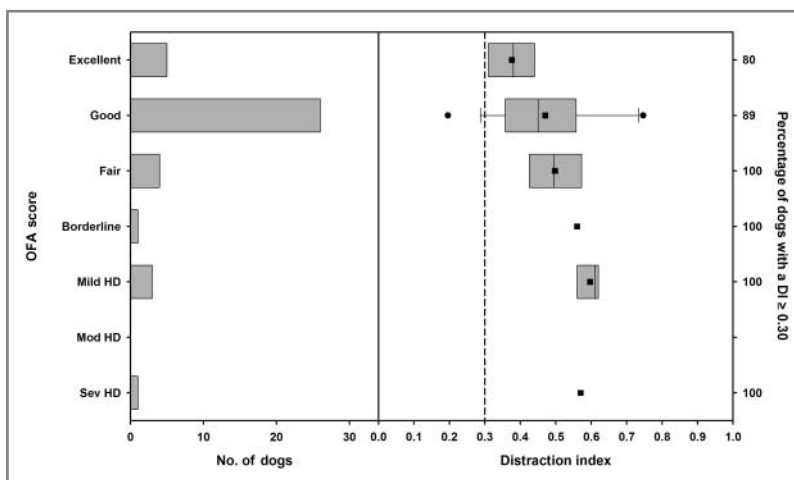


Figure 3—Distribution of OFA scores (left) and associated box-and-whisker plots of DIs (right) for 40 Labrador Retrievers  $\geq 2$  years of age that underwent routine hip joint screening at a veterinary teaching hospital from June 1987 through July 2008. See Figure 1 for key.

triever, and Rottweiler) among the 439 study dogs was compared with the mean hip joint laxity of the corresponding breeds in the larger PennHIP database (Table 4). The mean DIs for study German Shepherd Dogs and Rottweilers were significantly smaller (hip joints tighter) than the cor-

responding means in the PennHIP database. Mean DIs for study Labrador Retrievers and Golden Retrievers were not significantly different than the corresponding mean DIs in the PennHIP database. Data from Golden Retrievers and Labrador Retrievers from the study were used to determine breed-specific relationships (Figures 2 and 3). The OFA certified for breeding (ie, rated as excellent, good, or fair) 77% of the Golden Retrievers and 88% of the Labrador Retrievers. Of the OFA-certified Golden Retrievers and Labrador Retrievers, 100% and 89%, respectively, were judged as osteoarthritis-susceptible by the DI method. There was no significant difference in mean DIs for the 3 passing OFA categories (excellent, good, and fair) for either Labrador Retrievers or Golden Retrievers.

## Discussion

In dogs, hip dysplasia is defined by radiographic evidence of hip joint laxity or signs of osteoarthritis, with passive hip joint laxity early in life as the primary risk factor for later development of osteoarthritis.<sup>6,11,20,24–30</sup> In the present comparison of 2 hip joint scoring methods (OFA score and PennHIP DI), a wide range in passive hip joint laxity as measured by DI existed in dogs judged phenotypically normal by use of the OFA hip joint score. The discord was often considerable, with some dogs being OFA certified for breeding with DIs as high as 0.77.

Our results confirmed that OFA scoring of an HE radiograph does not reveal the critical occult, passive hip joint laxity associated with osteoarthritis susceptibility.<sup>22,30,34</sup> Ventrodorsal, HE stress radiography of the pelvis has received worldwide acceptance for hip joint screening despite scant scientific evidence to validate the usefulness of this radiographic view and related scoring techniques for detecting hip dysplasia. In addition to the OFA, hip joint screening systems of the European FCI, British Veterinary Association/Kennel Club, and Australian Veterinary Association/Australian National Kennel Club among others rely solely on the HE stress radiograph for hip joint screening.<sup>4,8,36,37</sup> Biomechanical studies<sup>6,38,39</sup> have revealed that passive hip joint laxity as detected via the HE stress radiograph is artificially minimized because of a “windup” of the joint capsule and that neutral positioning of the hip joint reveals the maximum passive laxity distraction method of radiography.

