Comparison of estimates of hip dysplasia genetic parameters in Estrela Mountain Dog using linear and threshold models

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ABSTRACT: Genetic parameters, breeding values, and genetic trends of hip dysplasia in Estrela Mountain Dogs were estimated using a linear model (LM) and a threshold model (TM). A database with 313 animals was used. Right and left hip joints were individually scored, according to the Fédération Cynologic Internationale grading rules of the canine hip dysplasia system, as normal (1), borderline (2), slight (3), moderate (4), and severe (5 and 6). The estimate of repeatability was lower in LM (0.86) than in TM (0.90). The same tendency was verified with the heritability because its estimate in LM was 0.38 and in TM was 0.43. However, these results did not establish any statistical differences between the models. The genetic trend of canine hip dysplasia for LM and TM showed a similarity in shape, but considerable individual differences were found in the EBV ranking lists. Therefore, the selection of breeding animals would not be the same with the 2 methodologies. To select the best method for genetic evaluation of hip dysplasia, further studies using more data and other dog breeds are required.

Key words: dog, genetic parameter, hip dysplasia, linear model, threshold model

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INTRODUCTION

The Estrela Mountain Dog (EMD) is the most popular autochthonous dog breed in Portugal, with approximately 1,000 pups registered each year (Ginja, 2006). Canine hip dysplasia (CHD) has a high prevalence (67%) in the breed (Ginja, 2006). In addition, CHD shows a polygenic inheritance influenced by environmental factors, and estimates of heritability range from 0.1 to 0.6 (Distl et al., 1991). Despite control schemes against the disease in some countries for more than 40 yr using radiographic phenotypic mass selection, the disease continues to affect dog populations (Flückiger et al., 1999; Leppänen et al., 2000). However, BLUP has not been used routinely in such populations. This methodology accounts for all available information simultaneously (environmental effects and relatives), allowing more reliable EBV in dogs (Flückiger et al., 1999).

The scoring of CHD is recorded in classes according to the Fédération Cynologic Internationale (FCI) rules (Morgan and Stephens, 1985). However, most research in genetic parameters has treated CHD as a continuous trait with linear models (LM), thereby ignoring its categorical nature (Lingaas and Klemetsdal, 1990; Mäki et al., 2000). In theory, methods used for analyzing continuous data are not suitable for categorical data (Gianola and Foulley, 1983; Ramirez-Valverde et al., 2001; Hansen et al., 2004). Gianola and Foulley (1983) developed the threshold model (TM) for genetic evaluation of categorical traits. The TM takes into account the asymmetry and extreme incidence of some categories (Arango et al., 2005). However, there is no research regarding the use of threshold models for CHD.

The main objectives of this study were to estimate variance components and genetic parameters for CHD in EMD using LM and TM, and to compare animal evaluations achieved from the 2 methodologies.

MATERIALS AND METHODS

All procedures involving animals were performed with clinical purposes in a canine hip dysplasia control program. The clinical work was conducted in accordance with principles and guidelines outlined by Portuguese animal care and use committee (Direcção Geral de Veterinária, Lisbon-Portugal).
Data

During the period from 2002 to 2006, 313 EMD (197 females and 116 males) were examined at the veterinary medical teaching hospital of the University of Trás-os-Montes e Alto Douro. The age of the screened dogs varied from 12 to 168 mo (28.3 ± 19.6 mo) and the BW from 26 to 65 kg (40.5 ± 7.0 kg). The dogs were sedated using medetomidine (0.02 mg/kg i.v.), butorphanol (0.1 mg/kg i.v.), and atropine (0.02 mg/kg i.v.), and the standard ventrodorsal view of the pelvis was performed, with the coxofemoral joints fully extended and the knees internally rotated, as described in previous work (Morgan and Stephens, 1985).

The FCI grading system for CHD was used in the evaluation of hip radiographs. The form of the femoral head and the acetabulum, joint space, and Norberg angle were checked, and the coxofemoral joints were classified into 5 classes, from A to E (Morgan and Stephens, 1985). The letter E, representing the severely affected joints, was subdivided in E1 and E2, as was suggested in previous work (Mäki et al., 2000). The category E2 represents the most severely affected joints (Norberg angle less than 80° or luxation). This strategy was followed for the reason that apparently in some cases the phenotypic difference between dogs classified with letters D and E is greater than the phenotypic difference between dogs classified with any other consecutive letters (Mäki et al., 2000).

