High Intensity Interval Training Benefits Right Heart Function in a Rat Model of Pulmonary Arterial Hypertension

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Pulmonary Arterial Hypertension (PAH) is a disease of progressive remodeling in pulmonary arteries that elevates pulmonary pressures and eventually leads to right ventricular (RV) failure and death. The purpose of this study was to examine the benefit and detriment of high intensity interval training (HIIT) to the RV in a monocrotaline (MCT) PAH rat model. It is hypothesized that HIIT will improve indicators of RV function without increasing myocardial inflammation or apoptosis. Male Sprague Dawley rats were injected with either MCT (40 mg/kg, \(n=14\)) to induce mild PAH or saline for healthy controls (CON, \(n=9\)). A subgroup of MCT (\(n=8\)) and CON rats (\(n=6\)) performed a 6 week treadmill HIIT program 5x/week using short bouts of alternating high intensity (2 min, 85-90% \(\text{VO}_2\max\)) and low intensity (3 min, \(~30\% \text{VO}_2\max\)) running for 30 min/session. Histochemistry/immunohistochemistry was performed on cryofixed or formalin-fixed/paraffin-embedded RV sections to assess indicators of inflammation (CD45+ cells), apoptosis (TUNEL), fibrosis (trichrome) and was imaged using epifluorescence or brightfield microscopy. Image quantification was performed using ImageJ. For the HIIT rats, a reduction in MCT-induced RV hypertrophy was observed, as measured echocardiographically, and by the calculated ratio of RV mass relative to LV+Septum mass. RV function was better preserved for HIIT vs. sedentary MCT, as indicated by stroke volume and cardiac index (cardiac output normalized by body weight) in echocardiography. MCT-induced RV fibrosis as measured by trichrome staining was lower for HIIT, also indicating a healthier myocardium. HIIT did not prompt greater counts per field of CD45+ cells and TUNEL+ cells in HIIT vs. sedentary MCT RV myocardium. In conclusion, in the monocrotaline rat model of PAH, HIIT appears to be a beneficial exercise approach that improves RV function without exacerbating RV inflammation or apoptosis. Future work will examine effects in other PAH models and ultimately in patients with disease.

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