Subjective hip joint scoring of the HE radiograph reportedly has poor interrater agreement, with the same hip joints often receiving vastly different scores from different radiologists.<sup>40,h</sup> An examination of the FCI hip joint screening system revealed poor interrater agreement across 41 observers, leading the authors to conclude that the “FCI screening method for canine hip dysplasia, using the standard HE radiographic view, as currently applied in most European countries, is questionable.”<sup>40</sup>

In the present investigation, dogs with considerable hip joint laxity as judged by DI, and therefore susceptible to hip joint osteoarthritis, were certified for breeding on the basis of the OFA hip joint screening method. Such dogs could be considered false-negative diagnoses, meaning they are phenotypically normal on the HE radiograph at the specific age of evaluation but genotypically abnormal and therefore susceptible to os-

teoarthritis. Evidence<sup>22,24,25,41</sup> from multiple institutions suggests that osteoarthritis susceptibility increases in dogs with DIs  $\leq 0.30$  and that breeds of dogs with a negligible incidence of hip dysplasia such as performance Borzois and Greyhounds have uniformly tight hip joints.<sup>22,42,43</sup> An obvious limitation of the present study was that dogs were not followed longitudinally; therefore, we could not definitively confirm that those dogs with a DI  $> 0.30$  would indeed acquire the osteoarthritis of hip dysplasia if followed long enough. It could therefore be argued that the term false-negative diagnosis has been inappropriately applied. Such an argument, however, would apply equally to the OFA method of hip joint evaluation for which positive or negative predictive values of hip joint subluxation seen on the HE view have not been determined or published. According to the OFA grading system, laxity (subluxation) alone without radiographic signs of osteoarthritis equates to a diagnosis of hip dysplasia,<sup>44</sup> even though long-term studies have not confirmed that subluxation will ultimately result in osteoarthritis of the hip joint nor is there evidence that dogs without subluxation at 2 years of age will remain free of OA for life.

A DI of 0.30 is the cutoff between osteoarthritis-susceptible and osteoarthritis-nonsusceptible dogs, and by extension, we believe it scientifically justified to compare OFA scores to this threshold. When this threshold was used, the rate of false-negative diagnoses with the OFA method was 82%. The negative predictive value was extremely low at 20%. There was concordance, however, when comparing mean hip joint laxity (DI) with OFA score: as OFA hip joint score improved, the corresponding mean DI also improved (hip joints got tighter). Because both methods focus on hip joint laxity as a diagnostic metric, it was not surprising that there was a significant correlation of the 2 methods between OFA score excellent  $<$  good  $<$  fair  $<$  borderline  $<$  dysplastic and mean DI for each OFA category. The strength of this correlation has been reported elsewhere.<sup>22</sup> Dogs judged as excellent had a mean DI of 0.32, compared with mean DIs of 0.41 for dogs judged as good and 0.47 for dogs judged as fair. The OFA and PennHIP methods, however, cannot be considered surrogates for each other because of the wide range of DIs within each subjective OFA scoring category. Interestingly, tight hip joints as identified by the PennHIP DI ( $< 0.30$ ) always corresponded to passing OFA scores; however, the converse was not true: passing OFA hip joint scores were associated with a wide range of hip joint laxity as suggested by the DIs, with most dogs having DIs in the osteoarthritis-susceptible range.

