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Impact of cardiorespiratory diseases on morbidity and mortality in Irish wolfhounds

Lovisa Orleifson

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Impact of cardiorespiratory diseases on morbidity and mortality in Irish wolfhounds

Inverkan av kardiorespiratoriska sjukdomar på sjuklighet och dödlighet hos irländska varghundar

Lovisa Orleifson

Supervisor: *Jens Häggström, Department of Clinical Sciences*

Assistant Supervisor: *Ingrid Ljungvall, Department of Clinical Sciences*

Assistant Supervisor: *Katja Höglund, Department of Anatomy, Physiology and Biochemistry*

Examiner: *Henrik Rönnerberg, Department of Clinical Sciences*

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SUMMARY

Irish wolfhounds have the highest probability of death at a young age of all breeds, according to Swedish animal actuarial data. The breed is 29 times more likely to die from cardiac causes than the baseline breed. In European studies, dilated cardiomyopathy (DCM) is shown to be hereditary in Irish wolfhounds with a prevalence ranging from 24 – 43 %. Studies have also shown that the breed has an increased risk to die from tumors, musculoskeletal, gastrointestinal and respiratory diseases. Few studies describe respiratory diseases in Irish wolfhounds, but studies conducted in Australia and North America show that pneumonia has a high incidence in the breed and that several cases have a fatal outcome.

The aim of this study was to study impact of different health issues on morbidity and mortality in Swedish Irish wolfhounds, with focus on DCM and pneumonia. Questionnaires were sent to owners of purebred Irish wolfhounds born during 2006 – 2008. A total of 100 questionnaires were completed resulting in an overall response rate of 36 %. The study population consisted of 49 males and 51 females and among those 72 dogs were dead and 28 dogs were still alive at the end of the study.

The results from this study showed that the most common causes of death were tumors, heart disease and pneumonia. These findings are partly supported by previous studies. Our study revealed pneumonia as one of the most common causes of death, which has not been shown before. Sixteen percent of the dogs included in the study were affected by DCM. Percentage of dogs with pneumonia on at least one occasion during their lifetime was 37 % and a majority of them had recurrent episodes. DCM was more common in males than in females, however, the difference was not significant. No sex predisposition was found regarding pneumonia.

This study showed that DCM and pneumonia are common in Irish wolfhounds in Sweden. Because these diagnoses also have been reported as the most common causes of death, they should be given attention in the course of improving the general health in the breed. Further research is warranted regarding etiology, diagnosis and different treatment regimens concerning respiratory disease in the breed.

SAMMANFATTNING

Enligt försäkringsstatistik har svenska irländska varghundar högre sannolikhet att dö vid yngre ålder jämfört med andra raser. De löper en 29 gånger högre risk att dö av hjärtsjukdom. Europeiska studier har visat att dilaterad kardiomyopati (DCM) är ärftligt i rasen och har en hög prevalens (24 – 43 %). Studier har också visat att irländska varghundar har en ökad risk att dö av tumörsjukdomar, sjukdomar i rörelseapparaten samt av gastrointestinala- eller respiratoriska sjukdomar. Få studier finns tillgängliga rörande lunginflammationer i rasen, men utländska studier har visat att incidensen sannolikt är hög och att sjukdomen kan ha en dödlig utgång.

Målet med denna studie var att undersöka sjuklighet och dödlighet hos svenska irländska varghundar med särskild fokus på DCM och lunginflammation. Enkäter skickades ut till ägare av renrasiga irländska varghundar födda under åren 2006 – 2008. Totalt besvarades 100 enkäter vilket resulterade i en svarsfrekvens på 36 %. Studiepopulationen bestod av 49 hanar och 51 tikar, varav 72 hundar var döda och 28 hundar fortfarande i livet vid studiens slut.

Resultaten från denna studie visade att de vanligaste dödsorsakerna var tumörsjukdom, hjärtsjukdom och lunginflammation. Detta överensstämmer delvis med tidigare studier. Vår studie visade att lunginflammation var en av de vanligaste dödsorsakerna, vilket inte har visats tidigare. Av hundarna i studiepopulationen hade 16 % DCM. Andelen av hundarna som varit drabbade av lunginflammation vid minst ett tillfälle var 37 % och majoriteten av dessa hade återkommande episoder. DCM var vanligare hos hanar jämfört med hos tikar men skillnaden var ej signifikant. Gällande lunginflammation förelåg ingen tydlig könspre disposition.

Denna studie visade att DCM och lunginflammation är vanligt hos irländska varghundar i Sverige. Eftersom dessa diagnoser också rapporterats vara några av de vanligaste dödsorsakerna, bör de uppmärksammas i arbetet med att förbättra hälsan i rasen. Ytterligare forskning kring respiratoriska sjukdomar i rasen behövs med avseende på etiologi, diagnosställande och olika behandlingsregimer.

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INTRODUCTION

Heart disease is the fourth most common cause of death in Swedish insured dogs (Bonnett *et al.*, 2005). Egenvall *et al.* (2005) found that Irish wolfhounds had the highest probability of death by 5 years, 8 years and 10 years of age compared to all other breeds in the insurance database of over 350 000 insured Swedish dogs. Indeed, the probability of death by 10 years of age was as high as 91 % in Irish wolfhounds. Compared to baseline breeds, the breed was 29 times more likely to die from cardiac causes. Mortality rate ratios concerning tumors and musculoskeletal disorders showed that Irish wolfhounds were also more likely to die of those causes compared to other breeds. Moreover, studies have shown a high incidence of pneumonia in the breed and respiratory disease has been reported a common cause of death (Fleming *et al.*, 2011; Greenwell & Brain, 2014)

Dilated cardiomyopathy (DCM) is a common disease in European Irish wolfhounds (Vollmar, 2000; Distl *et al.*, 2007). Although the insurance data is a valuable source of information to characterize the general health situation and causes of death in specific breeds in Sweden, the resolution of the information is limited and the database does not include old dogs. The aim of this study was, therefore, to study impact of different health issues on morbidity and mortality in the breed with focus on DCM and pneumonia. The results from this study will hopefully be useful to further evaluate the need of a breeding program regarding heart disease and reveal other important health issues. Because many of the Irish wolfhounds have at least one foreign parent, this study may provide information about the overall population of Irish wolfhounds (Wink, T., Swedish Kennel Club, pers. communication, 2015).

LITERATURE REVIEW

The canine heart

The heart is located in the center of the thoracic cavity and consists of two atria and two ventricles. From the left atrium oxygenated blood flows to the left ventricle and from there, by the aorta, blood flows throughout the body to distribute oxygen and nutrients. From the organs the blood transports carbon dioxide and waste products, and through the veins blood flows back to the heart entering the right atrium by the posterior and anterior vena cavae. Blood flows from the right atrium to the right ventricle and then to the lungs where the blood takes up oxygen and releases carbon dioxide. The blood then returns to the heart by the pulmonary veins, entering the left atrium. In order for the blood to flow in the right direction, valves are located between the atria and ventricles and between the ventricles and the major arteries leaving the heart (aorta and the pulmonary artery). The valves open and close depending on the hydrostatic pressure. The valve between the left atrium and left ventricle is called the bicuspid valve or the mitral valve and the valve between the right atrium and right ventricle is called the tricuspid valve. The blood volume pumped by the ventricles during one minute is called the cardiac output (CO) and is dependent on the heart rate and the blood volume pumped out of each ventricle during one contraction; the stroke volume (Sjaastad *et al.*, 2010).

