EFFECTS OF ONE YEAR EXERCISE TRAINING WITH A DRUG TO BREAK ADVANCED GLYCATION END-PRODUCT CROSS-LINKS ON CARDIAC FUNCTION IN OLDER INDIVIDUALS

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Background: Life-long accumulation of irreversible advanced glycation end-products leads to ventricular stiffening. Endurance training preserves left ventricular compliance. The advanced glycation end-product cross-link breaker Alagebrium (ALT) decreases ventricular stiffness in animal studies. We examined the effects of 1-year treatment with ALT on cardiac function in healthy older subjects, and combined it in a factorial design with exercise training (ExT).

Methods: Subjects were randomized into 4 groups in a double-blind placebo controlled randomized trial with a 1-year intervention: 1) ExT & ALT 200 mg/day; 2) ExT & placebo; 3) no ExT & ALT 200 mg/day; 4) no ExT & placebo. We performed a maximal exercise test (VO2max) and measured left ventricular function using echocardiography. Two-dimensional speckle tracking was used to measure longitudinal strain, global systolic (SRS), early (SRE) and late (SRA) strain rate and global myocardial velocity (MVS, MVE and MVA). Statistical differences between the 4 groups in response to the interventions were analyzed using the Linear Mixed Model.

Results: Forty-four subjects (age 70±4 years) completed the 1-year intervention (4 groups, n=11). Although VO2max improved significantly, by 15% (ExT pre 23.9±4.5 vs. post 27.2±4.6 mlO2/min/kg, p<0.001), cardiac function did not improve with 1-year ExT. Preservation of diastolic function was seen in the ALT groups, while the placebo groups showed deterioration of left atrial volume (pre 47±12 post 45±13 ml vs. pre 45±11 post 51±14 ml, respectively, p=0.006), SRA (pre 1.22±0.15 post 1.18±0.18 s-1 vs. pre 1.19±0.23 post 1.27±0.24 s-1, respectively, p=0.075), MVA (pre -6.02±1.03 post -5.78±1.28 cm/s vs. pre -5.41±1.30 vs. post -6.10±0.90 cm/s, respectively, p=0.004) and MVE/MVA ratio (pre 0.70±0.19 post 0.71±0.25 vs. pre 0.86±0.23 post 0.70±0.16, respectively, p=0.002).

Conclusion: One year of exercise training significantly improved physical fitness, however despite the established benefits, exercise did not reverse the effects of sedentary aging. On the other hand, one year treatment with ALT might attenuate the decrease in diastolic function associated with one year of physiological aging.