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Diet-Mediated Dilated Cardiomyopathy in the Canine

Ada-Miette J.Thomas, BSc[1]; Alison Ramser, PhD[2*]; Sami Dridi, PhD[2]

[1]*Department of Food Science, University of Arkansas, Fayetteville, AR 72701, USA*
[2]*Department of Poultry Science, University of Arkansas, Fayetteville, AR 72701, USA*

[*]***Corresponding author***
Alison Ramser, PhD
Postdoctoral Fellow, Department of Poultry Science, University of Arkansas, Fayetteville, AR 72701, USA; E-mail: atramser@uark.edu

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ABSTRACT

Dilated cardiomyopathy (DCM) is a disease of the heart muscle resulting in decreased myocardial function and is the second most common myopathy in canine. Previously, canine dilated cardiomyopathy was considered to be an inherited disease among large and giant breeds, however, recent reports suggest a possible link between certain grain-free diets and this condition. Several investigations into the incidence of this condition in relationship to grain-free diet consumption have been conducted in recent years. The most recent research shows a static overall trend in the incidence of DCM despite a five-fold increase in the sales of grain-free pet foods. Inadequate intake of protein, taurine, and specific sulfur-containing amino acids may have a potential role in the development of DCM, as these nutrients are crucial for cardiac muscle development and function. However, significant research remains to be done on the topic to discern any potential definitive causation.

Keywords
Dilated cardiomyopathy (DCM); Cardiomyopathy; Quince Fruit; Grain-free; Nutrition; Baltistan.

INTRODUCTION

Dilated cardiomyopathy (DCM) is a significant cause of morbidity and mortality in canines.[1] This condition is characterized by dilation and compromised contraction of the left or both heart ventricles. DCM has been the subject of much research in recent years. In 2019, the Food and Drug Administration (FDA) raised concerns about a potential link between pulse ingredient-rich diets (grain-free diets) and DCM related to taurine deficiency. As a result, current research has focused on discerning a link between grain-free diets and the incidence of DCM.[2] Recent research has suggested a possible affiliation of DCM with a deficiency in other amino acids and their precursors as well (Figure 1).

DILATED CARDIOMYOPATHY IN CANINES

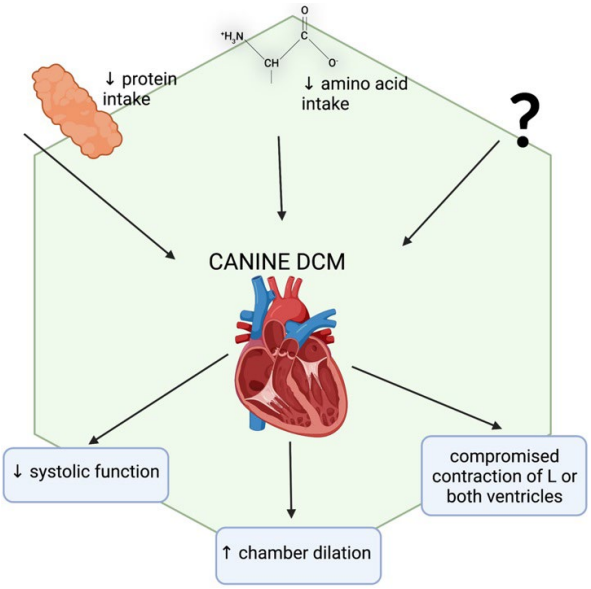
Incidence

Dilated cardiomyopathy is the second most common heart disease in canines.[3,4] Concerns have arisen that the incidence of this condition is increasing. Previously, canine DCM was primarily considered to be an inherited disease among specific breeds, however, there have been recent reports suggesting a possible link between certain types of diets and this disease.[5-9] This condition is more prevalent in large and giant breeds (e.g., Irish Wolfhounds, German Shepherd Dogs, Doberman Pinschers, Golden Retrievers, etc.).[4,10,11] Veterinary cardiologists have reported subjectively more frequent diagnoses of DCM in atypical breeds.[10,12,13] Recent studies have sought to investigate an increased incidence of DCM due to variety of factors. There may be a potential link between this condition and environmental/regional, breed-specific, and/or diet factors.[14] Currently, research is primarily focused on diet-mediated DCM, as concerns were raised by the FDA over incidence of this condition and grain-free pet food sales.[4,15] An incidence rate of 0.4% was reported among all patients assessed at a specific veterinary teaching hospital in the United States from 1995-2010.[16] Interestingly, a European study reports an incidence rate of 1.1%.[17] Concerns over the incidence of this condition are rising, however, research shows a static overall trend in the incidence of DCM over time.[14] The etiology of this condition still requires much research to identify.

