

Characterizing the cardiac phenotype in Quarter horses with equine neuroaxonal dystrophy

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Introduction and Rationale



- Equine neuroaxonal dystrophy (eNAD) is an inherited neurological condition
- eNAD clinically resembles two human disorders:
 - Ataxia with vitamin E deficiency (AVED)
 - Friedreich's Ataxia (FA)
- Cardiomyopathy is reported in the majority of Friedreich's Ataxia patients, contributing to death in 83.3% of cases

Objective: To characterize the cardiac phenotype of eNAD affected horses to improve understanding of the systemic effects of this condition

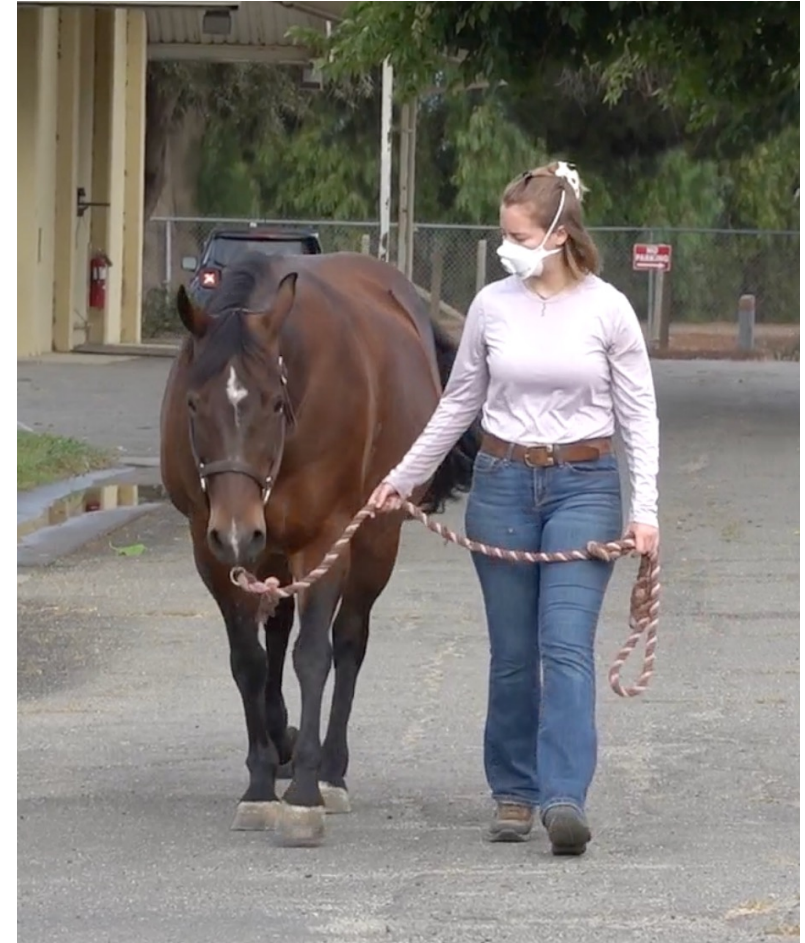
Hypothesis

Quarter horses with eNAD exhibit subclinical cardiomyopathy that manifests as myocardial thinning, a higher prevalence of arrhythmias, and histologic evidence of myocardial degeneration.

Aim 1: *In Vivo*

Aim 1: Define the cardiac structure and function in Quarter horses with eNAD as compared to unaffected controls using echocardiography, electrocardiography, and cardiac serum biomarkers.

- **Study population:** 7 eNAD suspect Quarter horses and 7 breed/age matched controls
 - Co-housed at the Center for Equine Health