Hip dysplasia is a quantitative genetic trait, with multiple genes and nongenetic factors playing a role in disease expression. The principles of quantitative genetics<sup>45,46</sup> dictate that to make genetic improvement in a characteristic such as hip joint status, selection pressure must be applied. Selection pressure is achieved by breeding dogs with better-than-average hip joints for the breed (and preferably much better than average, to make more rapid genetic change). As previously mentioned, the maximal selection pressure that can be applied through use of the OFA scoring system would

be to mate 2 dogs with OFA-rated excellent hip joints. In our study, however, the mean OFA hip joint score fell between fair and good, and according to published OFA data,<sup>5</sup> the mean hip joint phenotype is squarely in the good category. Therefore, the mean OFA hip joint score is only 1 category from excellent. Random selection of dogs from the pool of 60 dogs with excellent hip joints in our sample, while maximizing selection pressure according to OFA scoring, would not result in much selection pressure according to the DI (Figure 1). In fact, the net effect of randomly mating excellent dogs with this distribution of DIs would be to reproduce a similar DI distribution in the progeny (like begets like), meaning 52% of the offspring would be susceptible to osteoarthritis. This particular prediction is based on the population-specific association between an OFA-rated excellent hip joint score with DI in our nonrandom sample of 439 dogs. The prediction may not be generalizable to all breeds and samples of dog: Golden and Labrador Retrievers will be discussed next. For our sample and the breeds therein, it was not likely that continued OFA hip joint screening would result in further improvement in the hip joints of subsequent generations.

An examination of the relationship of OFA score with PennHIP DI in specific dog breeds yielded some interesting observations. For example, only 2 of the 62 Golden Retrievers in the present study received an OFA rating of excellent; however, both dogs had hip joint laxity, with DIs of 0.54 and 0.41. Although a dog breeder would greatly appreciate having dogs with excellent OFA hip joint scores, in fact, breeding these 2 excellent dogs would apply no greater selection pressure with respect to DI than if one were to randomly breed from the pool of Golden Retrievers with OFA-rated good hip joints (Figure 2). Thirty of the 62 Golden Retrievers were OFA-rated good, but all 30 dogs had DIs > 0.30, ranging up to as high as 0.64. Forty-eight (77%) of the Golden Retrievers were considered phenotypically normal by OFA standards, of which 100% had a DI  $\geq$  0.30. There was no significant difference between mean DIs corresponding to each OFA passing category; however, this result could be attributable to small sample size of Golden Retrievers and the few dogs with excellent hip joint scores. As of August 2009, the mean DI for Golden Retrievers in the PennHIP database ( $n = 12,367$ ) was 0.55 and only 1.2% of these Golden Retrievers had DIs < 0.30. Over generations of selective breeding based on the OFA score, some genetic improvement may have taken place, thereby reducing the mean DI of the Golden Retriever breed to 0.55. Correspondingly, the mean DI of OFA-rated normal (excellent, good, or fair) Golden Retrievers in the study was somewhat better at 0.48. The predicament is that breeding Golden Retrievers with OFA-rated normal hip joints would exert scant selection pressure ( $0.55 - 0.48 = 0.07$  DI units). Even breeding Golden Retrievers with good or excellent hip joints would not improve the situation appreciably. The mean DI for Golden Retrievers with OFA-rated good hip joints was 0.46, which is a degree of passive hip joint laxity corresponding to a considerable risk for OA-HD.<sup>24</sup>

Similar to the Golden Retrievers, Labrador Retrievers in the present study that were OFA-rated normal

had a wide range of laxity. Five of the 40 Labradors were judged to have OFA-rated excellent hip joints, with a mean DI of 0.38 (range, 0.29 to 0.50), but 4 of these 5 dogs had DIs in the osteoarthritis-susceptible range. The mean DI for all Labrador Retrievers in the PennHIP database (as of August 2009;  $n = 18,966$ ) was 0.49, and the mean DI of OFA-rated good Labrador Retrievers in our study was 0.47, suggesting that breeding OFA-rated good dogs will result in little selection pressure to make hip joints appreciably tighter (selection pressure =  $0.49 - 0.47 = 0.02$ ) than currently exists. This conclusion is supported by actual OFA data<sup>5</sup>: the mean OFA hip joint score of 102,960 Labrador Retrievers evaluated by the OFA was good (on a 7-point scale, with 1 = excellent and 7 = severe hip dysplasia), meaning that no further genetic improvement would occur by pairing dogs with OFA good hip joint scores. To make further genetic improvement in Labrador Retrievers, one must exclusively breed dogs rated excellent by OFA standards. However, as shown from this study (admittedly small), this would result in 80% of the offspring being susceptible to osteoarthritis according to the DI system. In summary, the high proportion of OFA-rated normal Golden and Labrador Retrievers that harbored excessive passive hip joint laxity in our study, and the small amount of selection pressure that could be applied through their breeding, makes it highly improbable that the continued breeding of OFA-rated normal dogs (excellent, good, or fair) would appreciably improve the breeds' overall laxity profile and related osteoarthritis susceptibility.

