Characterizing the cardiac phenotype in Quarter horses with equine neuroaxonal dystrophy

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UC DAVIS VETERINARY MEDICINE
Students Training in Advanced Research

Background and Rationale

Equine neuroaxonal dystrophy (eNAD) is an inherited neurodegenerative disease characterized by early onset ataxia and histologic lesions within the caudal brainstem and spinal cord.[1] The clinical and histologic features of eNAD resemble an inherited neurodegenerative condition in humans known as ataxia with vitamin E deficiency (AVED).[2] AVED was once referred to as Friedreich's Ataxia with isolated Vitamin E deficiency because the neurologic deficits associated with Friedreich's Ataxia are indistinguishable from those of AVED. Cardiomyopathy is reported in the majority of Friedreich's Ataxia patients, contributing to death in 83.3% of cases in one postmortem study.[3,4,5,6] The goal of this project is to compare the cardiac structure and function evaluated by echocardiography and electrocardiography in Quarter horses with eNAD and unaffected breed-matched controls. Characterizing the cardiac phenotype of horses affected by eNAD will improve understanding of the systemic effects of this complex heritable condition.

Hypothesis

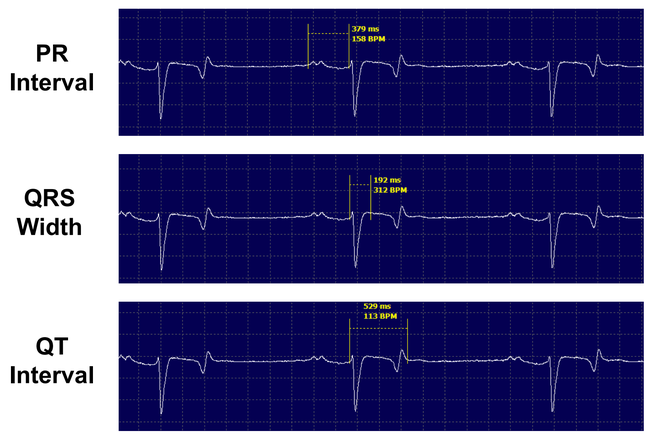
Quarter horses with eNAD exhibit subclinical cardiomyopathy that manifests as myocardial thinning and a higher prevalence of arrhythmias.

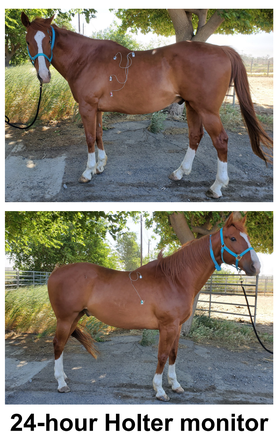
Methods

Study Population

Horses for this study were selected from the Center for Equine Health (CEH) herd at UC Davis. Cases included 7 eNAD suspect Quarter horses and 7 age and breed-matched controls.

Electrocardiography: Cardiac Electrophysiology





24-hour Holter monitor

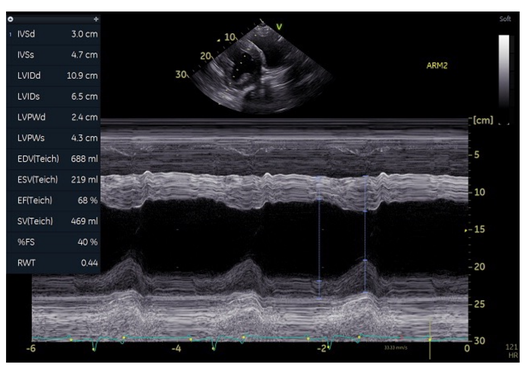
Blinded electrocardiographic data available from 24-hour Holter monitors was semi-automatically analyzed and used to compare prevalence and type of arrhythmias and heart rate variability estimates between eNAD suspect and unaffected horses. Duration of complexes and relevant intervals were manually measured and compared between groups.

