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Genetic evaluation of elbow scores and the relationship with hip scores in UK Labrador retrievers

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ABSTRACT

A linear mixed model analysis of elbow and hip score data from UK Labrador retrievers was used to estimate the heritability of elbow score (0.16–0.19) and to determine a moderate and beneficial genetic correlation with hip score (0.40). A small improvement in the genetic trend of elbow score was observed during the years 2000–2008, equivalent to avoiding only the worst 3–4% of scored dogs for breeding, but close to what may have been anticipated if the current British Veterinary Association-approved guidelines were followed.

Calculations suggested that a correlated response to indirect selection on hip score may elicit a greater response than direct selection on elbow score and that the genetic trend in elbow score may be explained as a consequence of the stronger selection pressure that has been placed on hip score. Increases in the accuracy of estimated breeding values for elbow score of 4–7% for dogs with elbow data only and 7–11% for dogs with both hip and elbow score were observed from bivariate analysis of elbow and hip data. A selection index confirmed the benefits of bivariate analysis of elbow and hip score data by identifying increases in accuracy (directly related to the response to selection) of 14% from the use of optimum coefficients compared to use of hip data only.

The quantified genetic correlation means that hip score effectively acts as a 'secondary indicator' of elbow score in this breed and the preponderance of hip data means that it acts as a major source of information that may be used to improve the accuracy of estimates of genetic risk for elbow dysplasia.

Introduction

Recent studies have demonstrated that the application of quantitative genetic techniques, in particular the calculation of estimated breeding values (EBVs), will lead to substantial improvements in the response to selection against complex canine inherited disease (Malm et al., 2008; Hou et al., 2010; Lewis et al., 2010a,b). Such studies have tended to focus on hip dysplasia (HD) due to the existence of large datasets from longstanding evaluation schemes with good rates of participation. Work is underway in several countries to make available to the public EBVs for HD (as graded by official scoring schemes).

Elbow dysplasia (ED) is another developmental orthopaedic abnormality which has long been recognised as a major problem in the larger pedigree breeds of dog (Hodgman, 1963). Historically, ED has received less attention than HD, with fewer studies researching the underlying genetics and other risk factors. Possibly as a result of this, screening schemes for ED were developed more recently than for HD and, since they have attracted fewer participants, there is still a relative paucity of scoring data.

The term ED is used to describe a number of abnormalities associated with developmental physiological incongruity of the elbow joints that often result in debilitating and incurable osteoarthritis (Hazewinkel, 2007). Incongruity of the elbow, usually either unequal growth of the radius and/or ulna, or dysmorphia of the trochlear notch (the receptacle for the head of the humerus), causes abnormal distribution of pressure within the joint during weight bearing and can lead to fragmentation of immature bone surfaces, termed 'primary lesions' (Samoy et al., 2006).

There are three common types of primary lesion: (1) ununited anconeal process (UAP), (2) fragmented coronoid process (FCP) and (3) osteochondritis dissecans (OCD), although incongruity itself is also often classed as a primary lesion (Hazewinkel, 2007). Surgical removal of loose fragments of bone is only partially successful in curing the associated lameness, possibly due to remaining joint incongruity (Samoy et al., 2006), which can only be corrected by more drastic surgical techniques. Thus, as with HD, genetic selection against ED is the only means to provide widespread and consistent improvement in the welfare of affected breeds.

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The pattern of inheritance of ED is unclear, but the emerging evidence is of a multifactorial complex disease (Maki et al., 2002), although there are possible indications of a major gene effect (Maki et al., 2004). Varying disposition to the specific primary lesions across different pedigree breeds suggests that the primary lesions are different genetic syndromes (Clements, 2006; Hazewinkel, 2006a) and has prompted research into the pathogenesis of ED and the genetic analysis of specific primary lesions (Ubbink et al., 2000; Gemmill and Clements, 2007; Temwichitr et al., 2010).

The sensitivity of radiographs for the detection of primary lesions of ED is known to be sub-optimal, with diagnosis often based solely on the radiographic presence of signs of secondary osteoarthritis (Gemmill and Clements, 2007). Nevertheless, the affordability and technical simplicity of radiographic examination compared to other more sensitive detection methods, such as arthroscopy or CT scan (Hazewinkel, 2006b), have led to its adoption with the hope of encouraging higher participation in screening schemes.

In the UK, an ED scoring scheme based on radiographs is run by the British Veterinary Association (BVA) and the UK Kennel Club (KC) along guidelines set by the International Elbow Working Group (IEWG[1]) and is intended to provide the means for breeders to select against ED.

The genetic parameters for elbow score and the various assessments of HD are important for evaluating not only the potential for selection against ED, but also for taking a bivariate approach to predicting breeding values from the screening data. For example, where the genetic correlation is moderate or strong, there are important benefits from bivariate evaluations, since they offer increased accuracy through the pooling of information across traits, which can be particularly valuable when one disease is more widely, or more rigorously, screened than the other, as is the case with ED and HD.

Estimates of the genetic correlation between ED and HD have been obtained for several breeds (Maki et al., 2002; Malm et al., 2008) and the evidence from those studies with reasonable power suggests that the correlation is weak. This would indicate that selection for improvement in one disease will lead only to a small improvement in the other. However, genetic correlations estimated in one breed are specific to that breed and can only be regarded as a preliminary indicator of the value of the correlation in another breed. Therefore, in breeds with large populations and with active screening programmes for both diseases, such as the UK Labrador retriever, it is important to estimate the genetic parameters for ED and HD that are specific to that breed.