Horse Summary

Control group

7 Quarter horses

3 mares, 4 geldings

Mean age: 12 years old

Mean BCS: 7

Mean weight: 576 kg

eNAD group

7 Quarter horses

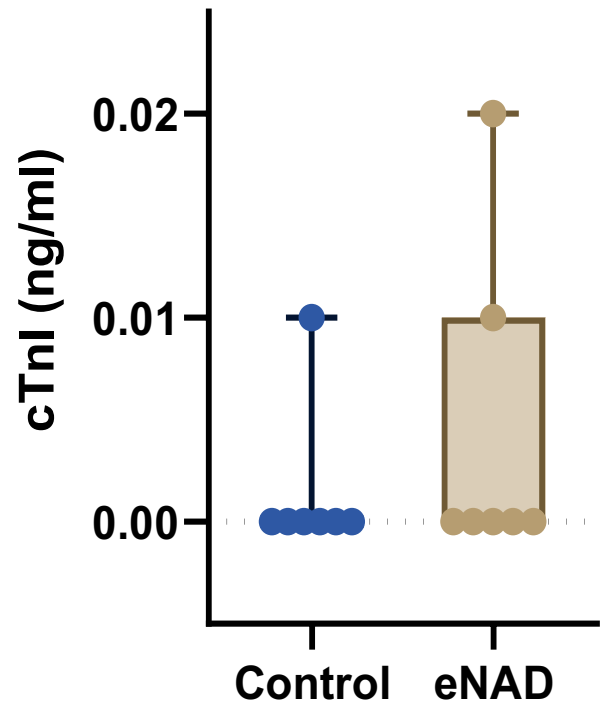
4 mares, 3 geldings

Mean age: 9 years old

Mean BCS: 7

Mean weight: 533 kg

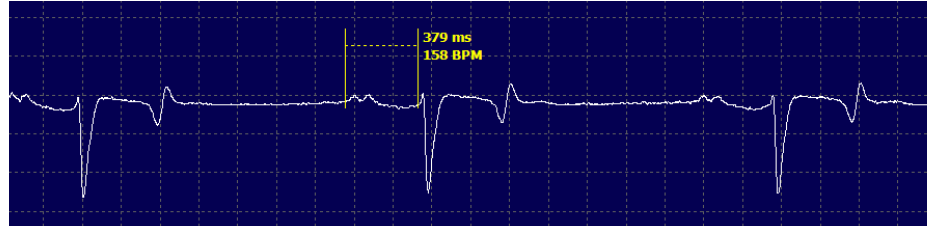
Methods: Bloodwork



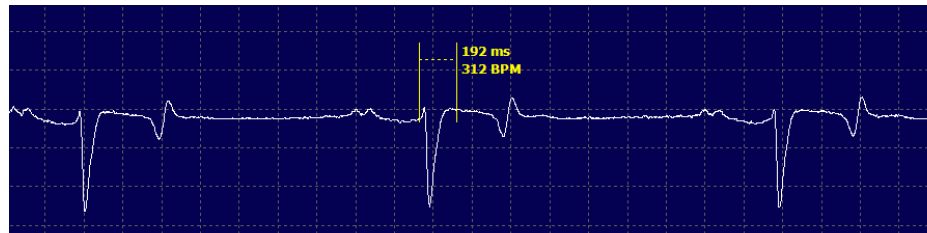
University of Pennsylvania cTnI reference range: 0-0.07 ng/ml