The heart mainly consists of striated muscle cells and this part of the heart is called the myocardium. The muscle cells occur in two types: contractile cells and autorhythmic cells. Ninety-nine percent of the muscle cells are contractile cells, which depolarize secondary to

stimuli. As opposed to the contractile cells, the autorhythmic cells depolarize spontaneously and this occurs most rapidly in the sinoatrial node, which is a cluster of cells located in the right atrium functioning as the heart's main pacemaker. From there, the action potential is propagated through the myocardium; generating a contraction, a heartbeat (Sjaastad *et al.*, 2010).

Congestive heart failure

The heart can be affected by different pathological processes which may result in cardiac dysfunction, such as for example myopathies, valvular diseases and congenital heart diseases. To maintain adequate CO and systemic blood pressure in the presence of a dysfunctional heart, several compensatory mechanisms are available. The heart rate and the peripheral resistance increase. The myocardium may increase in mass, i.e. hypertrophy, and, in the case of cardiac volume overload, it may stretch which results in cardiac dilation. Up to a certain limit, cardiac muscle cell can stretch which will result in an increased stroke volume, but when dilation exceeds optimum for the cells, the stroke volume will instead decrease. This is known as the Frank Starling's law (Sjaastad *et al.*, 2010; Miller *et al.*, 2012). Other compensatory mechanisms include increased blood volume and redistribution of blood to vital organs. These mechanisms can be sufficient to maintain CO even in severe heart disease. When CO decreases because of a gradual loss of pump function, the pulmonary and systemic venous and capillary pressures increase, which may lead to congestive heart failure (CHF). The reduced cardiac pump function leads to a tendency for a lowered blood pressure, which stimulates several neuroendocrine systems, such as the renin-angiotensin-aldosterone system (RAAS). This response is compensatory in nature and results in increased retention of sodium and water, which increase the extracellular fluid compartment, including the plasma volume. The increase in plasma volume results in higher workload for the already failing heart and excess of fluid accumulates in body cavities. In case of left-sided CHF fluid accumulates in the lungs or the thoracic cavity and in case of right-sided or bilateral CHF, hepatic congestion and ascites are observed (Miller *et al.*, 2012).

Clinical signs associated with CHF are tachycardia, weak arterial pulse, labored breathing due to fluid retention in the lungs or thoracic cavity, slow capillary refill time, ascites and hepatic congestion (Lombard, 1984; Tidholm & Jönsson, 1997). In Irish wolfhounds one of the leading signs in severe CHF is pleural effusion (Vollmar, 1999).

Cardiomyopathy

Cardiomyopathy is characterized by pathological changes, associated with cardiac dysfunction, in the myocardium. Cardiomyopathy is classified into four different groups by the WHO-ISFC task force: dilated, hypertrophic, restrictive cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy (Richardson *et al.*, 1996). Dilated cardiomyopathy is characterized by uni- or bilateral cardiac dilation and reduced systolic function. Hypertrophic cardiomyopathy is recognized by ventricular myocardial hypertrophy, which results in myocardial stiffness and impaired ventricular filling. Restrictive cardiomyopathy is characterized by comparably normal ventricular dimensions and wall thickness, but increased ventricular stiffness, which results in impaired ventricular filling. Arrhythmogenic right ventricular cardiomyopathy is characterized

by a fibrous fatty infiltration in the right ventricular wall, which results in clinical signs such as arrhythmias and sudden death (Richardson *et al.*, 1996).

Dilated cardiomyopathy

Dilated cardiomyopathy is characterized by dilatation of the left ventricle or of both ventricles and thinning of the ventricular walls, which leads to cardiomegaly and decreased systolic function (Lombard, 1984; Sandusky *et al.*, 1984; Richardson *et al.*, 1996). Grossly all heart chambers show slight to moderate dilation, but in dogs examined by Janus *et al.* (2015) only the left ventricle showed significant dilation. When histologically examining the myocardium in dogs diagnosed with DCM, two types of histological changes have been described: attenuated wavy fibers and fatty infiltration degenerative type (Tidholm & Jönsson, 1997; Janus *et al.*, 2015). The fatty infiltration degenerative type is the predominating type in Dobermanns (Calvert *et al.*, 1997a; Everett *et al.*, 1999) while attenuated wavy fibers type is frequently seen in other medium, large and giant breeds (Sandusky *et al.*, 1984; Tidholm *et al.*, 1998 & 2000; Dambach *et al.*, 1999). Genetic factors have been shown to influence the development of DCM in several breeds and the disease has been suggested to be inherited as an autosomal dominant trait in Newfoundland dogs, Dobermanns and Great Danes (Dukes-McEwan & Jackson, 2002; Meurs *et al.*, 2007; Stephenson *et al.*, 2012). In some studies, other modes of inheritance have been suggested such as an autosomal recessive trait in young Portuguese water dogs (Dambach *et al.*, 1999) and an x-linked recessive trait in Great Danes (Meurs *et al.*, 2001). However, dogs of atypical breeds may also develop DCM. The etiology in these cases is unidentified, but theories such as infectious organisms and nutritional imbalances have been brought forward or the disease is considered as idiopathic (Meurs, 2010).

Clinical signs

The most common clinical signs associated with DCM are dyspnea and cough (Tidholm *et al.*, 1997; Martin *et al.*, 2009). Other common clinical signs are exercise intolerance, weakness, weight loss, reduced appetite, collapse and lethargy. During physical examination typical clinical findings are tachycardia, weak pulse, gallop sound, systolic heart murmur, pale mucous membranes and ascites (Tidholm & Jönsson, 1997; Brownlie & Cobb, 1999; Martin *et al.*, 2009). In the retrospective study by Tidholm and Jönsson (1997), the majority of dogs affected by DCM did not have a heart murmur, but of the dogs presented with a murmur (25 %), 78 % of the described murmurs were grade II-III/VI. Similar findings have been reported by Martin *et al.* (2009) where a majority of the recorded murmurs were grade I-III/VI. Vollmar (2000) found when examining Irish wolfhounds with DCM that mild to severe mitral or tricuspid valve regurgitation was present in most patients that had a noticeable enlarged left or right ventricle. Arrhythmias are common and atrial fibrillation is most frequently recorded in giant dogs. The second most common arrhythmia is ventricular premature complexes (VPCs) (Tidholm & Jönsson, 1997; Martin *et al.*, 2009), which differs from some other breeds where DCM is common for example Boxer and Dobermann, where VPCs instead is the most common arrhythmia (Martin *et al.*, 2009).