Clinical Signs and Diagnosis

The clinical phase of DCM can be identified by decreased systolic function typically followed by chamber dilation, often progressing to congestive heart failure, arrhythmias, and in some cases,

Figure 1. *Graphical Summary: Decreased protein and amino acid intake leads to canine dilated cardiomyopathy, which is characterized by decreased systolic function, increased chamber dilation, and impaired contraction of left or both heart ventricles. Much research remains to be done to determine further definitive causation of this disease. Created with* BioRender.com



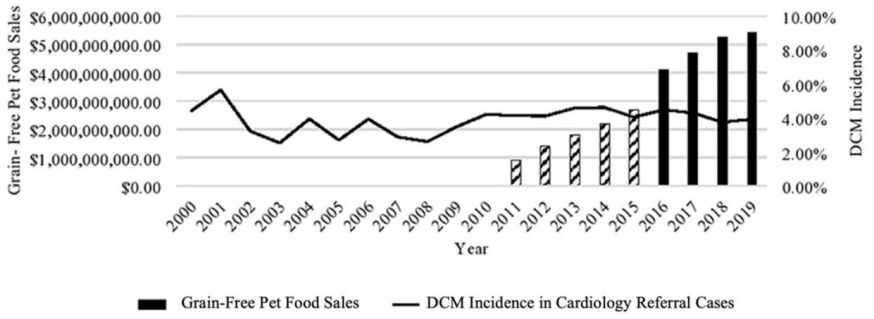
sudden death.[14] This condition is characterized by dilation and compromised contraction of the left or both heart ventricles.[18] A 2022 study also characterized the metabolomic profile of canines with DCM and found that oxidative stress was a major pathway implicated in DCM compared to healthy controls.[19] Often times, DCM can go unnoticed for the majority of the condition, as symptoms are often not readily present until further development. This leads to difficulty diagnosing the condition. Once the condition is symptomatic, active exclusion of other potential causes of these symptoms must take place before a definitive clinical diagnosis can be made.[18] Often, the clinical phase of DCM is a result of long-term progression. In fact, sudden cardiac death can sometimes be the first manifestation of the disease.[3,18,20] Pre-screening and diagnosis are paramount in the treatment of DCM.[21] Diagnosis of the disease is based on left ventricular dilation, depressed systolic function, altered geometry of the left ventricle (increased sphericity), left or bi-atrial enlargement, increased mitral valve M-mode E point to septal separation (EPSS), and arrhythmias recorded on the simultaneous electrocardiogram (ECG) through echocardiographic (echo) examination.[18,22] Diagnosis of this condition is primarily based on these findings as well as active exclusion of other cardiovascular conditions.[23] Veterinary cardiologists may employ a variety of diagnostic tests to evaluate the development of DCM. A definitive diagnosis can be made using echocardiographic findings to confirm symptoms such as reduced systolic function, enlarged left atrium, and/or dilated ventricular chambers.[24-26] Physical examination, imaging modalities, electrocardiogram evaluation, twenty-four-hour Holter monitoring, and cardiac biomarkers may be used to diagnosis this condition.[21,27] Physical examination of the canine may reveal irregular heart rhythm, weak pulse, systolic murmur with maximum intensity in the left sixth intercostal space.[14,24] Imaging modalities such as thoracic radiography and echocardiography are crucial when diagnosing DCM as they can reveal increased end-diastolic and end-systolic diameter of the left ventricle, as well as fractional shortening.[28,29] Arrhythmia of the ventricles can be detected using electrocardiographic evaluation, as well as atrial and ventricular enlargement.[14,30] Twenty-four-hour Holter monitoring, however, is the benchmark evaluation method for detection of arrhythmias.[31] Measurement of cardiac biomarkers such as cardiac troponin–I concentration (indicative of myocardial damage) offers a more complete analysis of the condition than other diagnostic tools alone.[14,32] In the case of DCM, increasing concentration of cardiac troponin–I is associated with increasing myocardial damage.[32]