Methods: Electrocardiography

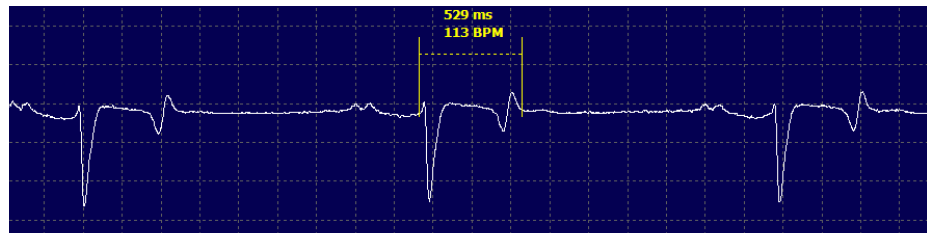
PR interval



QRS width



QT interval



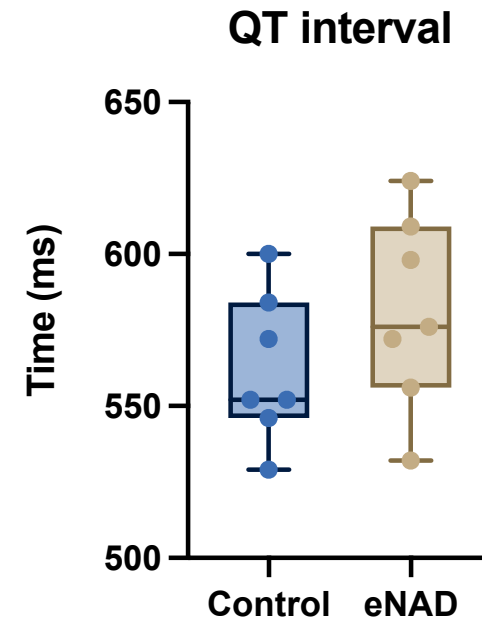
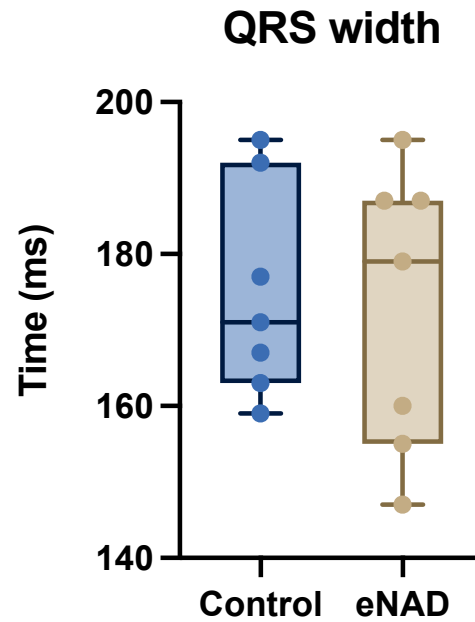
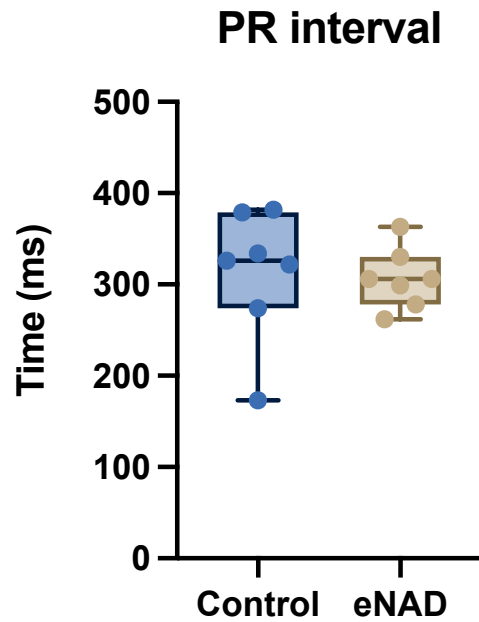
24 hour Holter monitor

Methods: Echocardiography

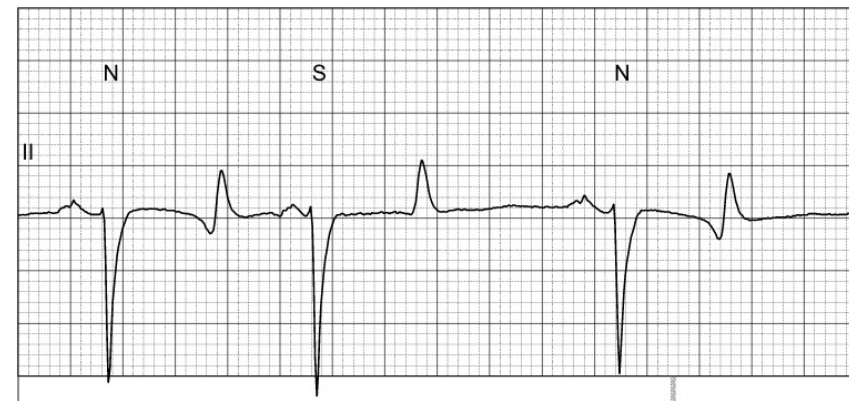
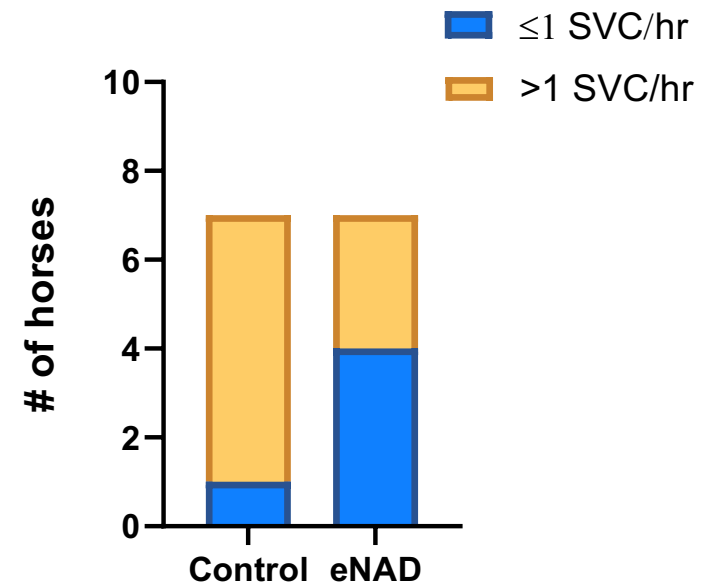
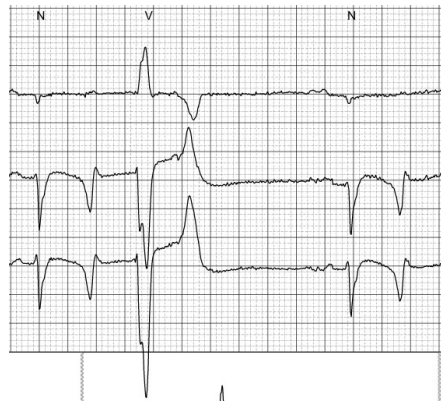
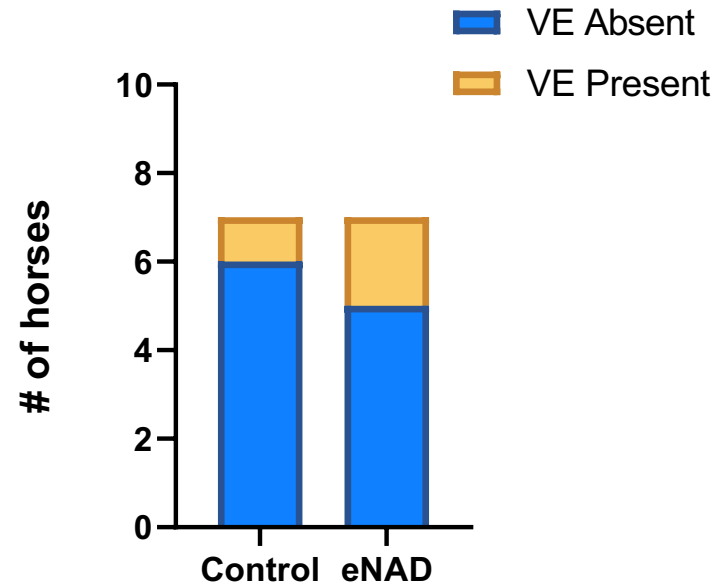


