Public Abstract
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Effects of treprostinil sodium in a monocrotaline-induced rat model of pulmonary hypertension
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In this study, we sought to elucidate the effects of treprostinil, a prostacyclin ($PGI_{2)}$ analog, on hemodynamics and vascular remodeling in a rat model of monocrotaline (MCT)-induced pulmonary hypertension. First, male, Sprague-Dawley rats were randomized to one of four treatment groups; control, MCT only, MCT with treprostinil (TRE) treatment, and TRE only. Next, rats received a one-time subcutaneous dose of MCT or saline and were administered either treprostinil or placebo for 28-days via an osmotic pump implanted subcutaneously. Finally, 28-eight days post-pump implantation, we recorded right ventricular systolic pressure (RVSP) and right ventricular size. Lung tissues were also collected and either paraffin embedded or snap frozen. MCT exposure caused significant increases in RVSP, right ventricular hypertrophy, medial wall thickening (MWT), and PPAR-γ protein expression. Treprostinil did not decrease elevations of RVSP, right ventricular hypertrophy, or MWT, but it significantly lowered PPAR-γ protein expression. In conclusion, we demonstrated that treprostinil therapy does not lessen increased RVSP, right ventricular hypertrophy and vascular remodeling associated with MCT-induced pulmonary hypertension. Conversely, treprostinil treatment attenuated increased PPAR-γ protein levels in whole lung homogenates of MCT-exposed rats. Although we have not yet established that PPAR-γ is an important therapeutic target for pulmonary hypertension, we speculate that further investigation of its role could reveal a mechanism in which PGI_2 elicits its effects on the pulmonary vasculature.