PREVALENCE AND GENETIC ANALYSIS OF SPONDYLOSIS DEFORMANS IN THE ITALIAN BOXER DOG POPULATION

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INTRODUCTION

The dog is the non-human species for which the largest number of genetic disorders is known, and, to date, over 370 genetic diseases have been documented (Ostrander *et al*., 2000). Some skeletal diseases, namely hip and elbow dysplasia, have been investigated, and genetic parameters for such disorders have been reported (Maki *et al*., 2000 ; Lippanen *et al*., 2000).
Conversely, genetic determinism of other diseases like spondylosis deformans has been less considered. Spondylosis deformans is a degenerative disease of the spine characterised by the presence of one or more osteophytes, showing different degrees of development, placed on the vertebral bodies (Hansen, 1952 ; Morgan, 1967). Severe spondylosis deformans causes stiffness in the back, lameness, change of gait and pain. Hence, reduction of incidence of spondylosis is advisable for increasing welfare and longevity of dogs.
In a survey on approximately 7,000 dogs, spondylosis was the most common disorder in the group of degenerative spinal diseases (Empel and Blenau, 1999). Incidence of spondylosis is particularly large in the Boxer breed (Murlebach and Freudiger, 1973 ; Eichelberg and Wurster, 1982), is higher in females (Eichelberg *et al*., 1989) and tends to increase and to be more severe at increasing age of dogs (Mattoon and Koblick, 1993).
Some studies (Murlebach and Freudiger, 1973 ; Eichelberg and Wurster, 1982) postulated that spondylosis has a genetic basis. Langeland and Lingaas (1995), in a study based on 353 boxers progeny of 24 sires, reported heritability estimates ranging from 0.42 to 0.62 for the maximum degree of osteophyte development and from 0.13 to 0.47 for the number of affected discs, but these estimates exhibited very large standard errors and did not differ significantly from zero.
The present study aimed to assess the prevalence and to investigate genetic aspects of spondylosis deformans in the Italian Boxer dog population.

MATERIAL AND METHODS

The data consisted of screening results of Boxer dogs enrolled from 1997 to 2001 in the spondylosis screening program arranged as a joint effort of Celemasche and the Italian Boxer Club, and included informations on the dates of birth and screening, the sex of the dog, the breeder, and the x-raying veterinarian. Age of animals at x-ray assay ranged from 10 to 84 months (mean ± SD : 20 ± 10 months). Dogs were x-rayed by 156 veterinarians and grading for the degree of development of osteophytes on the spine was carried out using a 4-grades linear system (Langeland and Lingaas, 1995) by a unique responsible. Records were grouped into 6 ages at screening classes (12 months or less, 13-16, 17-22, 23-28, 29-39, and 40 months or more). Linear scores at each intervertebral site (20 sites) were available for 849 dogs (468 females and 381 males) progeny of 329 sires and 552 dams. Pedigrees were provided by the Italian Association of Dog Breeders (E.N.C.I.) and were traced back for as many generations as

available, resulting in a total of 3087 animals in the analysis. Five intervertebral sites exhibited no phenotypic variation and were excluded from the analysis. Statistical analysis was performed considering scores at different intervertebral sites as different traits (15 traits). Effects due to age at screening, breeder and sex were significant ($P < .10$) and were included in final models. Dogs owned by a breeder were x-rayed by the same veterinarian, leading to a confounding of breeder and x-raying veterinarian effects. Estimation of variance components was conducted in two steps : a univariate bayesian analysis performing numerical integration via Gibbs sampling was performed in the first step and a multivariate REML analysis was used in the second step to estimate genetic correlations for different sites. Based on bayesian inference, sites showing a posterior probability of $h^2 > 0.10$ lower than 0.8 were not considered in REML analysis. Bayesian analysis was carried out generating a single Gibbs chain of size 1,200,000, saving samples every 10 iterates and discarding initial 200,000 samples (burn-in). Posterior densities of h^2 and variance components were estimated using a non-parametric density estimation technique based on average shifted histograms. The posterior median was used as point estimate of h^2 and variance components.

RESULTS AND DISCUSSION

Frequency of dogs by number of affected intervertebral sites is reported in Figure 1. Frequency of dogs showing no affected sites was 16% and prevalence of spondylosis in this Boxer population was comparable to that reported by Murlebach and Freudiger (1973), Eichelberg and Wurster (1982) and Langeland and Lingaas (1995) for other populations. Frequency of affected dogs was different for different sites and resulted higher from site T10-11 to site L2-3 and for L6-7 and L7-S1 sites.

