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Sex Differences in the Effects of Chronic Muscadine Grape Extract Treatment on Cardiac Function Parameters and Aortic Pulse Wave Velocity (PWV) in Hypertensive Transgenic (mRen2)27 Rats

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Muscadine grape extract (MGE) polyphenolics have potential beneficial cardiovascular effects. Whether the effects are sex-specific during progression of hypertension is unknown. We measured aortic arch PWV and cardiac function parameters using transthoracic echocardiography (Vevo LAZR 2100) after 15 weeks of MGE-treatment (0.2 mg polyphenolics /mL in drinking water) in transgenic hypertensive (mRen2)27 rats (n = 4 each, control male and female, MGE-treated female; n = 3 MGE-treated male) starting at 15 weeks of age. As expected, systolic blood pressure (SBP) measured via tail cuff after acclimation was higher in males than females at 15 weeks of age (179 ± 3 vs. 169 ± 3 mm Hg, $p = 0.04$). By 30 weeks of age, SBP did not differ between male and female rats (171 ± 4 vs. 171 ± 3 mm Hg). Body weight was higher in male than female rats (589 ± 8 vs. 326 ± 5 g, $p < 0.0001$); thus, cardiac output (CO), stroke volume (SV) and left ventricular mass (cLVM) were normalized to body weight. Systolic cardiac function was lower in male compared with female rats: SV (0.34 ± 0.04 vs. 0.59 ± 0.03 µL/g, $p < 0.001$); CO (0.13 ± 0.001 vs. 0.26 ± 0.02 mL/min/g, $p < 0.001$); ejection fraction (46 ± 4 vs. 74 ± 5 %, $p < 0.05$); fractional shortening (24 ± 3 vs. 45 ± 4 %, $p < 0.05$). In contrast, there was no difference between male and female rats in cLVM (2.35 ± 0.20 vs. 2.85 ± 0.14); heart rate (367 ± 19 vs. 432 ± 22 bpm); E/e' (12 ± 2 vs. 14 ± 0.4), or PWV (2.74 ± 0.21 vs. 2.85 ± 0.09 m/s). Sex differences in systolic cardiac function remained after 15 weeks of MGE treatment and MGE did not alter SBP or diastolic function (E/e'). However, aortic PWV was 36% lower in MGE treated males compared to control males (1.75 ± 0.13 vs. 2.74 ± 0.21 m/s, $p < 0.005$), which was also significantly lower than MGE treated females (2.40 ± 0.05 m/s, $p < 0.05$). Aortic PWV was 16% lower in MGE-treated females than control females, which did not reach significance (2.40 ± 0.05 vs. 2.85 ± 0.09 m/s). In conclusion, MGE intake improves arterial stiffness in male (mRen2)27 rats independent of differences in blood pressure or cardiac function. That aortic PWV in female rats did not derive benefit implies a potentially unique therapeutic profile for MGE in targeting mechanisms important for arterial stiffness in a sex-specific manner.

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