Diagnosis

Complete medical history and physical examination should be performed in all dogs. The terms preclinical (occult) and clinical (overt) dilated cardiomyopathy are used to describe different stages of the disease. Preclinical DCM refers to individuals without clinical signs of heart disease but in which DCM is detected after thorough examination. Clinical DCM refers to the stage when clinical signs are apparent (Meurs, 2010). To be able to diagnose preclinical and clinical DCM, and to differentiate it from other heart diseases, echocardiography is useful because an echocardiographic examination can evaluate the anatomy and the function of the heart (Dukes-McEwan *et al.*, 2003). Echocardiography makes it possible to diagnose DCM in individuals where no clinical signs are present, though repeated examinations may be necessary in some cases. It is also helpful to monitor the progression of the disease and evaluate the response to therapeutics (Vollmar, 1999).

Many dogs affected by DCM have arrhythmias (Martin *et al.*, 2009) and electrocardiography should be carried out to examine the presence and type of arrhythmia, because it can be an indicator for diagnosis of DCM in some breeds, and to evaluate the need for antiarrhythmic therapy (Brownlie & Cobb, 1999; Dukes-McEwan *et al.*, 2003). In some breeds, for example Dobermann, a 24-hour ambulatory electrocardiogram (Holter recording) can be useful to identify dogs of high risk of DCM (Calvert *et al.*, 2000). In case of suspected CHF, thoracic radiographs are useful to evaluate cardiomegaly and to diagnose pulmonary edema or pleural effusion as well as abdominal radiographs for diagnosis of ascites (Tidholm & Jönsson, 1997; Martin *et al.*, 2009). For a definitive diagnosis it is recommended that deceased dogs with diagnosis or suspicion of DCM should be examined post mortem (Dukes-McEwan *et al.*, 2003).

Prognosis

Generally the disease progresses quickly and overall prognosis is poor, however, a difference in progression is seen between breeds (Calvert *et al.*, 1997b; Dambach *et al.*, 1999; Brownlie & Cobb, 1999). Death occurs due to CHF or dogs can die suddenly without signs of CHF (Tidholm *et al.*, 1997; Janus *et al.*, 2015). A study of different breeds by Martin *et al.* (2009) showed that median duration of signs before referral was three weeks and by then the majority of the dogs had clinical signs of CHF. That study also showed that median survival time after referral in dogs with DCM was 19 weeks and the survival rate was found to be 28 % at one year and 14 % at two years from referral. A survival analysis on different breeds by Monnet *et al.* (1995) showed that there was a 50 % probability of survival 2,3 months after diagnosis had been made. At one and two years from diagnosis the probability of survival was 38 % and 28 %, respectively. In another study survival rates in dogs of different breeds with CHF caused by DCM were found to be 18 % at one year and 8 % at two years from time of initial diagnosis (Tidholm *et al.*, 1997). The effect of different cardiac therapies was not evaluated in the survival studies and more recent studies have shown a significantly increased lifespan when dogs affected by DCM have been treated with Pimobendan compared to those who have not received the drug (Fuentes *et al.*, 2002; O'Grady *et al.*, 2008). Poor prognostic indicators in DCM were presence of pleural effusion or pulmonary edema, young age at onset of clinical signs, dyspnea and ascites (Monnet *et al.*, 1995; Tidholm *et al.*, 1997). Some echocardiographic measurements of cardiac size and motion have also been shown to be predictive of outcome (Borgarelli *et al.*,

2006). Menaut *et al.* (2005) showed that dogs with atrial fibrillation without structural or functional heart disease had longer survival time compared to dogs with atrial fibrillation and structural heart disease or CHF.

Dilated cardiomyopathy in Irish wolfhounds

Irish wolfhounds have the highest mortality rate ratio regarding heart disease of all Swedish breeds, with a 29 times increased risk of death due to cardiac causes (Egenvall *et al.*, 2005). In a retrospective study including 500 Irish wolfhounds examined at a veterinary hospital in Germany, cardiovascular abnormalities were noted in 42 % and DCM was diagnosed in 24 % of the dogs. Affected dogs had a mean age of 4,2 years (Vollmar, 2000). In a study by Distl *et al.* (2007) the prevalence of DCM was 26 % and a more recent study by Vollmar *et al.* (2013) showed that 43 % of the Irish wolfhounds had DCM, the mean age for affected dogs in those studies were 4,4 years and median age 4,3 years, respectively. Philipp *et al.* (2012) found in their study that mean age of diagnosis of DCM in dogs from Europe was 4,9 years. Brownlie and Cobb (1999) found that the mean age at which CHF had developed in British Irish wolfhounds was 6,4 years in males and 7,2 years in females. Time from detection of heart disease to development of CHF in Irish wolfhound was very variable but was in that study 27 months in males and 24 months in females. Swedish insurance data has shown that median age at death of Irish wolfhounds with cardiac disease was 7,5 years (Egenvall *et al.*, 2006).

In the publication by Brownlie and Cobb (1999) 12 % of the Irish wolfhounds without clinical sign of heart disease had atrial fibrillation. Among dogs with DCM, 46 % had atrial fibrillation diagnosed at their first examination and by the time these individuals had developed CHF, all dogs suffered from atrial fibrillation. The authors, therefore, proposed that atrial fibrillation may be an indicator of preclinical DCM in Irish wolfhounds. Vollmar (2000) found that out of 121 Irish wolfhounds with DCM, 88 % had atrial fibrillation and 11 % had VPCs. Likewise, Martin *et al.* (2009) found atrial fibrillation in 94 % of Irish wolfhounds with DCM.

In a study performed to evaluate the prevalence of whole blood taurine deficiency in Irish wolfhounds with and without DCM, there was no association between occurrence of DCM and low taurine levels in the blood, based on measurements from one occasion (Vollmar *et al.*, 2013).

Inheritance

Distl *et al.* (2007) showed that males were affected by DCM significantly more often than females and Brownlie and Cobb (1999) found a trend of males being affected at a younger age compared to females. In a study performed to analyze the mode of inheritance regarding DCM in Irish wolfhounds Distl *et al.* (2007) found that a major gene model with a sex-dependent allele effect was most probable. They suggested that development of DCM can be attributed to a single gene locus and further polygenic effects. Philipp *et al.* (2012) also found that multiple loci potentially were associated with DCM in Irish wolfhounds.