- Full echocardiogram exam with 6 standard views in long axis (LAX) and short axis (SAX) from right side and left side long axis 2 chamber view
- Single lead ECG recorded simultaneously
- Views of interest:
 - **Left outflow tract** – aortic diameter
 - **Short axis of L ventricle** – linear M-mode
 - **2 chamber view** – left atrial diameter
 - **4 chamber view** – volume and area

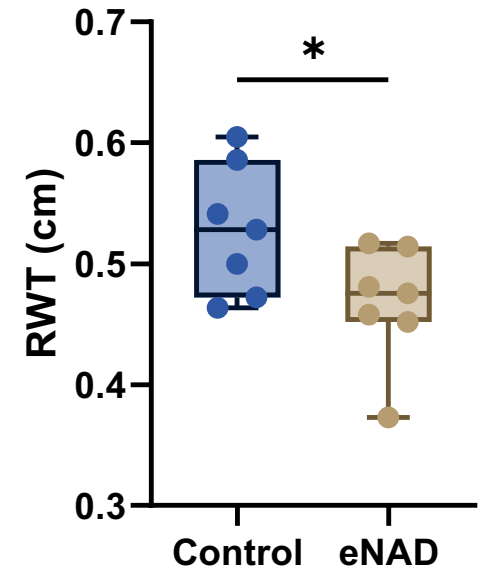
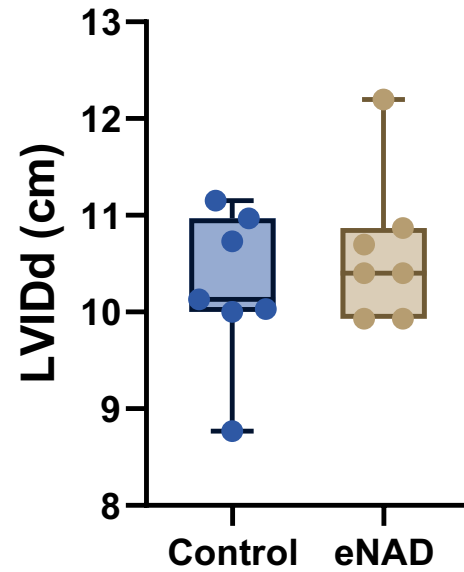
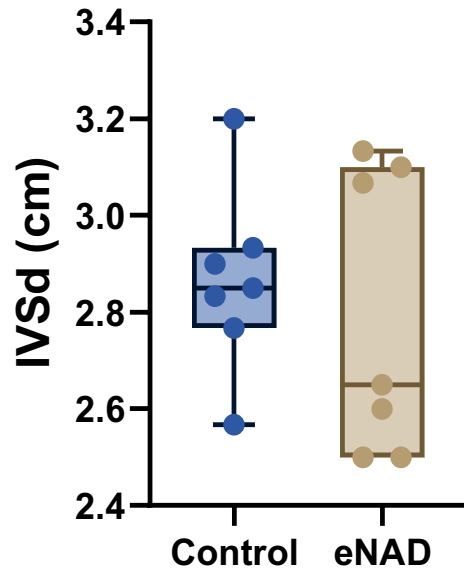
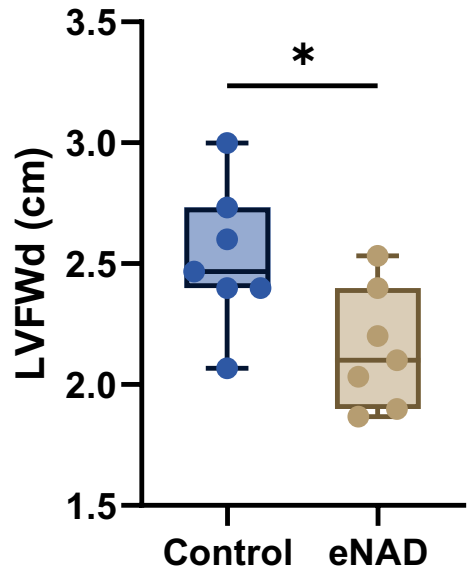
Basic Conduction Factors



