Effect of Obesity and Hypertension on Heart Biomechanics
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Introduction
Heart disease is the leading cause of death in the United States, causing over 600,000 deaths annually. Two of the most common risk factors associated with heart disease are obesity and hypertension, which combined, affect over 80 million adults every year. The economic and social costs of heart diseases exceed 207 billion dollars annually [1]. A possible cause for heart dysfunction may be revealed through analysis of the mechanical properties of the muscle fibers in diseased heart muscle.

To accurately model human function, two groups of rats, ZSF1CN and SDCN, were used in testing the mechanical properties of the heart. ZSF1CN rats are bred to be naturally and obese, are genetically predisposed to diabetes, and are hypertensive. The SDCN, or Sprague-Dawley control, are the control model. Within the heart muscles we looked specifically at the left ventricular papillary muscles since the fibers of this muscle are aligned to avoid complex force directions. Only the contractile apparatus of this muscle was examined, meaning only a constant contraction of muscle and not the twitching behavior the heart experiences in vivo. To examine contractile behavior, passive force and active force responses from the muscles tissue were collected. A force-length procedure, which uses various sarcomere lengths, collected passive force data. A length-ramp procedure, which consists of small perturbations of length above and below a set sarcomere length, collected active force data. The length data and corresponding force responses were used to create a mathematical model which represents underlying biophysical and biochemical theories of actin-myosin interactions [2]. There are five parameters that are incorporated into this Ford model. They are: distortion kinetic (c) and magnitude (ν0) parameters, recruitment kinetic (b) and distortion (λd) parameters, and the term for the interaction of the distortion and recruitment (γ). Distortion is the disassembling of cross-bridges and recruitment is their assembly.

Objective
The overall objective of the experiment was to determine if obesity and hypertension have a significant impact on the passive and or active properties of cardiac tissue mechanics.

Success Criteria
To confirm the success of our experiments we had to show the adequacy of the animal model (increased weight in ZSF1CN), acquire a minimum of six rats per group, and then prove the validity of the mathematical model for both stretches and releases of sarcomere length.

Methods
To begin the experiment, left ventricular papillary muscles were extracted from either the ZSF1CN or SDCN rats. A microscope and scalpel were then used to cut the muscles into strips for additional samples. The strips were then demembranated overnight using a relaxing solution containing 1% Triton X-100 to remove the sarcoplasmic membrane and allow constant calcium activation [3]. The skinned muscles were then placed in normal relaxing solution.

The skinned muscles were attached to aluminum t-clips and were placed on the hook of a displacement motor on one end and on the hook of force transducer on the other end. The muscles were then lowered into a 45 ml bath and cycled through relaxing, pre-activating, and activating solution to fully activate the muscle two times. Laser diffraction was used to determine quality of muscle preparation and the sarcomere length. The muscle length and passive force response was recorded for sarcomere lengths 1.8 to 2.4, by .1 increments. Passive force data was fit to an exponential equation to be used to determine active force more accurately.

The motor arm was then used to apply 0.5%, 1%, 1.5% and 2% stretches and releases. This was done for long and short sarcomere lengths, 2.3 um and 1.9 um respectively. Both lengths were also tested at both full and half maximal calcium activation. The force and length data was recorded at a sampling rate of 2000 Hz.

The Ford mathematical model of the underlying mechanical properties of the force change vs length change relationship was used to analyze cross-bridge mechanics. A series of MATLAB programs were improved upon and used to estimate the model parameters and additional basic force measurement from the force and length data coming from the stretches and releases. The values of the parameters for the passive and active information were compared for the ZSF1CN and SDCN groups.

Results
Data has not been fully collected from the Ford model analysis at this point in the experiment. However, all passive data and initial active force data has been retrieved for full activation at long sarcomere length. Figure 1 shows the success of the mathematical model, with a R² value of .92 for the greatest stretch and release. This was performed on a SDCN rat.
Discussion

The results of the current analysis do not support a functional difference between the force generation of control and obese/hypertensive rats. The cross-bridge dynamics have yet to be fully analyzed but the initial analysis of the magnitude parameters for distortion and recruitment show no significant difference. The passive force trends towards a significant value for the group data, meaning that the control rats may have higher passive tensions. Higher passive tension indicates a stiffer muscle fiber.

The decreased change in steady state force in the ZSF1CN could indicate an adaptive feature in the obese rats. A lower change in force means an ability to maintain force after initial contraction, which could be an adaption to increased work for obese rats. Additionally, the high R² value in the fit equation indicates the Ford model is sufficient to describe the force length relationship.

Unfortunately, there are not enough samples within the control group to be confident in any of the statistical analysis. More than double of the controls are in the process of analysis which will allow better understanding in the future.

Future research from the experiment include the analysis of the half maximal and the short sarcomere length data. Additionally, twitching muscle and force-pCa curves will be looked at for better physiological understanding.

Acknowledgments

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References


[2] Steven J. Ford, Murali Chandra, Ranganath Mamidi, Wenji Dong, and Kenneth B. Campbell, Department of Veterinary and Comparative Anatomy, Pharmacology, and Physiology, Washington State University, Pullman, WA 99164