Other health issues in Irish wolfhounds

The median age at time of death for British Irish wolfhounds was 6,2 years and mean age at time of death for Irish wolfhounds studied in Norway was 7 years (Michell, 1999; Anfinsen *et al.*, 2011). Swedish Irish wolfhounds have a 91 % probability of death at an age of 10 years (Egenvall *et al.*, 2005). Egenvall *et al.* (2005) also showed that Irish wolfhounds had an 8,9 times increased risk to die from tumors and 6,7 times increased risk to die from musculoskeletal disorders compared to baseline breeds, which place them among the breeds with the highest mortality rate ratios in these categories. This shows that, in addition to heart disease, there are also other diseases that are major contributors to the high overall mortality rate in the breed. Bonnett *et al.* (2005) presented that death due to heart disease accounted for 25 % of all deaths in the breed and death due to tumors accounted for 22 %. In North American Irish wolfhounds, the most common organ system registered for cause of death was musculoskeletal (22 %) and the breed was one of the top five breeds with musculoskeletal causes of death (Fleming *et al.*, 2011). Other common organ systems listed as cause of death were gastrointestinal (15 %), cardiovascular (13 %) and respiratory (12 %). When cause of death was categorized by pathological diagnosis, the most common cause in Irish wolfhounds was neoplastic disease, which accounted for 32 % of the deaths among these categories except for unclassified (36%). Likewise, in a survey performed on British dogs of different breeds, Irish wolfhounds were over-represented regarding tumors as cause of death (Michell, 1999).

Osteosarcoma

Osteosarcoma was the most frequently occurring bone tumor in dogs of different breeds and was likely to occur in large breed middle-aged dogs in the study by Liu *et al.* (1977). The risk of osteosarcoma has been shown to rise with increasing body weight, height and age, although a hereditary etiology in individual breeds could not be excluded (Ru *et al.*, 1998). In that study, Irish wolfhounds were shown to have an odds ratio of 20,7 for osteosarcoma, and thereby the highest risk of osteosarcoma of all included breeds. Swedish Irish wolfhounds had the highest incidence rate of all breeds regarding malignant bone tumors with an incidence rate of 99 cases per 10 000 dog-years at risk, based upon insurance data. The overall incidence rate was 5,5 cases per 10 000 dog-years at risk. The top five breeds at risk were all large or giant breeds (Irish wolfhound, St. Bernard, Leonberger, Great Dane and Rottweiler). Up to 10 years of age 12 % of the Swedish Irish wolfhounds were estimated to have developed malignant bone tumors based on 23 affected dogs (Egenvall *et al.*, 2007). In a retrospective population-based survey in Norway, Irish wolfhound had the highest incidence rate of primary bone tumors of the four breeds included, with a rate of 126 cases per 10 000 dog-years at risk (Anfinsen *et al.*, 2011). Most of the osteosarcomas originate in the appendicular skeleton (Liu *et al.*, 1977; Anfinsen *et al.*, 2011; Egenvall *et al.*, 2007). Clinical signs associated with osteosarcomas in the extremities are lameness, pain and swelling over the lesion (Liu *et al.*, 1977).

Pneumonia

A study describing 28 Irish wolfhounds from Europe and North America with clinical signs of rhinitis and bronchopneumonia showed that the majority of affected dogs had clinical signs present since birth (Clercx *et al.*, 2003). Common signs were intermittent or persistent mucoid or purulent nasal discharge, cough and dyspnea. In some of the dogs, recurrent acute episodes

of bronchopneumonia were present. Antibiotic treatment resulted in a positive response, but in several cases regular periodic treatment, or even continuous treatment, was required. Four of the dogs died at an age under 14 months due to severe pneumonia. Pedigree analysis of the dogs from Europe and Canada revealed that ancestors were shared, which according to the authors, suggests a heritable syndrome. Primary ciliary dyskinesia or primary immunodeficiency were not detected among the affected dogs and signs of heart disease were also absent. The rhinitis and bronchopneumonia syndrome described above was first reported by Wilkinson (1969). Wilkinson (1969) pointed out that the condition was well distributed through the breed and rather suggested the etiology to be a viral infection with secondary bacterial invasion. Different bacterial organisms were found in nasal discharge from affected puppies but healthy puppies did not develop infection when exposed to infected nasal discharge. In the majority of the cases, puppies from the same litters as the affected puppies remained healthy even though they lived in close contact with each other. A case report of three related Irish wolfhounds less than one year of age with clinical signs of respiratory disease instead indicated a primary cell-mediated immunodeficiency (Leisewitz *et al.*, 1997). In a more recent study, a retrospective analysis of medical records determining the incidence of pneumonia in dogs admitted to a veterinary hospital in Sydney during 2008 – 2012, Irish wolfhound had the highest incidence of all breeds based on 25 Irish wolfhounds. However, four of the affected Irish wolfhounds had a predisposing cause for aspiration pneumonia identified such as laryngeal paralysis, a choking episode and gastric dilation (Greenwell & Brain, 2014).

Other diseases

Gastric dilation volvulus has been seen with a higher incidence in some giant and large breed dogs, among them Irish wolfhounds, and the incidence increased with increasing age (Glickman *et al.*, 2000). Other known health issues in Irish wolfhounds are intrahepatic portosystemic shunts where an incidence of 3,4 % was reported when screening puppies in United Kingdom (Kerr & van Doorn, 1999). This disorder is likely hereditary (van Steenbeek *et al.*, 2009). Furthermore, Casal *et al.* (2006) described epilepsy to be hereditary in Irish wolfhounds with an incidence of 18 % among 120 related litters, however, neurological causes have not been reported as a common cause of death in the breed in Sweden (Egenvall *et al.*, 2005). Regarding developmental orthopedic diseases, LaFond *et al.* (2002) found that Irish wolfhounds had an increased risk for fragmented coronoid process, osteochondrosis in the stifle and in the shoulder and panosteitis, compared to mixed-breed dogs. Krontveit *et al.* (2010) found that the estimated incidence risk of hip dysplasia was 10 % in Irish wolfhounds which was the lowest incidence risk compared to the three other breeds included in the study.

MATERIAL AND METHODS

Study design

A retrospective study was performed by distributing a questionnaire to owners of purebred Irish wolfhounds born between January 1st 2006 and December 31st 2008 registered in the Swedish Kennel Club (SKK). These years were chosen because the dogs would have reached an age of 7-9 years, and possibly be affected by diseases, for example DCM. Furthermore, a majority of them would not be alive, which allows a possibility to study causes of death (Egenvall *et al.*,

2005; 2006). Moreover, the range of year of birth was chosen so that, in cases of death, this would not have occurred too long ago, which means that the owners may remember the details. The questionnaire was sent by mail to all owners where an address was available in the SKK's register, in total, 280 questionnaires were sent to 232 owners. Recipients that had not responded by the time required received one reminder. Reminding notices were also published at the webpage and the Facebook page of the Swedish Irish Wolfhound Club.

The questionnaire was divided into three sections, where the first consisted of questions regarding general information such as sex, number of identification, neutering status, weight, coat color, breeding history and the owners contact information. The first section was for everyone to answer. Moreover, the questionnaire was divided into one section for dogs that were dead and one section for dogs that were still alive. These sections contained questions about cause of death, time of death, a potential history of DCM, clinical signs observed by the owner and potential ongoing medical treatments. Questions were also asked about history of pneumonia, if and how they were treated, if they were recurrent, and if known relatives were affected. In this study, relatives were defined as mother, father, siblings and offspring. Furthermore, in the section for the dogs that were still alive more specific questions were asked whether heart and thorax of the dog had been examined by a veterinarian. The information from the questionnaires was treated completely anonymously and permission was asked for access to veterinary records if considered required. A translated English version of the questionnaire is attached in Appendix 1.