The family structure in the 313 screened EMD consisted of 55 groups of full brothers (3.4 dogs per group) and 73 groups of paternal half-brothers (3.3 dogs per group). Moreover, all known ancestors in 4 generations were considered, resulting in a pedigree file with 843 animals. All the pedigree information was obtained from the Portuguese Kennel Club (Lisbon, Portugal).

Models

Linear Model. In the linear model, the letters A, B, C, D, E1, and E2 were recoded with 1, 2, 3, 4, 5, and 6, respectively. The following linear model was assumed when estimating the variance components as well as the fixed and random effects for hip dysplasia:

\[ y_{ij} = \mu + \text{sex}_i + b_1 w_j + b_2 \text{age}_j + a_j + p\epsilon_j + e_{ij}, \]

where \( y_{ij} \) is the hip dysplasia score on animal \( j \) of sex \( i \), \( \mu \) is the overall mean, \( \text{sex}_i \) is the fixed effect of the \( i \)th sex class (male and female), \( b_1 \) is the fixed regression coefficient, \( w_j \) is the BW of animal \( j \), \( b_2 \) is the fixed regression coefficient, \( \text{age}_j \) is the age of animal \( j \), \( a_j \) is the random additive genetic effect of the \( j \)th animal, \( p\epsilon_j \) is the random permanent environmental effect of the \( j \)th animal with measurements, and \( e_{ij} \) is the random residual effect. In matrix notation, the model can be written as

\[ y = Xb + Za + Wpe + e, \]

where \( y \) is a vector of hip dysplasia scores, \( b \) is a vector of fixed effects, \( a \) is a vector of animal effects, \( p\epsilon \) is a vector of permanent environmental effects and nonadditive genetic effects, and \( e \) is a residual vector; \( X, Z, \) and \( W \) are incidence matrices relating the effects to the scores. The distributions of \( a, p\epsilon, \) and \( e \) were assumed to be normal, with zero mean and with \( \text{Var}(a) = A\sigma_a^2, \text{Var}(p\epsilon) = I\sigma_{pe}^2, \) and \( \text{Var}(e) = I\sigma_e^2 \). Covariances between \( a \) and \( e \) were assumed to be zero. The variance components in the model were estimated by REML using the ASREML software (Gilmour et al., 2000).

Threshold Model. In the threshold model, the observed outcome \( (y_{ij}) \) for hip dysplasia was assumed to be ordered in 6 categories. An unknown liability \( (U_{ij}) \) was assumed with 5 unknown thresholds \( [t = (t_1, ..., t_5)] \), which categorized the observed outcome:

\[ y_{ij} = \begin{cases} 1 & \text{if } -\infty < U_{ij} \leq t_1 \\ 2 & \text{if } t_1 < U_{ij} \leq t_2 \\ \vdots & \vdots \\ 5 & \text{if } t_4 < U_{ij} \leq t_5 \\ 6 & \text{if } t_5 < U_{ij} < \infty \end{cases} \]

For reasons of identifiability and without loss of generality, it was assumed that \( t_1 = 0 \) and \( t_2 = 1 \). In addition, it was assumed that the liabilities conditional on all of the effects were independent and normally distributed:

\[ U|b, a, p\epsilon \sim N(\mu(Xb + Za + Wpe), I\sigma_e^2). \]

The model in matrix notation was similar to the previous one, where \( U \) was a vector of liabilities:

\[ U = Xb + Za + Wpe + e. \]

Variance components and genetic parameters as well as solutions for fixed and random effects in threshold animal mixed models were estimated with THRGIBBS1F90 (Misztal et al., 2002), which is a Fortran90 program using a Bayesian approach via the Gibbs sampling algorithm (Lee et al., 2002). After 10,000 Gibbs samples were discarded as burn-in, 300,000 samples were used to calculate the posterior means and SD for variance components, repeatabilities, and heritabilities, and the highest probability density intervals (Smith, 2005).

Other Statistics

The Spearman’s rank correlation coefficient \( (r_s) \) was used to evaluate the association between EBV attained by LM and TM. Spearman’s rank correlation considers ranked EBV, rather than the EBV itself. Spearman’s method works by assigning a rank to each observation in each group separately. A value of \( r_s \) near 1 indicates good agreement; a value near 0 indicates poor agreement. The Pearson correlation coefficient \( (r_p) \) was used as well. Descriptive statistics based on absolute
values of the ranking position differences were also used to quantify individual differences in ranking positions.