Arrhythmia Prevalence



Cardiac Structure



RWT = [left ventricular free wall thickness in diastole (LVPWd) + intraventricular septal thickness in diastole (IVSd)]/left ventricular internal diameter in diastole (LVIDd)

Significance Summary

Cardiac troponin I quantification

Basic conduction factors

Heart rate variability

Arrhythmia prevalence

Cardiac function

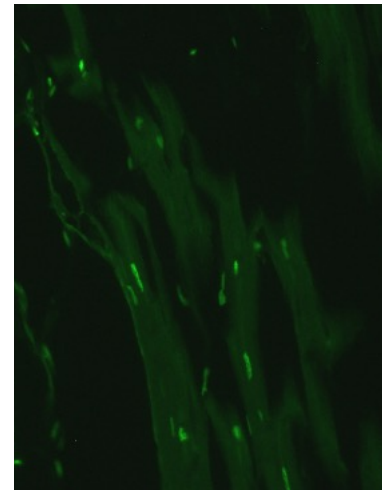
No significant differences detected between the two groups

Cardiac structure: Horses in the eNAD group had a significantly decreased left ventricular free wall thickness ($p=.024$) and significantly decreased relative wall thickness ($p=.047$).

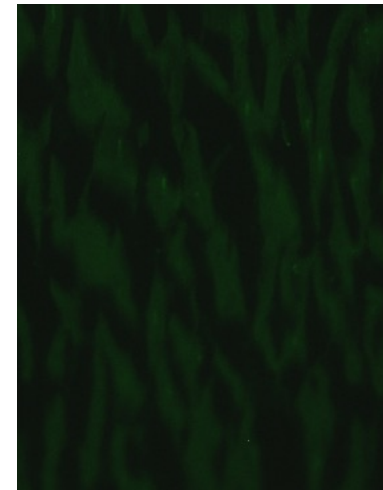
Aim 2: *In Vitro*

Aim 2: Identify evidence of changes in left ventricular mass, and accumulation of oxidative damage and apoptosis in the myocardium of horses with eNAD submitted for post-mortem evaluation compared to breed-matched controls.

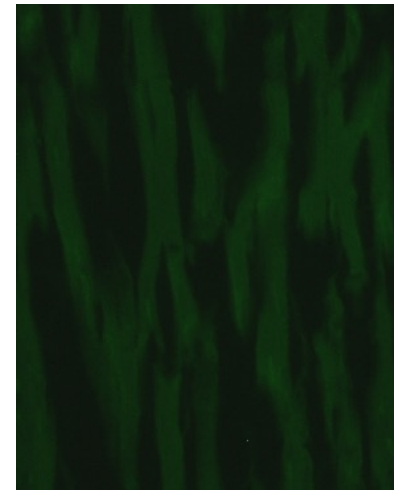
- **Study population**
 - 14 eNAD affected cases and 7 unaffected controls
- **Immunofluorescence assays:**
 - Apoptosis (TUNEL, ROCHE In Situ Cell Death Detection Kit, Fluorescein)
 - Oxidative damage to DNA (anti-oxo-8-guanine, Abcam).