Data management

The information from the questionnaires was entered into a Microsoft Excel document. Information about causes of death was divided into different main classes, which was used in the questionnaire. Complete and correct birth date was controlled for each dogs in the SKK's register as well as sex and coat color.

Information about clinical signs and results from examinations, that were associated with heart disease, were evaluated by the author to determine whether the dog in this study was to be classified to be affected by DCM or not. Dogs that had the diagnosis DCM based on clinical and echocardiographic examinations were classified as having DCM. Dogs with clinical signs such as atrial fibrillation, heart murmur and developing CHF were classified as being probably affected by DCM and dogs with CHF at time of euthanasia with no prior clinical signs were classified with suspicion of DCM. All these dogs were later included when calculating occurrence of DCM. Concerning frequencies of pneumonia, questions were not asked about how the dog had been diagnosed, but only if it had been affected by pneumonia on at least one occasion during the dog's lifetime.

Statistical analyses

Basic descriptive statistics was used to examine the study population regarding dog characteristics, causes of death and occurrence of diagnoses such as DCM and pneumonia. If owners had reported multiple causes of death for one dog, each diagnosis was accounted for in the statistical analysis. To test the hypotheses of difference in occurrence of DCM and

pneumonia between sexes, Fisher's exact test was used. This test was chosen because it is appropriate when sample sizes are small. Level of statistical significance was set to $p < 0,05$. The statistical analyses were carried out with a commercially available statistical software program^a.

RESULTS

During the years 2006 – 2008, 460 purebred Irish wolfhounds were born and registered in the SKK register. Of the 280 distributed questionnaires, 100 were completed and returned by mail to the Swedish University of Agricultural Sciences. Four letters were returned due to unknown recipients. This resulted in a total response rate of 36 %. Not all owners answered all the questions in the questionnaire, resulting in varying response rates for different variables in the calculations. The study population consisted of 49 males and 51 females. Summary statistics for the dogs included in the study are presented in Table 1.

Table 1. *Dog characteristics, number of dogs with dilated cardiomyopathy (DCM) and number of dogs with pneumonia, presented for dogs born in 2006, 2007 and 2008, respectively*

Group	2006	2007	2008
Number of dogs	42	37	21
Response rate	39 %	38 %	30 %
Alive/dead	9/33 (42)	10/27 (37)	9/12 (21)
Sex, male/female	22/20 (42)	18/19 (37)	9/12 (21)
Weight (kg)	69 (35)	67 (35)	68 (19)
Neutered	4 (38)	8 (34)	5 (20)
Coat color, B/RB/DB/F/W/Bl	25/1/0/3/6/7 (42)	26/2/1/4/2/2 (37)	16/0/1/1/1/2 (21)
Number with offspring	6 (42)	5 (36)	5 (20)
DCM	8 (42)	6 (37)	2 (21)
Pneumonia	13 (36)	14 (34)	6 (19)

Summary of dog characteristics. Weight is given as mean weight in kilograms, coat color brindle (B), redbrindle (RB), dark brindle (DB), fawn (F), wheaten (W) and black (Bl). Total number of values for each specific category is presented in parenthesis. Dogs that had been diagnosed with both DCM and pneumonia appear in both disease groups.

Cause of death

Of the 100 dogs included in the study, 72 dogs were dead. Twelve owners had reported multiple causes of death for the dog, which were all accounted for in the statistical analysis. The most common cause of death was tumors, heart disease and pneumonia (Figure 1). Tumors accounted for 24 % of the causes of death, where osteosarcoma and other tumors represented 9 % and 15 %, respectively. The proportion of heart disease consisted of dogs classified to have DCM, 16

^a JMP Pro v. 11.2.0, Cary, NC, USA.

%, and unclassified heart diseases, 1 %. The largest proportion of cause of death was represented by other causes of death which included dogs that had died due to gastric dilation volvulus 7 % (6 dogs), megaesophagus 3 % (3 dogs), paresis 3 % (3 dogs), epilepsy 2 % (2 dogs), pyometra 2 % (2 dogs), kidney disease 2 % (2 dogs), osteomyelitis or septic arthritis 2 % (2 dogs), diabetes mellitus 1 % (1 dog), traffic accident 1 % (1 dog), intoxication 1 % (1 dog), behavioral issues 1 % (1 dog), stiffness of the neck 1 % (1 dog), lethargy 1 % (1 dog) and old age 1 % (1 dog).

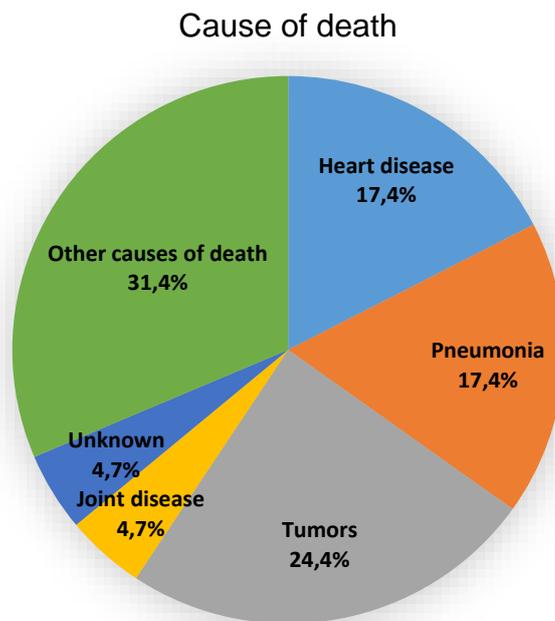


Figure 1. *Proportional mortality in 72 Irish wolfhounds.*

Of the deceased dogs, all but 5 dogs had been euthanized. The remaining 5 dogs had died suddenly, which result in a sudden death rate of 7 %. One of these dogs had undergone a post mortem examination and was diagnosed with acute circulatory failure with a strong suspicion of DCM. One other dog was diagnosed with DCM prior to sudden death, and in the other dogs the owners suspected gastric dilation volvulus in one case, and simply old age in another. There was one dog, which had died suddenly, where no specific disease was suspected as cause of death.

Dilated cardiomyopathy

Overall occurrence of DCM in the study was 16 % (16 dogs) based on 100 completed questionnaires. A majority of these dogs had either been diagnosed with DCM by an echocardiographic examination, or by post mortem examination (75 %). The other dogs were classified by the author as being probably affected by DCM, or with a strong suspicion of DCM based on presence of atrial fibrillation and/or clinical signs suggestive of CHF. The proportion of dogs affected by DCM are shown, divided by sex, in Figure 2. There was no significant difference in occurrence of DCM between sexes ($p = 0,28$).