Previous work has examined the genetic parameters for HD in the UK Labrador population (Lewis et al., 2010a,b). However, no corresponding analysis has been made for the accumulated data on ED. Therefore the objective of the present study was to extend the genetic parameterisation of Labradors by estimating the heritability of ED and its genetic correlation with HD. With such parameters for ED and HD, it is possible to quantify the relative value of ED and HD screening data for improving both the accuracy and intensity of selection for ED and to add further information on the underlying genetic relationships between the two diseases, based upon a data set of substantial size. This study uses two approaches to assessing the value of the ED and HD screening data for selection against ED, one based upon empirical accuracies and one based upon selection theory.

Materials and methods

Data

The BVA and the UK KC launched their elbow scoring scheme in 1998. It is voluntary and restricted to dogs over 1-year old to ensure skeletal maturity. Radiographs are taken of the lateral view of the elbow in a flexed and extended position by a veterinary surgeon in general practice, usually while the dog is anaesthetised or heavily sedated. Radiographs are submitted to the BVA and evaluated by two members of a panel of certified veterinary radiologists or small animal surgeons. Each elbow is graded based on the size of detectable primary lesions and the severity and extent of secondary osteoarthritis, with scores assigned as follows[2]: 0, normal, no primary lesion or osteoarthritis; 1, mild ED, presence of osteophytes <2 mm; 2, moderate ED, presence of osteophytes 2–5 mm or a primary lesion but no osteophytes; and 3, severe ED, presence of osteophytes >5 mm or primary lesion with osteophytes of any size (Fluckiger, 2007). The score of the worst elbow only is reported to the owner.

Data on left, right and total elbow scores were obtained from the KC and restricted to dogs scored from 2000 to 2008, since this restriction helped to minimise diagnostic drift. Other data obtained for the same dogs were their sex, coat colour, date of birth and date of radiograph. Data were also restricted to those records where sex was explicitly stated as male or female and coat colour was stated to be one of the 'permitted' colours (i.e. black, chocolate and yellow only) (Lewis et al., 2010a), the age at scoring was within the boundaries of $\geqslant 1$ and <3 years old, or 365–1,094 days inclusive, and the elbow score for each elbow was within the defined boundaries of 0 and 3.

The resultant dataset contained 3,613 single records of elbow score from radiographs. The data were unevenly divided between the sexes, with many more females than males scored: 67–33% (a similar ratio to that observed in the KC pedigree) and age at scoring (2,911 at 1-year-old or 365–729 days, 702 at 2-year-old or 730–1,094 days). The proportions of each colour were close to those in the KC pedigree (black, 53% in study vs. 52% in KC; chocolate, 19% vs. 14%; yellow, 28% vs. 29%, respectively). The records came from 1,298 unique sires, 2,487 unique dams and 2,891 unique litters, with an average of 2.78 offspring per sire, 1.45 offspring per dam, 1.25 records per litter and 1.16 litters per dam. The distribution of records over years of evaluation shows the increase in participation from 2000 (4.2%), 2001 (4.9%), 2002 (5.6%), 2003 (6.3%), 2004 (9.7%), 2005 (13.7%), 2006 (16.1%), 2007 (18.4%) to 2008 (21.2%).

Hip score data also came from the BVA/KC-administered hip score scheme. This scheme is also voluntary and restricted to dogs >1-year-old. Pelvic radiographs are evaluated by the same panel of clinicians as for elbows. The hip score sums the scores of nine features of the coxofemoral joint on both sides to give a total from 0 to 106, where 0 indicates no malformation and higher scores signify greater severity of HD. Left, right and total hip score data used in this study were as described by Lewis et al. (2010a) and consisted of 25,243 records of radiographs of 1- to 4-year-old (365- to 1,459-days-old inclusive) dogs from 2000 to 2007.

In total 26,266 dogs had data included in the study: 2,590 dogs had both elbow and hip score data, 1,023 dogs had elbow score data only (of which 74% were evaluated in 2008, outside the year of evaluation range for hip data) and the remainder had only hip score data. The data records were linked to the KC Labrador retriever pedigree database, using their unique registration number. All ancestors of the dogs with elbow score data were traced back to the founding generation, i.e. where the sire and dam are unrecorded, or to a maximum of four generations (great, great grandsires/dams). As a result, the pedigree used in the univariate analysis of elbow score comprised 17,194 animals and the pedigree used in bivariate analyses consisted of 59,714 animals.

Transformation of score data

Elbow score data is ordinal, with total score having seven classes with scores from 0 to 6. Firstly, the total score was evaluated in untransformed (E) format. Secondly, to address the lack of normality in the data, an underlying and normally distributed liability for elbow score was assumed and analyses were replicated using total elbow scores transformed to the mean value of the liability for the corresponding score, E_L (Table 1). This was done by first calculating the threshold values x_i for $i = 1$–6 for a $N(0, 1)$ distribution, such that the population frequency for grade 0 was given by Φ_1, for grades 1–5 by $\Phi_{i+1} - \Phi_i$ and for grade 6 by $1 - \Phi_6$, where Φ is the cumulative distribution function for $N(0, 1)$. Normal liability scores (s) for elbow grades 1–5 were calculated by:

$$s_i = \frac{\phi_i - \phi_{i+1}}{\Phi_{i+1} - \Phi_i}$$

where 'ϕ_i' is the density function for $N(0, 1)$ evaluated at threshold x_i. The liability scores for the lowest and highest elbow grades were:

$$s_o = \frac{-\phi_1}{\Phi_1} \quad \text{and} \quad s_6 = \frac{\phi_6}{1 - \Phi_6}.$$

Hip score is strongly positively skewed and, where it was to be included in bivariate models with measures of elbow score, it was transformed to better meet normality assumptions using $\log_e(1 + H)$, where H is the total score (Lewis et al., 2010a).

[1] See: www.iewg-vet.org/archive/protocol.htm.

[2] See: www.bva.co.uk/public/documents/Elbow_Dysplasia.pdf.