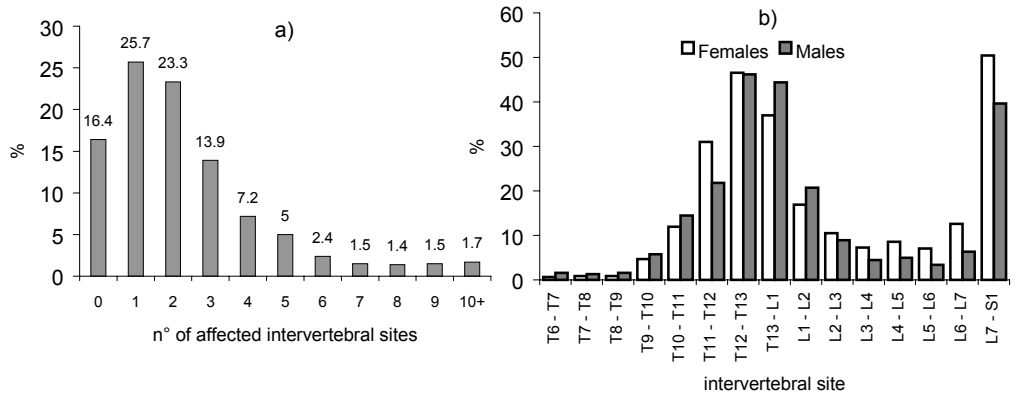

Figure 1. Frequency of dogs by number of affected intervertebral sites (a) and frequency of affected dogs by intervertebral sites (b). Site : T = thoracic, L = lumbar, S = sacral

Summary statistics of marginal posterior densities for variance components and heritability (h^2) obtained from univariate bayesian analysis are in Table 1. Point estimates of h^2 and additive genetic SD were heterogeneous across sites, ranging from 3 to 44%, and from 0.04 to 0.80 points, respectively. Probability of $h^2 > 10\%$ was higher than 0.8 for 8 sites. Despite frequency of affected dogs and attributed scores were similar for some sites, e.g. sites T12-13 and T13-

L1, magnitude of estimates of h^2 for these sites were quite different (33 vs. 17%). Moreover, some sites showing low incidence, e.g. T10-11 and L2-3, had h^2 estimates close to or greater than 30%. It can be pointed out that sites having major effects on clinical signs, namely T10-11, T11-12, and T12-13, evidenced noticeable levels of genetic variation.

Table 1. Summary statistics of marginal posterior densities of heritability and additive genetic SD for different intervertebral sites obtained in univariate bayesian analysis[A]

	h^2			σ_a	
Site	PM	PD95%	P $h^2 > 0.10$	PM	PD95%
T6-7	0.10	0.01, 0.24	0.46	0.051	0.019, 0.083
T7-8	0.03	0.00, 0.13	0.07	0.042	0.000, 0.079
T8-9	0.08	0.00, 0.24	0.41	0.069	0.000, 0.123
T9-10	0.22	0.04, 0.41	0.90	0.190	0.083, 0.264
T10-11	0.29	0.12, 0.47	0.99	0.409	0.255, 0.538
T11-12	0.44	0.25, 0.63	1.00	0.569	0.414, 0.706
T12-13	0.33	0.12, 0.53	0.99	0.598	0.353, 0.803
T13-L1	0.17	0.02, 0.39	0.73	0.383	0.137, 0.604
L1-2	0.19	0.04, 0.38	0.86	0.329	0.150, 0.476
L2-3	0.37	0.13, 0.61	0.99	0.435	0.244, 0.585
L3-4	0.07	0.01, 0.23	0.33	0.170	0.000, 0.326
L4-5	0.08	0.00, 0.24	0.37	0.189	0.000, 0.353
L5-6	0.10	0.01, 0.28	0.51	0.202	0.002, 0.354
L6-7	0.27	0.04, 0.51	0.92	0.360	0.142, 0.516
L7-S1	0.35	0.13, 0.57	0.99	0.797	0.478, 1.066

[A]Median (PM), symmetric density region at 95% (PD95%), and probability of heritability value greater than 0.10 (P $h^2 > 0.10$). Site : T= thoracic, L = lumbar, S = sacral.