DIETARY MEDIATION

Diet Composition

In July 2019, the Food and Drug Administration (FDA) released a public statement reporting a total of 560 canines with diagnosed with possible diet-mediated cardiomyopathy.[4,15] More than 90% of the diets consumed by the subjects at the time of diagnosis were grain-free and 93% of the diets contained peas and/or lentils.[15] Several investigations into the incidence of this condition in relationship to grain-free diet consumption have been conducted in recent years as a result.[33-36] In a study of 86 golden retrievers, researchers hypothesized that dogs eating non-traditional diets (e.g., grain-free diets containing peas and/or lentils) are at higher-risk for contracting diet-mediated DCM than dogs eating traditional diets (e.g. grain-inclusive diets).[37] Results of this study suggested increased incidence of DCM in canines eating non-traditional diets, however, study design and statistical analysis are

Figure 2. *Annual Average Incidence Rate of DCM and Grain-free Pet Food Sales from 2000-2019*[14]



questionable as comparisons made between groups of differing sample sizes were done using the mean when the coefficient of variation should have been used. Additionally, the inclusion criteria for the non-traditional diet was very strict and required all five of the outlined criteria to be met, while inclusion criteria for the traditional diet was very broad and only required meeting two or more of the outlined criteria.[37] Most recently, a meta-analysis reported a static overall incidence of the condition over time, while there was a five-fold increase in grain-free pet food sales (Figure 2). This study concluded there was no correlation between incidence of the condition and consumption of grain-free diets.[14] Further research on dietary-mediation of the condition suggests that diets low in protein, taurine, and specific sulfur-containing amino acids may have a significant role in the development of DCM, as these nutrients are crucial for cardiac muscle development and function.[3] Diets high in insoluble fiber have been shown to have antinutritive effects relating to decreased crude protein digestibility in the gut.[38,39] A decrease in crude protein digestibility can affect the bioavailability of taurine, carnitine, and other amino acids.[40] In a separate, non-controlled study, canines diagnosed with DCM who consumed diets supplemented with taurine and L-carnitine showed reduced clinical signs and longer lifespan.[41] Therefore, diet-mediated DCM could be influenced by the metabolism of protein, taurine, and specific amino acid precursors. Future dietary mediations could also target oxidative stress and overall inflammation as both have been shown to be associated with DCM in canines.[19]

Nutrient Deficiencies

Cardiac muscle function is largely affected by taurine and it's precursors (methionine and cysteine), and carnitine and it's precursors (methionine and lysine).[3,42] Copper, potassium, thiamine, selenium, and vitamin E deficiencies are also linked to myocardial damage, however, further research is required to determine a connection.[3] Although non-essential, taurine is an important sulfur-containing amino acid that largely affects the functions of the cardiovascular, skeletal, and central nervous systems. Methionine and cysteine are sulfur containing amino acids that form the non-essential amino acid, taurine.[43] The bioavailability of these precursors can affect the endogenous synthesis of taurine in the liver.[43] Another important nutrient to consider is carnitine. Deficiencies in taurine and carnitine have been shown to be correlated with decreased myocardial function.[44,45] Carnitine is endogenously synthesized in the liver as well and the bioavailability of its precursors, methionine and lysine, can affect the synthesis of the amino acid.[46] In a human survival study, administration of carnitine in patients with DCM showed statistically significant survival rates when compared to a control group.[47] Similarly, in a study conducted on a family of dogs with DCM, supplementation with carnitine showed greatly improved myocardial function. Withdrawal of carnitine supplementation lead to development of clinical symptoms of DCM.[45]

CONCLUSION

Recent reports from the FDA suggest a potential dietary-mediation in the incidence of DCM. As a result, much research has been done to investigate possible causation of this condition due to grain-free pet food. The most recent meta-analysis shows no correlation between incidence of the condition and grain-free pet food sales. Protein, taurine, and specific sulfur-containing amino acids are crucial for cardiac muscle development and function. Diets low in these nutrients may have a significant role in the development of DCM, however, much research remains to be done before definitive conclusions can be made on the etiology of the condition.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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