Blood work: Cardiac Troponin I

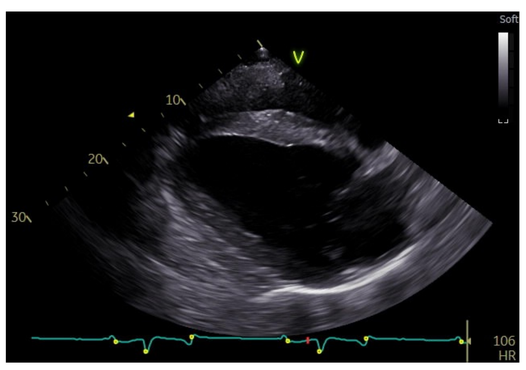
Blood drawn at the time of each horse's ECG was evaluated at the University of Pennsylvania for cardiac troponin I quantification.

Echocardiography: Cardiac Structure and Function

Echocardiography was performed with the Vivid Iq Ultrasound system, using 6 standardized equine echocardiographic views in short and long axis and a long axis 2 chamber view from the left.[7]



Short axis of the left ventricle- M-mode



Long axis 4 chamber view

Statistics

Data was assessed for normality using a Shapiro-Wilk test, and most variables were compared between cases and controls with a student's T-test or Mann Whitney-U test, where appropriate. Arrythmia prevalence data was compared between cases and controls using a chi-squared test.

Acknowledgements

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Results

Cardiac Structure

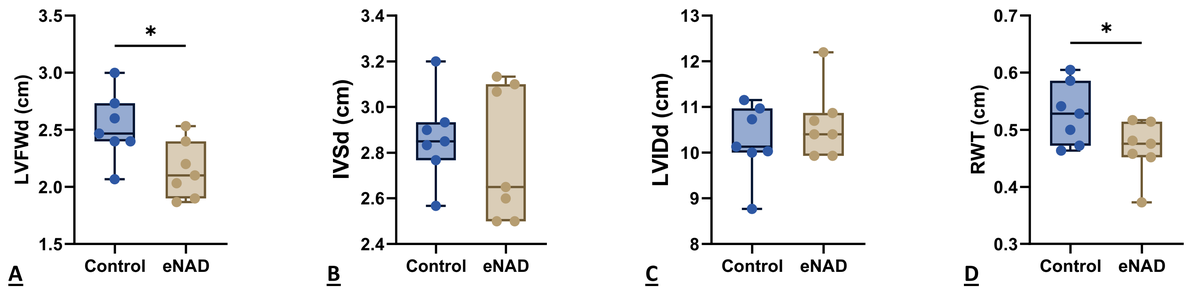


FIGURE 1 | Box and whisker plots of selected cardiac structural measurements performed on echocardiograms of horses with equine neuroaxonal dystrophy (eNAD) compared to controls. **(A)** Left ventricular free wall in diastole (LVFWd) **(B)** Interventricular septum in diastole (IVSd) **(C)** Left ventricular internal diameter in diastole (LVIDd) **(D)** Relative wall thickness of the left ventricle (RWT) was calculated as [left ventricular free wall thickness in diastole (LVFWd) + intraventricular septal thickness in diastole (IVSd)]/left ventricular internal diameter in diastole (LVIDd). *= p≤0.05. LVFWd and RWT were significantly decreased in eNAD horses compared to controls consistent with myocardial wall thinning.

Basic Conduction Factors

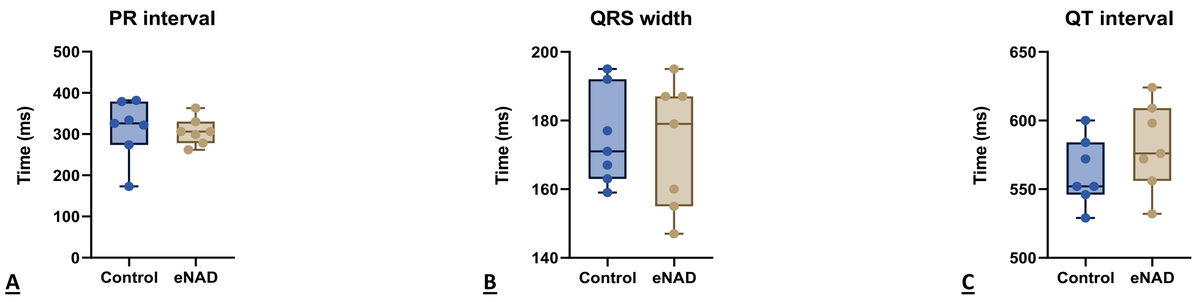


FIGURE 2 | Box and whisker plots of basic conduction factors in horses with equine neuroaxonal dystrophy (eNAD) compared to controls. **(A)** PR interval, a measure of conduction through the atrioventricular node. **(B)** QRS width, a measure of ventricular depolarization. **(C)** QT interval, a measure of ventricular repolarization. No significant differences were detected between the eNAD and control horses in any conduction factors measured.