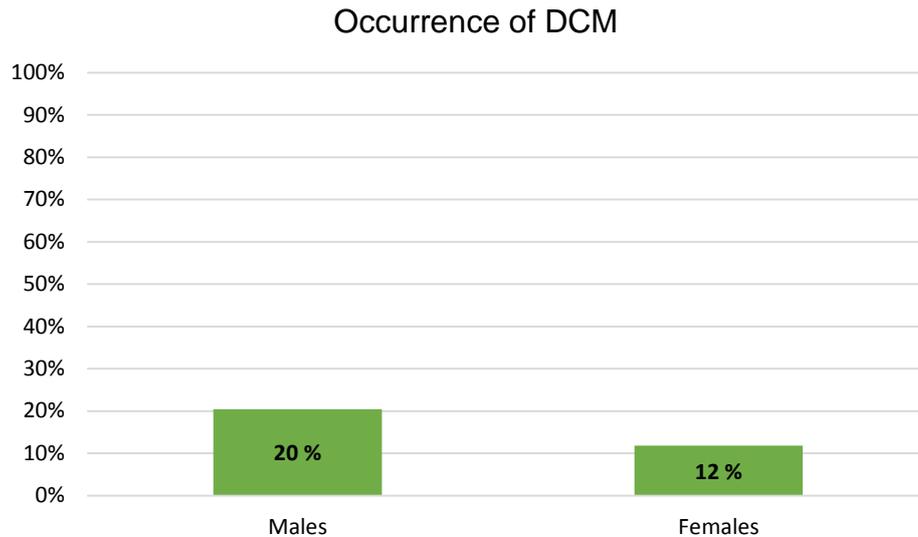


Figure 2. *Proportion of dogs with dilated cardiomyopathy by sex, based on data from 49 males and 51 females. The difference between sexes was not significant.*

Pneumonia

The total proportion, where the owners had answered that the dog had pneumonia on at least one occasion, was 37 % (33 dogs). Number of values for this question were 89 answers. The proportions of dogs with at least one episode of pneumonia presented by sex are shown in Figure 3. There was no significant difference in occurrence of pneumonia between sexes ($p = 0,83$).

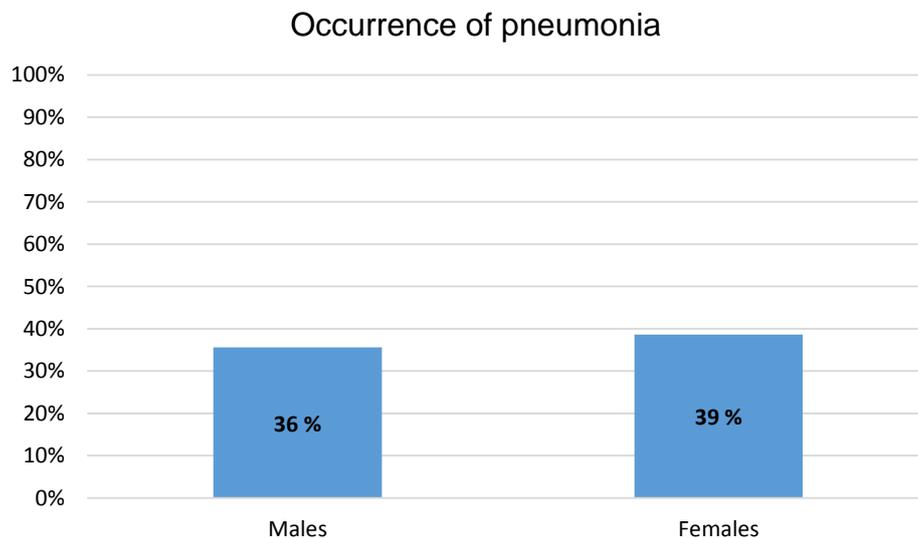


Figure 3. *Proportion of dogs with at least one episode of pneumonia by sex, based on data from 45 males and 44 females. The difference between sexes was not significant.*

Among the dogs with a history of pneumonia, all 33 owners had answered the question regarding recurrence. Eighteen dogs had recurrent episodes of pneumonia and 11 of them had

pneumonia three times or more. Two dogs had developed pneumonia up to 14 times during their lifetimes. The proportions of dogs with only one episode of pneumonia and dogs with recurrent pneumonias are shown in Figure 4.

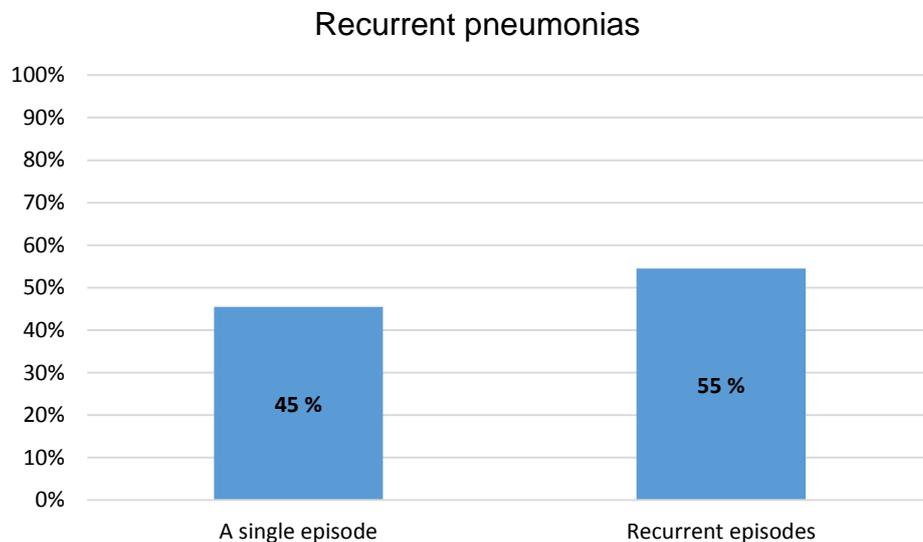


Figure 4. *Proportion of dogs with a history of only one episode of pneumonia and dogs with recurrent episodes of pneumonia.*

Among the 33 dogs with at least one episode of pneumonia, 16 % (5 dogs) had also been diagnosed with DCM. Among those, one dog had pneumonia a total of 14 times during its lifetime. In 3 of the 33 dogs, the owners had reported other concurrent disease, such as megaesophagus. Of the deceased dogs (27), with at least one episode of pneumonia, 52 % had pneumonia listed as a cause of death.

DISCUSSION

The study population included purebred Irish wolfhounds born during 2006 – 2008. Dogs fitting these criteria were 460 dogs, but for 180 dogs no contact information was available and therefore these dogs were not included. Only a minority of the dogs born during these years compose the study population, and results from this study may not entirely be representable for the general Swedish Irish wolfhound population. However, there were no indications that dogs whose owners not had reported their contact information to the SKK, would be more or less affected by diseases than the others, and, thus, not introducing a systematical error. The survey had a response rate of 36 % consisting of 100 dogs, which may provide valuable information from a comparably large group of Irish wolfhounds. The response rate in this study is comparable to other studies with a similar study design, such as Mandigers *et al.* (2006), which had a response rate of 37 %. Other similar studies, with small differences in study design, have reached response rates of 21 % (Proschowsky *et al.*, 2003), 36 % (De Risio *et al.*, 2015) and 51 % (Anfinsen *et al.*, 2011), which suggests the response rate in this study to be reasonable.