RESULTS AND DISCUSSION

The distribution of hip dysplasia scores by right and left hip joint is shown in Table 1. The high frequency of the most severity grades of CHD (E1 = 11.0% and E2 = 6.4%, Table 1) in the breed contrast with other studies in other breeds (E = 0; Ohlerth et al., 2003) and is in part reflection of an absence of screening programs and breeding strategies.

Variance components and genetic parameter estimates (phenotypic variance, additive genetic variance, permanent environmental variance, residual variance, repeatability, and heritability) of CHD with LM and TM models are in Table 2. The estimate of repeatability was lower in LM (0.86) than in TM (0.90). The same tendency was verified with the heritability; its estimate in LM was 0.38 and in TM was 0.43. Results here achieved for repeatability are in agreement with the assumption that measurements made on right and left hip joints are repeated observations of the same trait. However, no results were found in the bibliography for repeatability of CHD. Estimate of heritability using LM reported by Lingaas and Klemetsdal (1990) and Mäki et al. (2000) was 0.17 and 0.58, respectively. Andersen et al. (1988), who also used TM, reported heritability estimate equal to 0.35. Results reported on this study fall inside this large range. Additionally, approximate confidence intervals for LM and the highest probability density intervals for TM are also in Table 2. In both models, repeatabilities were estimated more precisely than heritabilities as shown by intervals with smaller range of variation. Also, the observed overlapping among intervals does not allow drawing a conclusion about the existence of differences between LM and TM parameters estimations.

The genetic trend of CHD in birth years between 2000 and 2005 for LM and TM, calculated as EBV average by year of birth, are given in Figure 1. The similarity between the shapes achieved by genetic trends with the 2 methodological approaches is evident. The same result was reported in other traits of farm animals by Heringstad et al. (2003) and Hansen et al. (2004). The EBV longitudinal evolution shows moderate decrease of hip quality between birth years 2000 and 2003, and a genetic improvement in 2004 and 2005, because aver-

Table 1. Distribution of hip dysplasia scores by right and left hip joint

<table>
<thead>
<tr>
<th>Category</th>
<th>Right hip joint</th>
<th>Left hip joint</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of dogs</td>
<td>%</td>
</tr>
<tr>
<td>A</td>
<td>67</td>
<td>21.4</td>
</tr>
<tr>
<td>B</td>
<td>55</td>
<td>17.6</td>
</tr>
<tr>
<td>C</td>
<td>82</td>
<td>26.2</td>
</tr>
<tr>
<td>D</td>
<td>54</td>
<td>17.3</td>
</tr>
<tr>
<td>E1</td>
<td>37</td>
<td>11.8</td>
</tr>
<tr>
<td>E2</td>
<td>18</td>
<td>5.8</td>
</tr>
</tbody>
</table>

1The scoring of CHD was recorded in categories according to the Fédération Cynologic Internationale rules (Morgan and Stephens, 1985).

Table 2. Genetic parameter estimates of canine hip dysplasia with a linear model (LM) and a threshold model (TM)

<table>
<thead>
<tr>
<th>Item</th>
<th>LM</th>
<th>TM</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\sigma^2_p$</td>
<td>2.29 ± 0.197</td>
<td>3.81 ± 0.681</td>
</tr>
<tr>
<td>$\sigma^2_a$</td>
<td>0.87 ± 0.297</td>
<td>1.67 ± 0.583</td>
</tr>
<tr>
<td>$\sigma^2_p_e$</td>
<td>1.97 ± 0.197</td>
<td>1.75 ± 0.482</td>
</tr>
<tr>
<td>$\sigma^2_e$</td>
<td>0.31 ± 0.025</td>
<td>0.38 ± 0.073</td>
</tr>
<tr>
<td>R</td>
<td>0.86 ± 0.016</td>
<td>0.90 ± 0.015</td>
</tr>
<tr>
<td>$h^2$</td>
<td>0.38 ± 0.110</td>
<td>0.43 ± 0.113</td>
</tr>
<tr>
<td>Bounds (R)</td>
<td>0.83 to 0.89†</td>
<td>0.87 to 0.93‡</td>
</tr>
<tr>
<td>Bounds ($h^2$)</td>
<td>0.16 to 0.60†</td>
<td>0.21 to 0.65‡</td>
</tr>
</tbody>
</table>

$1\sigma^2_p =$ phenotypic variance, $\sigma^2_a =$ additive genetic variance, $\sigma^2_p_e =$ permanent environmental variance, $\sigma^2_e =$ residual variance, $R =$ repeatability, and $h^2 =$ heritability.