Arrythmia Prevalence

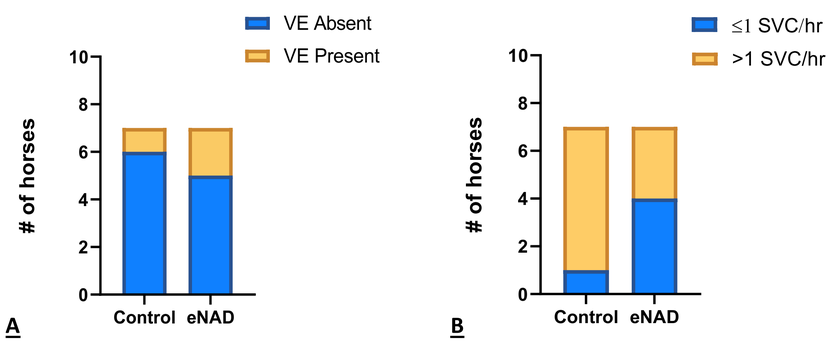


FIGURE 3 | **(A)** Number of horses with ventricular ectopy. **(B)** Number of horses with supraventricular ectopy defined as more than one supraventricular premature complex per hour. No significant difference in arrhythmia prevalence was detected between the horses with equine neuroaxonal dystrophy (eNAD) and control horses.

Cardiac Troponin I

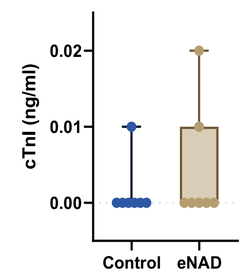


FIGURE 4 | Box and whisker plot of cardiac troponin I (cTnI) for horses with equine neuroaxonal dystrophy (eNAD) compared to controls. No significant difference in cTnI was detected between eNAD and control horses.

Cardiac Function

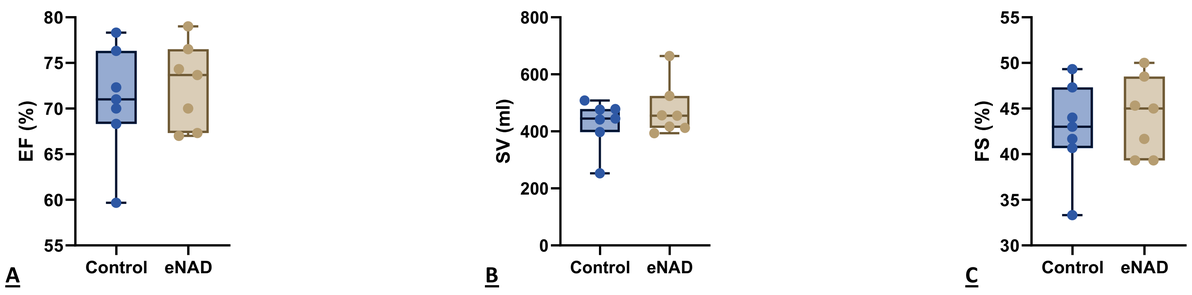


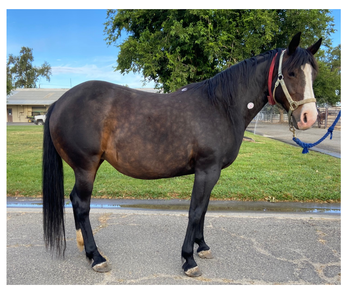
FIGURE 5 | Box and whisker plots of selected measures of cardiac function in horses with equine neuroaxonal dystrophy (eNAD) compared to controls. **(A)** Ejection fraction **(B)** Stroke volume **(C)** Fractional shortening. No significant differences in cardiac function measurements were detected between eNAD and control horses.

Conclusions and Future Directions

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

No significant differences were detected between the two groups in:

- Cardiac electrophysiology
- Cardiac troponin I levels
- Cardiac function



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

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