Sites showing probability of $h^2 > 10\%$ greater than 0.8 were considered in REML multivariate analysis aimed to estimate genetic correlations. Results are presented in table 2. Multivariate analysis led to h^2 estimates higher than those obtained in the univariate procedure. Increase of h^2 estimates ranged from 1 to 11 points. Three sites exhibited estimates greater than 40%. Such values were comparable to estimates of h^2 reported by Langeland and Lingaas (1995) for maximum score for osteophytes development. In that study standard errors of estimates were very large due to small sample size and method of estimation used. Standard errors of estimated h^2 obtained in the present study were small, ranging from 0.05 to 0.07. Phenotypic correlations (table 2) for different sites were generally moderate, ranging from 0.05 to 0.60. Genetic correlations were higher and heterogeneous across sites. As expected, size of genetic correlations for adjacent sites were higher than those between sites far away. All thoracic sites exhibited correlations larger than 0.85. Likewise, the first and the second lumbar sites showed a large correlation (0.91). Conversely, the genetic relationship between L6-7 and L7-S1 sites was moderate. These sites exhibited also weak relationships with all remaining sites, whereas estimates of genetic correlations between thoracic and cranial lumbar sites ranged from 0.5 to 0.9. Evidence of heterogeneous correlations indicates that scores for spondylosis affection at different sites should be considered as measures of different traits. This should be taken into

account in genetic evaluation programs and selection procedures to reduce prevalence of this disease.

Table 2. Estimates of genetic parameters obtained for different intervertebral sites in multivariate REML analysis[A]

	T9-10	T10-11	T11-12	T12-13	L1-2	L2-3	L6-7	L7-S1
T9-10	**0.31**	0.86	0.88	0.86	0.74	0.76	0.66	0.46
T10-11	0.50	**0.33**	0.96	0.87	0.72	0.53	0.55	0.29
T11-12	0.44	0.54	**0.46**	0.94	0.88	0.72	0.45	0.23
T12-13	0.29	0.36	0.60	**0.43**	0.91	0.84	0.24	0.07
L1-2	0.32	0.27	0.40	0.41	**0.25**	0.91	0.19	0.09
L2-3	0.33	0.27	0.35	0.36	0.59	**0.48**	0.14	0.16
L6-7	0.18	0.19	0.17	0.19	0.27	0.30	**0.29**	0.70
L7-S1	0.10	0.05	0.10	0.14	0.13	0.11	0.19	**0.36**

[A]Heritabilities on the diagonal, phenotypic and genetic correlations below and above the diagonal, respectively. Standard errors of heritabilities ranged from 0.05 to 0.07, s.e. of genetic correlations from 0.03 to 0.14.

CONCLUSIONS

Results from this study provide evidence that spondylosis deformans is a polygenic genetic disorder showing estimates of h^2 for linear scores for the degree of osteophytes development of intermediate magnitude. This ensures feasibility of selection programs to reduce prevalence of the disease and offers the opportunity of implementing genetic evaluation procedures mostly based on phenotypic observations, i.e. x-ray assays, of candidates to selection. Definition of a selection index considering appropriate weighting factors for different sites will be the aim of a future study.

REFERENCES

Eichelberg, H. and Wurster, H. (1982) *Kleintierpraxis* **27** : 59-71.
Eichelberg, H., Veit, C., Loeffler, K. and Brehm, H. (1989) *Tierarztlkiche-Praxis* **17** : 403-406.
Empel, W and Blenau, B. (1999) *Zycie Weterynaryjne* **74** : 556-558.
Hansen, H.J (1952) *Acta Orthopaedica Scandinavia* **11** : 1-118.
Langeland, M and Lingaas, F. (1995) *J. Small Anim. Practice* **36** : 166-169.
Leppanen, M., Maki, K., Juga, J. and Saloniemi, H. (2000) *J. Anim. Breed.Genet.* **117** : 97-103.
Maki, K., Liinamo, A.E. and Ojala, M. (2000) *J. Anim. Sci.* **78** : 1141-1148.
Mattoon, J.S. and Koblik, P.D. (1993) *Vet. Radiol. and Ultrasounds* **34** : 194-206.
Morgan, J.P. (1967) *J. American Vet. Radiol. Soc.* **8** : 17-22.
Mürhlebach, R. and Freudiger, U. (1973) *Schweizer Archiv. Tierheilkunde* **115** : 539-556.
Ostrander, E.A., Galibert, F. and Patterson, D.F. (2000) *Trends Genet.* **16** : 117-124.