+ control



Test sample

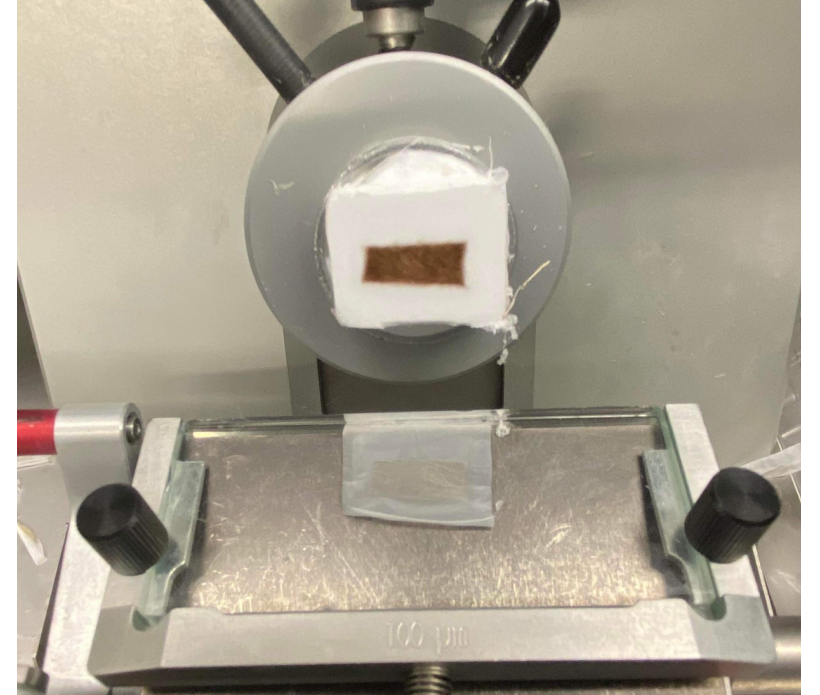


- control

Acknowledgements

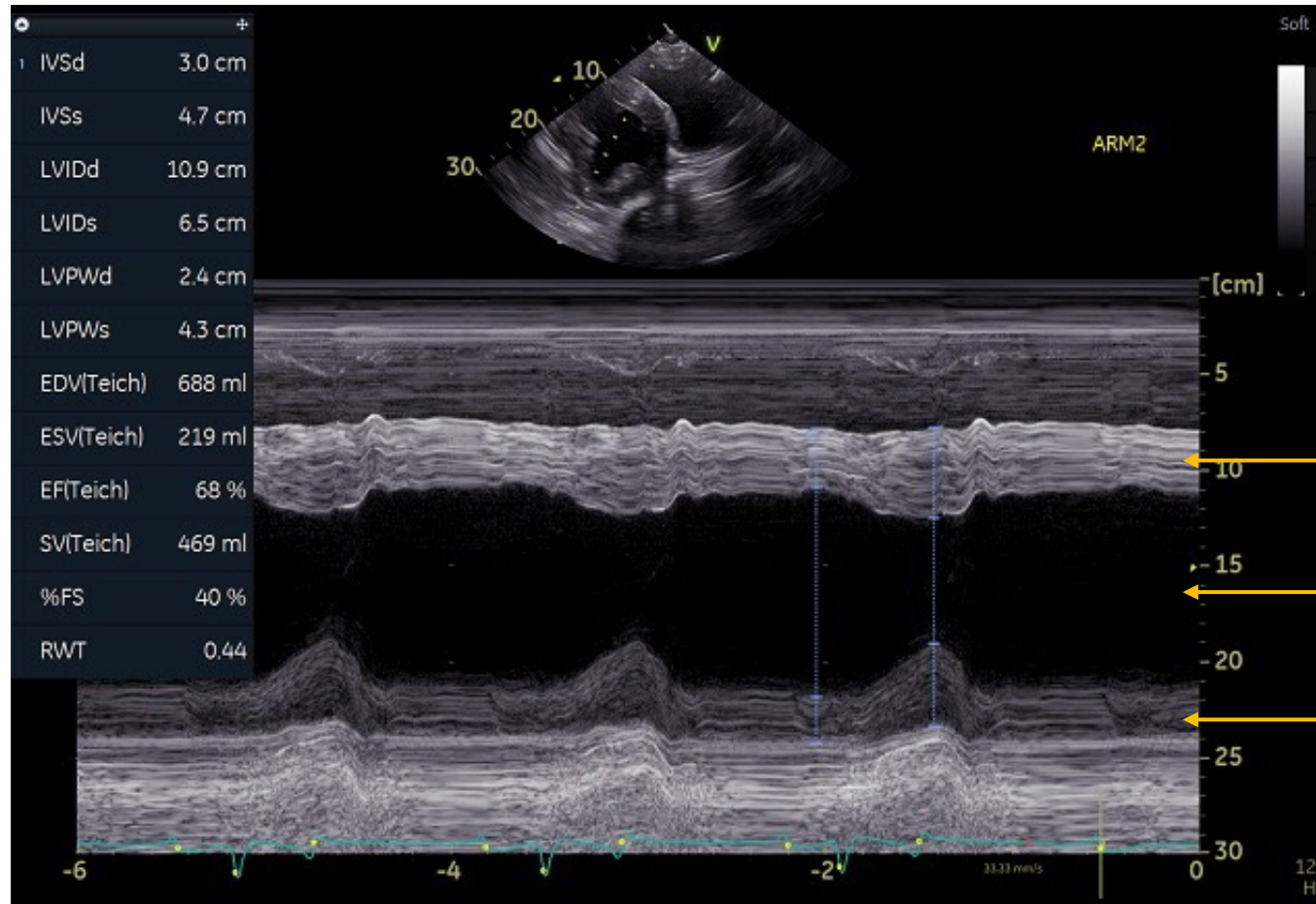