From a genetic perspective, the high number of false-negative diagnoses is sobering. In the PennHIP database, there are a few breeds of dogs such as the Cardigan Welsh Corgi that have no members with hip joint laxity < 0.30. In such breeds, it is possible that hip dysplasia is genetically fixed, meaning that the desirable genes that would code for tighter hip joints no longer exist within the breed. Although it may be possible to apply selection pressure to decrease the mean hip joint laxity within such a breed, the laxity profiles would conceivably not cross the DI threshold of 0.30, and while future generations of dogs may have less susceptibility to osteoarthritis, they would all retain some susceptibility. In breeds having only a few members with DIs < 0.30 such as the Golden Retriever (1.2%), it is imperative to methodically apply selection pressure through use of DI as a metric to ward off losing these remaining critical genes. For breeds in which hip dysplasia has become a fixed trait, the only means to replenish desirable genes is to outcross from breeds known to have the desired genes.

A paucity of evidence exists to support the effectiveness of selecting breeding candidates from hip joint screening on the basis of subjective scores of HE radiographs. Several studies involving German Shepherd Dogs have shown that by mating only phenotypically normal dogs (subjectively scored), the number of phenotypically normal offspring ranged from a high of 81.2% to a low of 27.7%.<sup>11,13-19,47</sup> In another study,<sup>3</sup> 10,335 German Shepherd Dogs were evaluated from 1985 through 1997, with the conclusion that "no clear improvement could be found" in hip dysplasia preva-

lence or estimated breeding value when subjective hip joint scores were used as a selection criterion. Only 1 study,<sup>48</sup> to our knowledge, has shown a definitive reduction in hip dysplasia prevalence through selection of breeding dogs on the basis of subjective scoring of ventrodorsal HE radiographs. In that study, through fewer than 5 generations of selection, the prevalence of hip dysplasia in young (12- to 14-month-old) dogs decreased from 30% to 10% in Labrador Retrievers and from 55% to 24% in German Shepherd Dogs. It is important, however, to consider 2 things: first, this reduction was reported for young dogs and no long-term results indicating ultimate hip phenotype were included, and second, this reduction was accomplished through use of estimated breeding values of candidate breeding dogs and not simply via mass selection, the method of selection most commonly used worldwide. The use of estimated breeding values incorporates hip joint scores of relatives of the dogs considered for breeding and is therefore a much more powerful tool to improve hip joint integrity than use of mass selection alone, which bases breeding decisions on the phenotype of the individual dog, exclusive of family members. The breeding value calculation requires meticulous record keeping and knowledge of the pedigree, and it is not commonly used by breeders to select candidate dogs for breeding. Despite the apparent early success in reducing the prevalence of hip dysplasia at The Seeing Eye Inc,<sup>6</sup> further hip joint improvement slowed. Therefore, in 1989, it was decided to incorporate hip joint laxity measured by the PennHIP distraction index to improve the overall health and longevity of the guide dogs.<sup>48</sup> As in the present study, all of the breeding dogs and most of the progeny at The Seeing Eye Inc had radiographically normal hip joints evident on the HE radiograph after 3 to 4 generations of selection, and a method was needed to distinguish hip joint quality among the normal dogs to facilitate making further genetic progress. The Seeing Eye Inc consequently chose to use the DI as a means of assessing hip joint quality.

