AMERICAN KENNEL CLUB
CANINE HEALTH FOUNDATION
PREVENT TREAT & CURE

RESEARCH PROGRESS REPORT SUMMARY

Grant 01994: Early and Accurate Prediction of Mitral Valve Disease Development

Principal Investigator: Dr. Sydney N. Moise, DVM

Research Institution: Cornell University

Grant Amount: $29,501.81

Start Date: 1/1/2014 **End Date:** 12/31/2014

Progress Report: End-Year 1 FINAL

Report Due: 12/31/2014 **Report Received:** 2/16/2015

Recommended for Approval: Approved

(Content of this report is not confidential. A grant sponsor's CHF Health Liaison may request the confidential scientific report submitted by the investigator by contacting the CHF office. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:

In the dog, 75% of heart disease is caused by myxomatous mitral valve degeneration (MMVD). Yet between 1960 and 2012 less than 12% of publications concerned MMVD even though it affects ~75% of older small breed dogs. The cause of MMVD likely involves the interplay of genetics, aging, and mechanical insult. A dog's mitral valve opens and closes ~120,000/day under a constant barrage of mechanical forces. With such stress, the struggle of the valvular tissue to stay 'normal' is constant. Our overall hypothesis is that dogs that suffer from MMVD have altered strain profiles on the mitral valve leaflets. This altered strain will be related to the structure of the mitral valve apparatus, which in turn is linked to breed size and/or chondrodystrophic features of the dog. Using our computer algorithm to assess the motion of the mitral valve leaflets the mechanical signatures of valvular strain can be determined. We believe that these signatures are identifiable at a young age in the breeds most commonly affected with MMVD. Although MMVD may afflict the majority of dogs of some breeds, some individuals are not affected even at an advanced age. We believe such a cohort of aged dogs of high risk breeds have strain patterns matching those of dogs of low risk breeds. A quantitative understanding of mitral leaflet strain will both improve our ability to predict MMVD susceptibility and increase the power and resolution of gene mapping efforts, and if successful will inform new targets and timelines for therapeutic intervention.

Grant Objectives:

To obtain a quantitative understanding of mitral leaflet strain that will both improve the ability to predict MMVD susceptibility and increase the power and resolution of gene mapping efforts.

Publications:

None at this time.

Report to Grant Sponsor from Investigator:

Myxomatous degeneration of the mitral valve (MMVD) is the most common cardiac disease of dogs. Research into the underlying mechanisms of this disorder is uncommon with most studies concerning the treatment of advanced disease. The cause of MMVD likely involves the interplay of genetics, aging, and mechanical insult. Likely dogs that suffer from MMVD experience altered mechanical strain on the leaflets of the mitral valve that amplifies the degenerative process. Consequently, we hypothesize that certain mechanical signatures of valvular strain exist in dogs of breeds at risk to develop MMVD and that these signatures are identifiable at a young age. We believe that dogs with abnormal strain patterns will have a mitral valve apparatus that differs structurally from dogs with normal strain patterns and that these profiles of strain will be related to dog size/chondrodystrophic phenotype. Although MMVD may afflict the majority of dogs of some breeds, some individuals are not affected even at an advanced age. We believe such a cohort of aged dogs of high risk breeds have strain patterns matching those of dogs of low risk breeds. We will determine if the morphology of the mitral valve apparatus differs in this cohort. The in vivo leaflet kinematics of the mitral valve will be quantified by computational analysis of image datasets obtained non-invasively by echocardiography. We believe establishing correlations of leaflet strain with structural anatomy and/or breed morphometry will both improve our ability to predict MMVD susceptibility and increase the power and resolution of gene mapping efforts.

At this point our progress since the beginning of our grant which was January 16, 2014 has included the acquisition of the quantification of phenotype and echocardiographic examination of a subset of dogs to obtain preliminary data. Due to funding constraints about which the Canine Health Foundation is aware uncertainty about the future has led to the loss of our assistance in the biomedical engineering department. However, Dr. Moise and Dr. Butcher are diligently working together during the next couple of months to identify another individual to assist the cardiologist at Cornell University with this investigation. We are dedicated to the completion and implementation because we believe in the value of this study.