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Exploring a Potential Relation Between Autonomic and Myocardial Function in Duchenne Muscular Dystrophy

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Duchenne muscular dystrophy (DMD) is a rare muscle wasting disorder with a high cardiovascular mortality rate. Structural remodeling of the myocardium is present early in the disease as fibrosis, later progressing to left ventricular (LV) dysfunction and dilated cardiomyopathy. Heart rate variability (HRV) is a robust measure of cardiac autonomic balance impaired in boys with DMD. However, the relation between cardiac autonomic and mechanical function in DMD is not yet understood. **PURPOSE:** To (1) characterize cardiac autonomic balance and LV function in boys diagnosed with DMD (n=8; 15±6 yrs. old) as compared to typically developing controls (n=20; 14±5 yrs. old) and (2) explore a potential relation. **METHODS:** Error-free HRV during quiet breathing was assessed using 3-lead electrocardiogram for 5 continuous minutes. HRV was calculated from heart rate recorded on an individual beat basis in the time-domain as root mean square of the successive differences (RMSSD). Mitral early (E) and late (A) diastolic filling velocities, and E-wave deceleration time (DTE), were measured using pulsed-wave Doppler echocardiography. Early diastolic tissue velocity $e\dot{c}$ was measured as the average of the septal and lateral region using tissue Doppler imaging and used to calculate the E/ $e\dot{c}$ ratio. The mitral E/A ratio was calculated by the division of the highest E and A measured using a sample of 3-5 cycles. Group differences were compared using Mann-Whitney *U* tests and correlations using Pearson's test. **RESULTS:** Parasympathetic activity, as assessed by RMSSD, was reduced in the boys with DMD (DMD: 33±21 vs. Con: 87±42 ms, p=0.002). The mitral E/A ratio was also significantly reduced in the boys with DMD (DMD: 1.51±0.26 vs Con: 2.51±0.66, p <0.001), driven by a significant increase in the A wave velocity (DMD: 0.51±0.10 vs Con: 0.33±0.08 m/s, p<0.001). Although no difference in the E wave velocity was observed, the DTE was significantly lower in the DMD group (DMD: 150±25 vs Con: 194±47 ms, p=0.008). Average $e\dot{c}$ was reduced in the DMD group (DMD: 0.11±0.02 vs Con: 0.15±0.02 m/s, p<0.001), which translated to an augmented E/ $e\dot{c}$ (DMD: 7.33±2.19 vs Con: 5.29±1.06, p=0.007). Importantly, RMSSD was moderately associated with DTE (r=0.58;p=0.003), A wave velocity (r=-0.45,p=0.02), average $e\dot{c}$ (r=0.63;p<0.001), and average E/ $e\dot{c}$ (r=-0.63;p<0.001) when all data were pooled. **CONCLUSIONS:** Preliminary findings suggest reduced vagal tone and impairments in global LV diastolic function in patients with DMD, with a possible relation between cardiac autonomic and mechanical function. **SIGNIFICANCE/NOVELTY:** The identification of a relation between parasympathetic control of the heart and global diastolic function in DMD is of clinical importance in establishing non-invasive, early markers of cardiac dysfunction in this patient population. Larger scale longitudinal studies are indicated for further investigation.

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