Because 43 % of the Swedish Irish wolfhounds born during 2006 – 2008 had at least one foreign parent (Wink, T., Swedish Kennel Club, pers. communication, 2015), this study may also provide some information about the overall population of Irish wolfhounds. Most common

countries the parents came from during these selected years were Sweden, Great Britain, Italy and from other Scandinavian countries. The years were specifically chosen to allow studies of morbidity and mortality, because the dogs had reached an age where many events may have occurred, but not too far back in time for the owner to forget details of their dog's health situation. The latter represents one important limitation with retrospective survey studies, because important details about clinical signs, cause of death and time of death might have been forgotten or mixed up with other dogs in the household. When a retrospective survey is performed, information concerning clinical signs and diagnoses are based on the owners' perceptions and knowledge about type of examinations that were performed. Naturally, this is very dependent on how good the communication between owner and veterinarian has been. For example, this means that dogs with preclinical stages of DCM will be undiscovered unless the owner has brought the dog to the veterinarian for heart evaluation. However, an advantage with a survey compared to clinical case series including dogs visiting veterinary hospitals, is that the results will not be skewed by selection bias. Dogs attending veterinary clinics are more likely to have disease, which would lead to higher prevalence of disease. The information from the questionnaire was treated completely anonymously, which means that owners could share information about their dogs without risking this information to be spread to others.

Cause of death

Only two of the deceased dogs had undergone a post mortem examination, which means that causes of death were determined with different degrees of certainty for the dogs. The results from this study with tumors, heart disease and pneumonia as the most common causes of death, are partly supported by previous studies based on Swedish insurance data by Egenvall *et al.* (2005) and Bonnett *et al.* (2005), where the breed was found to have an increased cause specific mortality rate for heart disease and tumors. Other studies have also reported neoplastic disease to be over-represented as cause of death in the breed (Michell, 1999; Fleming *et al.*, 2011). In this study osteosarcoma accounted for a large portion of all the tumors, and other studies have also shown bone tumors to be a common cause of death (Egenvall *et al.*, 2007; Anfinson *et al.*, 2011). Furthermore, Egenvall *et al.* (2005) and Fleming *et al.* (2011) found that musculoskeletal disorders were reported as a common cause of death in Irish wolfhounds. In the study by Egenvall *et al.* (2005), osteosarcoma was not included in this category, but in the study by Fleming *et al.* (2011) the category included all diseases localized to the specific organ system which allowed tumors such as osteosarcoma to be included. Regarding other musculoskeletal disorders, for example hip dysplasia, a low incidence has been shown in the breed (Krontveit *et al.*, 2010). In our study, joint disease only accounted for 5 % of the deaths. However, some owners reported other causes of death, which cannot with certainty be distinguished from musculoskeletal or neurological disorders, for example paresis (3 %) and stiffness of the neck (1 %). Previous studies have shown diseases in the gastrointestinal organ system to be a common cause of death (Fleming *et al.*, 2011), and in our study, gastric dilation volvulus accounted for 7 % of the causes of death, which actually is a higher proportion than joint disease (5 %).

In our study we also found a high proportion of deaths due to pneumonia, which previously has not been presented in Swedish studies. However, a few other studies have shown an increased

incidence of pneumonia in the breed and also that several dogs affected by respiratory disease eventually were euthanized due to that cause (Clercx *et al.*, 2003; Greenwell & Brain, 2014). Fleming *et al.* (2011) also presented respiratory disease to be one of the most common causes of death in North American Irish wolfhounds.

Dilated cardiomyopathy

Among the Swedish owners of Irish wolfhounds, DCM has attracted great attention because it is fatal, and insurance data has pointed out heart disease in the breed as a major cause of death (Egenvall *et al.*, 2005). This may result in an interest to participate in this study, particularly owners or breeders of dogs having died from DCM or those highly committed to improve the general health situation in the breed are likely to respond to surveys like the present. However, a retrospective study like this will only identify dogs diagnosed with DCM, but not the dogs with preclinical DCM, unless they were examined by echocardiography. Brownlie and Cobb (1999) reported that 12 % of Irish wolfhounds without clinical sign of heart disease had atrial fibrillation (which is an indication of preclinical DCM), which means that the occurrence of DCM among the Irish wolfhounds may be higher than reported in the present study. When comparing the occurrence of DCM in this study population (16 %) one has to remember that in other studies with higher prevalence of DCM (24 %, 26 % and 43 %) dogs have been classified by an echocardiographic examination and preclinical cases are probably included (Vollmar, 2000; Distl *et al.*, 2007; Vollmar *et al.*, 2013). On the other hand, four of the dogs classified to have DCM in this study, were not diagnosed by post mortem examination or echocardiography but were classified as probably affected or with suspicion of DCM by the author. Therefore, a few individuals may have been misdiagnosed concerning DCM. Nevertheless, this study supports the fact that DCM is common in the breed.

When comparing the occurrence of DCM by year of birth, the disease seems to be more common among the dogs born 2006 and 2007 compared to 2008. This is most probable an effect of the lower response rate for dogs born in 2008 and therefore smaller sample size. Another possibility is that dogs born 2008 were younger (7 years old to current date) and had not yet developed DCM. However, studies have reported the mean age of being diagnosed with DCM to be 4-5 years (Vollmar, 2000; Distl *et al.*, 2007; Philipp *et al.*, 2012). The majority of the dogs born 2008 would therefore already have developed the disease if they had the predisposition. A third possibility is that the disease could be declining in incidence in the breed and further research may be warranted.

The number of dogs with DCM in this study was small (16 dogs), but a difference in occurrence between sex was present, however this was not significant. A sex predisposition has been shown in a previous study where DCM in Irish wolfhounds was more common among males than females (Distl *et al.*, 2007). The lack of a significant result in the present study may be due to the small sample size.

Pneumonia

Few studies have been published regarding pneumonia in Irish wolfhounds. These studies report that the incidence in the breed is high and respiratory disease is frequently reported as a

cause of death (Fleming *et al.*, 2011; Greenwell & Brain, 2014). Our study showed that 37 % of the study population had a history of pneumonia on at least one occasion. The occurrence of pneumonia was nearly equally distributed among males and females, and the difference was not significant. These calculations were based on 89 dogs, which is a larger sample size than in a previous study by Greenwell and Brain (2014). In our study, fifty-five percent of the dogs with history of pneumonia had at least one recurrent episode. The combination of a comparably high number of dogs where the owner had reported recurrent episodes of pneumonia, and pneumonia as cause of death, suggest that respiratory disease is a serious problem in the breed. In this study, insufficient information was available to determine how the dogs had been diagnosed and how they had been treated. Questions were asked about course of treatment, time of recurrence and if full recovery was made, but these questions were often answered inadequately, and did not allow any further analysis. Greenwell and Brain (2014) found a predisposing cause for aspiration pneumonia in 44 % of the Irish wolfhounds. In our study, three of the dogs had megaesophagus, which may be suggestive as a predisposing cause for pneumonia. Only sixteen percent of the dogs (5 dogs) with history of pneumonia had also been diagnosed with DCM. Nevertheless, a possible association between pneumonia and DCM would be of interest to explore further in the future. The results from this study showed that more research is warranted regarding pneumonias in the breed, because little is known regarding etiology and predisposing factors.