In the United States, hip joint scoring by the OFA has received the widest use; however, definitive reduction of the incidence of hip dysplasia has not been demonstrated over the years of the scoring system's use.<sup>1-4</sup> The OFA database was used to compare the proportion of dogs with hip dysplasia born between 1972 and 1980 with the proportion of dogs with hip dysplasia born between 1981 and 1988.<sup>2</sup> A comparison of the 3 most popular breeds (German Shepherd Dog, Golden Retriever, and Labrador Retriever) born in the 2 periods revealed no significant change in proportions. It is recognized that the OFA policy of voluntary submission of films for hip joint scoring creates selection bias, making valid prevalence analyses tenuous. In 1 study,<sup>35</sup> the likelihood of hip dysplasia was 10 times higher in dogs that had HE radiographs withheld from submission to the OFA, compared with the likelihood of CHD in dogs that had HE radiographs submitted for official evaluation. It is generally agreed that the prevalence of hip dysplasia is higher than that reported by the OFA.<sup>35,49,50</sup> In the present study, although official OFA reports were received for 439 HE radiographs, it was unknown how many owners intentionally chose not to submit radiographs for OFA evaluation. It is also possible

that some owners submitted radiographs to the OFA without the authors' knowledge. Some information about the possible bias in our study can be estimated by examining mean breed-specific hip joint laxity values for the 4 most common breeds in the study, compared with corresponding mean hip joint laxity values obtained from the larger PennHIP database (Table 4). If prescreening of OFA films took place, then one would expect breed-specific hip joint laxity values from the sample of 439 dogs to be less than (ie, hip joints would be tighter than) that in the larger PennHIP database to which submission of all PennHIP radiographs is mandatory. Such was the situation for Rottweilers and German Shepherd Dogs, with study dogs having significantly better DIs than the overall population. This was not the situation, however, for Golden Retrievers and Labrador Retrievers. The results indicating prescreening bias in this group of Rottweilers and German Shepherd Dogs would mean that an even greater percentage of these breeds would be susceptible to osteoarthritis if selection bias attributable to OFA voluntary film submission did not exist.

In a recent study,<sup>5</sup> 431,483 OFA radiographic scores collected from 1989 through 2003 were analyzed. No reduction in the frequency of hip dysplasia could be documented over the 14-year period either because there was no reduction or, alternatively, because selection bias from voluntary film submission made the assessment unreliable. The investigators, however, believed that it was justified to examine just the dogs that received passing scores by OFA standards, reasoning that prescreening of hip joint films does not substantially distort (bias) the sample of hip joint radiographs received for phenotypically normal dogs. A small increase (0.8% to 3.5%) was evident in excellent OFA scores for Labrador Retrievers, Golden Retrievers, German Shepherd Dogs, Rottweilers, and Bernese Mountain Dogs. Interestingly, a slight reduction in excellent hip joint scores was detected in the pool of dogs made up of all other breeds ( $n = 214,324$ ). The proportion of dogs with OFA-rated good scores increased in the popular breeds by 3% to 5% over the study period. It was concluded that dog breeders can use OFA hip joint classification to improve hip joints of future generations. However, given the findings in the present study, these small percentage improvements in excellent and good subjective hip joint scores over a 14-year period appear clinically unimportant.

The presumption that there is negligible selection bias in OFA scoring for the sample of dogs with phenotypically normal hip joints can be questioned. A study<sup>35</sup> conducted to evaluate bias in the OFA database found that selection bias occurs in film submission for both healthy and diseased hip joints. In that study, 92% of the dogs with failing hip joint scores were not submitted for official OFA analysis, which was not unexpected. However, of the radiographically normal dogs, 50% also did not have films submitted. The study did not explore the reasons dog owners withheld normal hip joint films from official OFA analysis. Such a high degree of selection bias in either direction is attributable to voluntary film submission and makes one question the reliability of hip dysplasia prevalence figures as well as the claimed improvement in hip joint phenotype achieved with OFA hip joint screening.