$2$On the underlying scale.

$†$Approximate confidence interval (prediction $± 1.96 \times SE$ of prediction); and ‡highest probability density intervals, $P = 0.95$. 

Figure 1. Genetic trend of canine hip dysplasia per year of birth (2000 to 2005), estimated with A) linear and B) threshold models.
age EBV decrease on those birth years. The mentioned genetic improvement was most likely due to voluntary mass selection based on x-raying after 2002 (Ginja, 2006). The FCI and other grading systems for CHD used in mass dog selection for reproduction are less accurate for measuring genetic differences between phenotypically selected dogs (Swenson et al., 1997). Recognizing CHD as a polygenic trait, LM and TM methodologies allow estimation of BV using all available information (own phenotype, relatives). Records of siblings and ancestors provide early information that could reveal some of the differences among selected dogs, and thereby improve the EBV, compared with estimations based only on individual records (Swenson et al., 1997; Flückiger et al., 1999; Leppänen et al., 2000). Family records have already been shown to be of importance when selecting against CHD in a smaller population of German Shepherd dogs (Hedhammer et al., 1979), and in other traits in farm animals (Tempelman, 1998), being considered the most effective way to further improve the CHD breeding programs, increasing the selection differential and genetic progress (Linggaas and Klemetsdal, 1990; Swenson et al., 1997). Results shown on Table 3 for data set 2 are important because some of these animals are already parents, whereas others are candidates for breeding. Therefore, and from an individual point of view, it must be emphasized that 50% of the dogs occupied positions in the ranking lists for LM and TM with differences greater than 36. Also, the substantial maximum difference of 212 in a ranking list of 313 (Table 3) should be noted. For example, the top 10 ranking list according to LM includes only 1 dog of the TM’s top 10 ranking list. Consequently, these individual differences will have practical consequences for the selection of dogs for breeding.

Table 3. Comparison of estimated breeding values ranking lists for linear and threshold models, considering all individuals (data set 1) and individuals with records (data set 2)

<table>
<thead>
<tr>
<th>Item</th>
<th>Data set 1 (n = 843)</th>
<th>Data set 2 (n = 313)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>183</td>
<td>50</td>
</tr>
<tr>
<td>Median</td>
<td>138</td>
<td>36</td>
</tr>
<tr>
<td>Q1</td>
<td>61</td>
<td>17</td>
</tr>
<tr>
<td>Q3</td>
<td>274</td>
<td>76</td>
</tr>
<tr>
<td>Maximum</td>
<td>656</td>
<td>212</td>
</tr>
<tr>
<td>rs</td>
<td>0.53***</td>
<td>0.73***</td>
</tr>
<tr>
<td>rp</td>
<td>0.55***</td>
<td>0.74***</td>
</tr>
</tbody>
</table>

Q1 = the first quartile, Q3 = the third quartile, rs = the Spearman correlation coefficient, and rp = the Pearson correlation coefficient. ***P < 0.001.

In farm animals, advantages of threshold over linear models have been reported with simulated data (Meijering and Gianola, 1985; Hoeschele, 1988). However, variable results have been found using field data. Similar performance of threshold and linear models (Weller et al., 1988; Matos et al., 1997) and advantages of linear over threshold models (Hagger and Hofer, 1990, Carlén et al., 2006) have been reported. Varona et al. (1999), using only data from large herds and the animal model, showed no advantage of univariate threshold over lin-
ear models for calving ease but superior performance of a bivariate threshold model. Lingaas and Klemetsdal (1990) used LM on CHD, but recommended the future use of TM.

From a practical point of view, LM and TM can be used to perform genetic evaluation of CHD and are preferable to the mass selection. Indistinguishable heritability, repeatability, and genetic trends estimates were attained with both models. However, differences were found between EBV ranking lists. Thus, because LM can only be viewed as an approximation to the TM for categorical data (Gianola, 1982), we recommend the use of a TM for genetic evaluation of EMD for CHD. Nevertheless, low rank correlations between EBV of CHD from a linear and a threshold model found in this study in relation to other categorical traits of farm species need to be confirmed with further studies using more data and other dog breeds. Even with clear theoretical advantages for analyzing categorical data, perhaps due to its more recent implementation, the threshold model has not yet achieved the popularity of the linear model.

LITERATURE CITED