CONCLUSIONS

The most common causes of death among the Irish wolfhounds participating in this study were tumors, heart disease and pneumonia. Occurrence of DCM in the studied population was 16 % and occurrence of pneumonia on at least one occasion was 37 %. These results support previous results from other studies that DCM and respiratory disease are common in the breed. DCM was more common in males than in females, but the difference was not significant. No sex predisposition was found regarding pneumonia. A high proportion of dogs with history of pneumonia had recurrent episodes. Because DCM and pneumonia also were reported as common causes of death, they should be given attention in the course of improving the general health in the breed. Further research regarding respiratory disease in the breed is warranted.

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APPENDIX 1

Survey

- a health evaluation of Irish wolfhounds

All information about You and Your dog will be treated confidentially

*Mandatory questions are marked with **

Part 1

Information about the dog

Reg. no: *	Breed: Irish wolfhound	
Registered name: *	ID: chip and/or tattoo:	
The dog's name:	Date of birth: *	Coat color:
Sex * <input type="checkbox"/> Male <input type="checkbox"/> Female	Neutered or spayed * <input type="checkbox"/> Yes Date: _____ <input type="checkbox"/> No	
Weight _____ kg <input type="checkbox"/> Normal weight <input type="checkbox"/> Under normal weight <input type="checkbox"/> Overweight		
Has the dog been used for breeding? <input type="checkbox"/> Yes <input type="checkbox"/> No If Yes, how many offsprings does it have? _____		
Have relatives to the dog been diagnosed with dilated cardiomyopathy? <i>(Parents, siblings and offspring are defined as relatives)</i> <input type="checkbox"/> Yes <input type="checkbox"/> No If Yes, which? _____		
Owner		
First name: *	Surname: *	Country: *
Street: *	Postal code: *	City: *
e-mail:	Telephone: Home: Cell phone: Office:	

Continue to part 2 if the dog is DEAD or to part 3 if the dog is ALIVE

PART 2: The dogs is DEAD

How did the dog die *

Euthanasia

Spontaneously

Other.....

If Other, specify: _____

Date of death/euthanasia: * _____

Cause of death *

Dilated cardiomyopathy (congestive heart failure)

Other heart disease

Bone cancer (osteosarcoma).....

Other tumor

Pneumonia

Joint disease

Unknown cause

Other

If Other, specify: _____

The diagnosis was made by *

Echocardiography

Radiography

Necropsy

Unknown

Other

If Other, specify: _____

Was the dog diagnosed with dilated cardiomyopathy prior to death? *

Yes No

If Yes, approximate date: _____

If Yes, did the dog receive any medical treatment due to heart disease?

Yes No

Specify which drugs: _____

If your dog was diagnosed with dilated cardiomyopathy, did the veterinarian diagnose congestive heart failure (fluid in the lungs and/or abdomen)?

Yes No Don't know

Did the dog have clinical signs prior to death? *

Yes No

If Yes, specify by checking below.

Clinical signs

Heart murmur

Irregular heart rhythm/arrhythmia

If arrhythmia, specify which sort: _____

Fatigue

Exercise intolerance

Breathing difficulties

If breathing difficulties, describe breathing pattern: _____

Cough
Abdominal distention
Poor appetite
Weight loss
Other
If Other, specify: _____

Was necropsy performed? * Yes No

Diagnosis from necropsy

Dilated cardiomyopathy
Tumor
Pneumonia
Joint disease
Trauma
Unknown
Other
If Other, specify: _____

Has the dog ever been diagnosed with pneumonia? *

Yes No
If Yes, approximate date: _____

How long was the dog treated for pneumonia? _____

Did the dog recover? Yes No

Did the dog have pneumonia on more than one occasion?

Yes No
If Yes, specify how many occasions and with approximate dates: _____

Have relatives to the dog been affected by pneumonia? *

(Parents, siblings and offspring are defined as relatives)
 Yes No If Yes, which? _____

Information about the veterinarian responsible for treatment

Name of veterinarian: _____

Name of veterinary clinic: _____

Address: _____

Postal code, city and country: _____

Telephone: _____ e-mail: _____

Owner gives us (J. Häggström, I. Ljungvall, K. Höglund eller L. Orleifson) permission to access the dog's case records:

Yes No

Thank you for your participation!

PART 3: The dog is ALIVE

Owner's description of the dog *

- Healthy
- Dilated cardiomyopathy, untreated, no clinical signs from the heart
- Dilated cardiomyopathy, receiving medical treatment but have never had clinical signs from the heart
- Dilated cardiomyopathy, receiving medical treatment and have had clinical signs from the heart
- Other
- If Other, specify: _____

Clinical signs

- Heart murmur
- Irregular heart rhythm/arrhythmia
- If arrhythmia, specify which sort: _____
- Fatigue
- Exercise intolerance
- Breathing difficulties
- If breathing difficulties, describe breathing pattern: _____
- Cough
- Abdominal distention
- Poor appetite
- Weight loss
- Other
- If Other, specify: _____

Veterinary examination has been performed *

- Yes No

Date: _____

Information about the veterinarian responsible for treatment

Name of veterinarian: _____

Name of veterinary clinic: _____

Address: _____

Postal code, city and country: _____

Telephone: _____ e-mail: _____

Owner gives us (J. Häggström, I. Ljungvall, K. Höglund eller L. Orleifson) permission to access the dog's case records:

- Yes No

Information from the veterinary examination

Echocardiography has been performed *

- Yes No

Diagnosis from the echocardiography examination

- Dilated cardiomyopathy
Congenital heart defect
Other heart disease
Other.....

If Other heart disease or Other, specify: _____

Thoracic radiographs have been taken *

- Yes No

Diagnosis from the radiography examination

- Pulmonary edema/fluid in the lungs.....
Heart enlargement.....
Pneumonia
Other.....

If Other, specify: _____

If your dog has been diagnosed with dilated cardiomyopathy, did the veterinarian diagnose congestive heart failure (fluid in the lungs and/or abdomen)?

- Yes No Don't know

Does the dog receive any medical treatment due to heart disease? *

- Yes No

Specify which drugs: _____

When did the medical treatment start; date: _____

Outcome of treatment

- No response
Improved
Good response
Other

If Other, specify: _____

Has the dog ever been diagnosed with pneumonia? *

- Yes No

If Yes, approximate date: _____

How long was the dog treated for pneumonia? _____

- Did the dog recover?** Yes No

Did the dog have pneumonia on more than one occasion?

- Yes No

If Yes, specify how many occasions and with approximate dates: _____

Have relatives to the dog been affected by pneumonia? *

(Parents, siblings and offspring are defined as relatives)

- Yes No If Yes, which? _____

Thank you for your participation!