The integrity of the test used to diagnose hip dysplasia is crucial for reducing the frequency of a quantitative



genetic disease like canine hip dysplasia. The test that is needed is one that yields results not confounded by environmental factors (ie, high heritability), has clinically optimal accuracy and precision, and facilitates the application of substantial selection pressure. The results of the present study are of clinical importance for several reasons, particularly for veterinarians advising breeders. First, in our study, HE radiographs and OFA scoring did not provide critical information needed to accurately assess passive hip joint laxity and therefore osteoarthritis susceptibility. We believe the insensitivity of the OFA method for detecting hip joint laxity is not the fault of the expert radiologist interpreting the HE radiograph but, rather, an inherent deficiency of the HE radiographic view.<sup>38,39</sup> Hip joint subluxation as seen on an HE radiograph markedly underestimated the osteoarthritis susceptibility of a fixed cohort of Labrador Retrievers followed for life in another study.<sup>d</sup> We suspect that all hip joint screening systems based on the HE radiograph have similar diagnostic deficiencies.<sup>41,e,f,g</sup> The second important finding is that continuing the practice of selecting breeding candidates on the basis of OFA scores will provide minimal selection pressure to improve hip joint quality further.

Reliance on subjective scoring of the ventrodorsal HE radiograph of the canine pelvis resulted in failure to appreciate osteoarthritis susceptibility in 80% of the dogs in our study that were judged phenotypically normal by OFA standards. An even greater percentage of false-negative diagnoses may have been appreciated if the dogs in the study were exactly 2 years of age rather than a mean age of 32.7 months. Older dogs have a greater likelihood of having dysplastic signs than do younger dogs.<sup>51</sup> The PennHIP DI is a continuous metric that can predict the risk of OA-HD, and importantly, it can be measured as early as 16 weeks of age.<sup>22</sup> By incorporating passive hip joint laxity as measured by DI with principles of quantitative genetics,<sup>45,46</sup> veterinarians can help breeders make real improvement in the hip joint integrity of future generations of dogs.

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## From this month's AJVR

### Erythrocyte survival time in Greyhounds as assessed by use of in vivo biotinylation

Catherine L. Garon et al

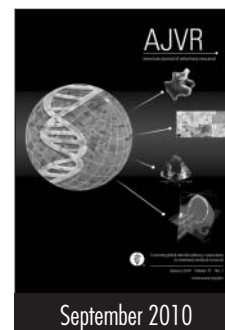
**Objective**—To determine erythrocyte survival time in Greyhounds.

**Animals**—6 Greyhounds used as blood donors and 3 privately owned non-Greyhound dogs.

**Procedures**—In vivo biotinylation of erythrocytes was performed by infusion of biotin-N-hydroxy-succinimide into each dog via a jugular catheter. Blood samples were collected 12 hours later and then at weekly intervals and were used to determine the percentage of biotin-labeled erythrocytes at each time point. Erythrocytes were washed, incubated with avidin-fluorescein isothiocyanate, and washed again before the percentage of biotinylated erythrocytes was measured by use of flow cytometry. Survival curves for the percentage of biotinylated erythrocytes were generated, and erythrocyte survival time was defined as the x-intercept of a least squares best-fit line for the linear portion of each curve.

**Results**—The  $R^2$  for survival curves ranged from 0.93 to 0.99 during the first 10 weeks after infusion of erythrocytes. Erythrocyte survival time for the 3 non-Greyhound dogs was 94, 98, and 116 days, respectively, which was consistent with previously reported values. Erythrocyte survival time for the 6 Greyhounds ranged from 83 to 110 days (mean, 93 days; median, 88 days). As determined by use of in vivo biotinylation, erythrocyte survival times in Greyhounds were similar to those determined for non-Greyhound dogs and did not differ significantly from erythrocyte survival times reported previously for non-Greyhound dogs.

**Conclusions and Clinical Relevance**—Erythrocyte survival time was similar in Greyhounds and non-Greyhound dogs. Greyhounds can be used as erythrocyte donors without concerns about inherently shorter erythrocyte survival time. (*Am J Vet Res* 2010;71:1033–1038)



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