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Causes of death and the impact of histiocytic sarcoma on the life expectancy of the Dutch population of Bernese mountain dogs and Flat-coated retrievers

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ABSTRACT

Bernese mountain dogs and Flat-coated retrievers are predisposed to hereditary oncological diseases. Since 1986 several authors have reported a high prevalence of tumours in both breeds, especially malignant histiocytosis/histiocytic sarcoma, which has a negative influence on life expectancy. However, many earlier reports included relatively low numbers of dogs, distributed over a small number of broad categories, often using outdated disease criteria. The aim of this study was to provide new data on causes of death, and the relative role of tumours, especially histiocytic sarcoma, collected and verified in a large number of dogs of both breeds in co-operation with dog owners and veterinarians.

The study demonstrates that the death of at least 55.1% of Bernese mountain dogs and 63.8% of Flat-coated retrievers is associated with malignant tumours. In addition, it appears that over 1/7 of all Bernese mountain dogs and Flat-coated retrievers die because of histiocytic sarcoma. This emphasises the need for further research on tumours, especially histiocytic sarcoma.

Introduction

While owners expect to buy a healthy pure-bred dog, evidence of the presence of hereditary diseases in dog breeds is accumulating. The Bernese mountain dog (BMD) and the Flat-coated retriever (FCR) are clear examples of such breeds. The BMD, which was originally bred in Switzerland as a multiple purpose farm dog, and the FCR, bred in the United Kingdom as a gundog, are now both often used as companion dogs. They have been reported to have a high prevalence of cancer (BMD: Bredal et al., 1994; Bonnett et al., 2005; Egenvall et al., 2005; Bronden et al., 2010; Nielsen et al., 2010; Fleming et al., 2011; FCR: The Kennel Club, 2004c; Dobson et al., 2009), especially histiocytic sarcoma (BMD: Moore and Rosin, 1986; Affolter and Moore, 2002; FCR: Brown et al., 1994; Morris et al., 2000; Affolter and Moore, 2002; Fidel et al., 2006; Gamlem et al., 2008; Dobson et al., 2009). They also die at a relatively young age compared to other breeds (BMD: Michell, 1999; Proschowsky et al., 2003; The Kennel Club, 2004b; Egenvall et al., 2005; Bronden et al., 2010; FCR: Michell, 1999; The Kennel Club, 2004c). These findings are of increasing concern to owners, breed societies, and veterinarians worldwide.

Histiocytic sarcoma (HS), previously called malignant histiocytosis, is a malignant neoplasia of histiocytes, which encompass macrophages and dendritic cells, normally responsible for antigen removal and presentation. HS can manifest itself as a single mass (localised HS) but may also be widespread throughout one or several organs (disseminated HS) (Affolter and Moore, 2002). The dendritic cell seems to be the cell of origin in most cases of HS (Affolter and Moore, 2002), but recently also a haemophagocytic macrophage variant has been recognised (Moore et al., 2006).

HS is one of the most aggressive, incurable and fatal tumours. It was first reported in humans in 1939 (Scott and Robb-Smith, 1939), followed by several other species including the dog (Scott et al., 1979). HS belongs to the spectrum of canine histocytic diseases, which also encompass benign neoplasia, called canine cutaneous histiocytoma, and reactive histiocytoses, called cutaneous and systemic histocytosis (Affolter and Moore, 2002).

Although many studies in the BMD and FCR report a relatively high prevalence of tumours, especially HS, others are less definitive (BMD: Nielsen et al., 2010; FCR: Michell, 1999). Such differences in reported prevalence may not only be explained by different regional subpopulations of dogs, but also by lack of verification (Michell, 1999), inaccuracies resulting from a small sample size, and different, often outdated clinicopathological criteria (Kerlin and Hendrick, 1996; Gamlem et al., 2008).

This raises questions as to whether the tumour prevalence and impact on the life expectancy of these breeds are indeed as big as some believe and how they compare to other factors causing morbidity or mortality. Actual insight into tumour prevalence

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among all other causes of disease and death are essential if we are to address this question. It may help to increase awareness of owners and breeders about health problems, support veterinarians in their diagnostic and counselling-process, and give directions for future attention points in veterinary research.

The aim of the present study was to provide an overview of all causes of death in the BMD and FCR and to identify important breed-associated diseases which determine the lifespan of dogs of both breeds.

Materials and methods

Selection of dogs

The Dutch BMD and FCR clubs both use a reporting system to get an insight into the lifespan of dogs and the incidence of diseases in each breed. Many owners and the majority of breeders in The Netherlands are members of these clubs and are encouraged to report the occurrence of diseases and the cause and date of death of their dogs, with the clinical or pathological diagnosis of the veterinarian in each case. Preferably this information is provided on a standardized notification form also signed by the veterinarian, accompanied by a copy of the pedigree certificate and, if available, a veterinary and/or pathological report. The causes of death and disease are archived in the reporting systems as indicated by the veterinarian. Over the past 15 years the usefulness of collecting such data has been recognised and reporting has increasingly intensified.

Permission for entry into both reporting systems was granted for this study and took place up to January 2012 (BMD) and up to January 2013 (FCR). Only BMDs and FCRs with (parents with) a pedigree-certificate, and known sex, age and cause of death were included in this study. Accuracy of the pedigree data was verified in the databases of the Dutch Kennel Club, which contain all registered pedigree dogs in The Netherlands.

