Characterizing the cardiac phenotype in Quarter horses with equine neuroaxonal dystrophy

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Equine neuroaxonal dystrophy (eNAD) is an inherited neurological condition. eNAD clinically resembles two human disorders: Ataxia with vitamin E deficiency (AVED) and 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.
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

- **PR interval**
  - Control: Range
  - eNAD: Range

- **QRS width**
  - Control: Range
  - eNAD: Range

- **QT interval**
  - Control: Range
  - eNAD: Range
Arrhythmia Prevalence

VE Absent
VE Present

≤1 SVC/hr
>1 SVC/hr

# of horses

Control  eNAD

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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: 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-gaunine, Abcam).
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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

**RMSSD (ms)**
- Control
- eNAD

**SDNN (ms)**
- Control
- eNAD

**SDANN (ms)**
- Control
- eNAD

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