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Methods: Echocardiography

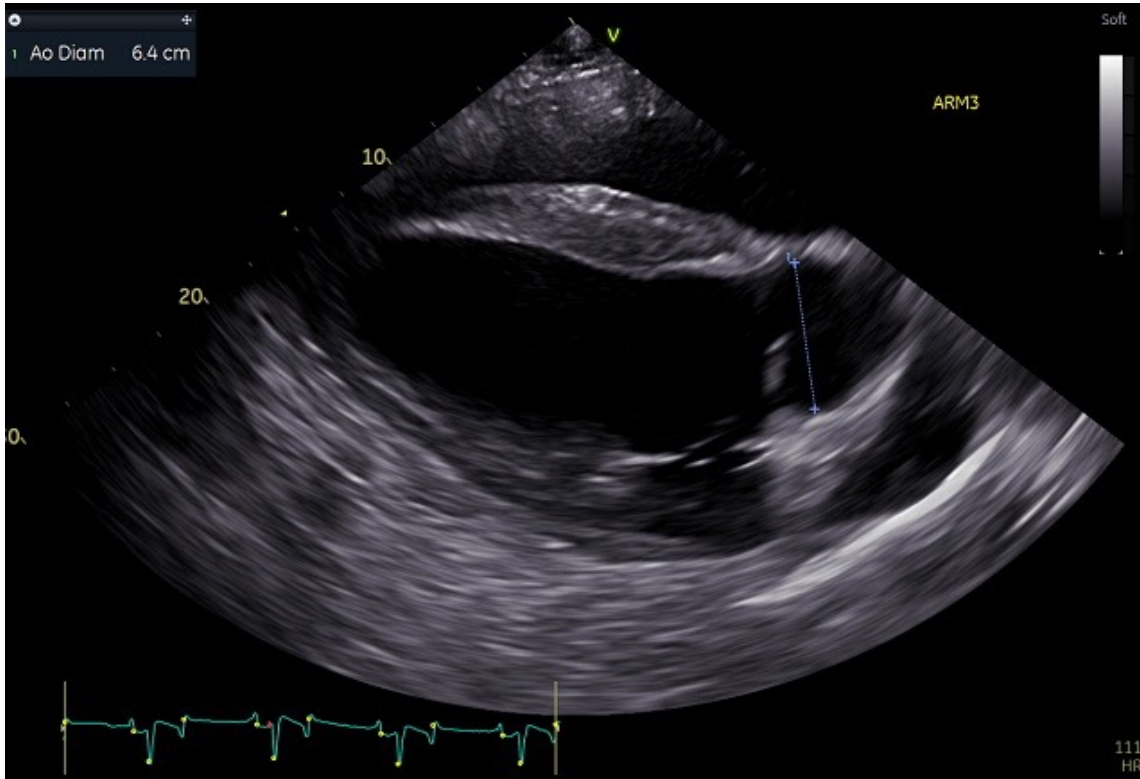


Interventricular septum (IVS)