Encoding

During the present study each cause of death was encoded in a combination of two parameters using a system with 17 codes for pathological process (PP) and 22 codes for organ system (OS). Those codes were, together with the remaining information, loaded in a digital database for analysis.

Analysis

The total number of dogs as well as the sex and age distribution of each breed was reported. Age at death was tested for normal distribution with the Kolmogorov–Smirnov test, followed by the Mann–Whitney test for sex differences. Differences in frequencies were calculated with the chi-square test.

The prevalence of each cause of death is shown, each separated in underlying PP as well as involved OS, and these are compared between the two breeds. Within the tumour-category of each breed the prevalence and impact of the different tumour types is specified. Of the BMDs and FCRs with HS an overview of age at death and sex distribution is given. PPs and specific high-impact diseases causing most of the deaths in each organ system are indicated, and the impact of each PP on the age at death is shown in a box-and-whisker plot for each breed.

Survival curves for dogs dying with HS, with other tumours, and without tumours were drawn with the Kaplan–Meier method. Significance of differences between the three groups was tested with the log rank (Mantel-Cox) test and the Breslow (Generalized Wilcoxon) test. $P < 0.05$ was considered to be significant. Statistics were performed with the statistical software programme SPSS (IBM SPSS Statistics 20.0.0).[1]

Results

Sex distribution

After fulfilling the inclusion criteria, 1092 BMDs and 536 FCRs were entered in the study. No significant difference in sex ratio was found for both BMD (male:female ratio 0.87) and FCR (ratio 1.14) when comparing the data to the sex ratios registered by the Dutch Kennel Club.

Age at death

Median age at death for all BMDs was 8.0 years (range 0.1–14.8 years), and a significant difference ($P < 0.001$) was found between males (7.3 years) and females (8.6 years). Of the BMD population 84.2% died before the age of 11 years. The median age at death for all FCRs was 9.5 years (range 0.0–16.2 years). No significant difference was found between males (9.2 years) and females (9.7 years). Of the FCRs 73.1% died before the age of 11 years.

Cause of death: Pathological process (PP)

A clear PP as cause of death was reported in 98.8% ($n = 1079$) of the BMDs and 96.8% ($n = 519$) of the FCRs. Tumours were the major cause of death in both breeds (Fig. 1). Total percentage of all tumour-associated deaths was significantly higher ($P < 0.001$) in the FCR (63.8%, $n = 342$) than in the BMD (55.1%, $n = 602$). No significant difference was found in the male:female ratio of tumour-bearing dogs in either breed.

In both breeds, about half of all of the tumours were of an unspecified type, followed by HS and other specified tumour types. Specified HS listed as cause of death accounted for approximately 1/7 of all deaths in the BMDs (15.3%) and the FCRs (14.3%) (Fig. 1). The precise tumour type was specified in 43.4% ($n = 261$) of the tumour deaths in BMDs and 64.4% ($n = 168$) of these were HS (Fig. 2). In the FCR 48.5% ($n = 166$) of the tumour types were specified and the most common reported tumour type was also HS ($n = 77$; 46.4% of known types) (Fig. 2).

With respect to non-tumour causes of death, the three most important causes in the FCR, in decreasing order, were old age, circulatory problems and degenerative pathologies, and in the BMD were old age, degenerative disease and metabolic pathologies (Fig. 1). Four BMDs and one FCR were placed in the separate category 'found dead', because they died without preceding symptoms, which could indicate circulatory pathology, but does not exclude other causes. Respectively, 14.1% ($n = 154$) and 9.3% ($n = 50$) of all BMDs and FCRs died of 'old age'. This was defined as death by ageing of several organ systems after passing the average lifespan of the breed and without an identifiable specific cause.

Cause of death: Organ system (OS)

Of 83.0% ($n = 905$) of the BMDs and 72.2% ($n = 387$) of the FCRs a distinct OS associated with the cause of death was reported (Fig. 3). Musculoskeletal, hepatic and cardiovascular systems were the three most important specific organ systems

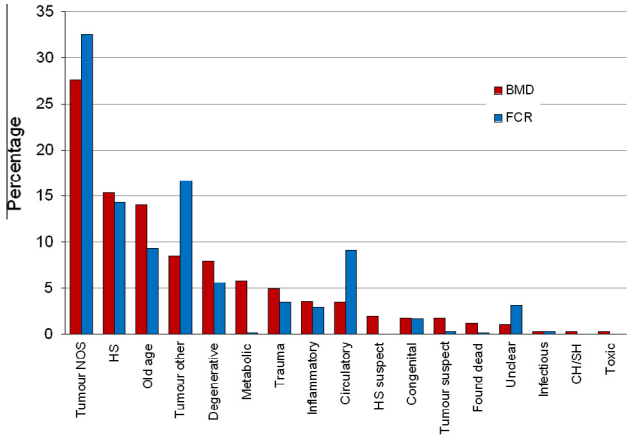

Fig. 1. Causes of death: pathological processes (PP) in the BMD ($n = 1092$) and FCR ($n = 536$). Tumour NOS, tumour type not otherwise specified; tumour other, specified tumour types other than HS; metabolic, metabolic and endocrine disturbances and renal failure; CH/SH, cutaneous/systemic reactive histiocytosis.

[1] See: www.ibm.com/software/analytics/spss.