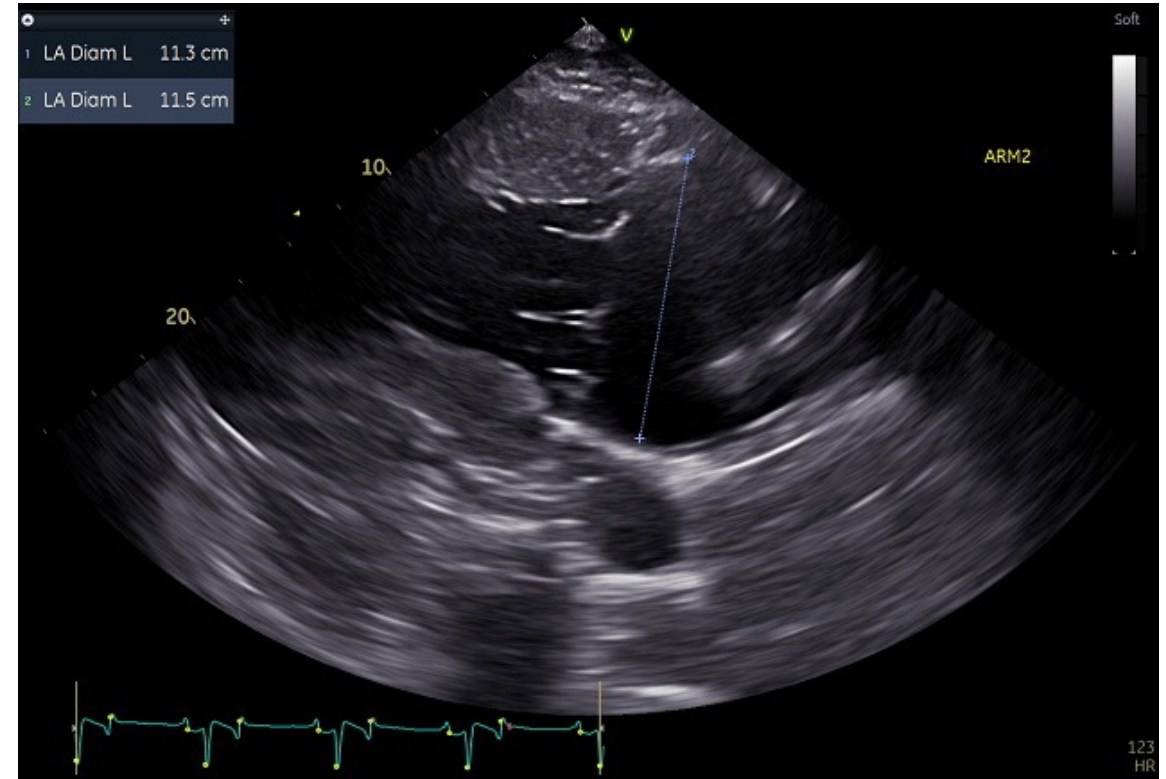
Internal diameter (LVID)

Ventricular free wall (LVPW)

Methods: Echocardiography

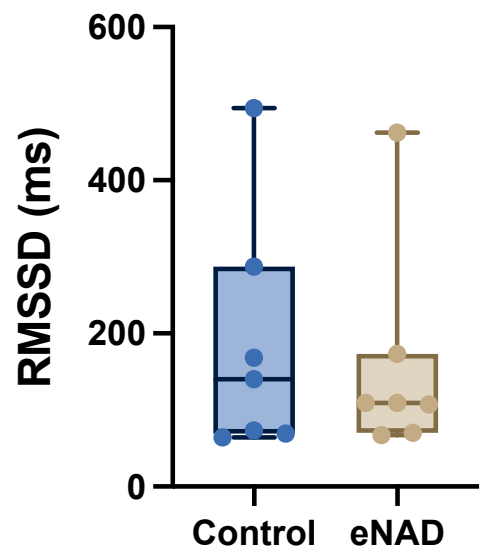


Left outflow view – Aortic diameter

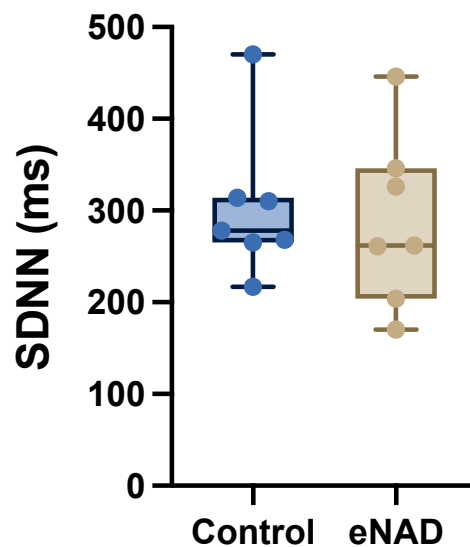


2 chamber view – Left atrial diameter

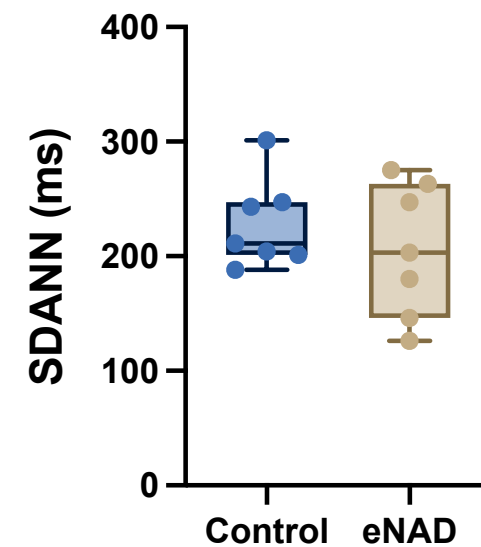
Heart Rate Variability



Root mean square of successive differences between normal heartbeats



Standard deviation of R-R intervals



Standard deviation of the average R-R intervals for each of the 5 min segments during a 24 h recording

Cardiac Function

