



*Enriching Research in Pulmonary Vascular Medicine*

*Embracing the Potential of*

**YOUNG  
INVESTIGATORS**

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*Inter-ventricular decoupling is an overlooked contributor to right ventricular myocardial stress and dysfunction in pediatric pulmonary hypertension*

### **INTRODUCTION:**

Pulmonary hypertension (PH) in children is a complex disease with multiple underlying etiologies, characterized by progressive pulmonary arterial (PA) and right ventricular (RV) dysfunction. Ongoing work has been successful in elucidating key events in the RVPA axis, but more is needed to investigate the role of the left ventricle (LV).

### **BACKGROUND:**

Previous studies have shown that LV contraction can generate almost 70% of the systolic pressure and 80% of the pulmonary flow in the passive RV of dogs, while the role of the RV is negligible for generating LV pressure. Therefore, the RV is relying in the contractile energy transfer from the LV to aid in perfusing the lungs, which is concerning given that echocardiographic evaluation of the LV has demonstrated reduced LV strain and strain-rate in pediatric PH patients. Thus, it is likely that PH patients could benefit both from therapies and diagnostic markers that target the RV-LV axis. Yet systematic studies to evaluate the underlying mechanical coupling between these two pumps in the face of hydraulic loading of one pump in the pediatric pulmonary hypertension population have not been performed. Further, connecting such mechanistic information to functional and biological markers that may provide early indicators of abnormal RV-LV coupling has likewise not been undertaken.

### **HYPOTHESIS AND OBJECTIVES:**

The overall hypothesis of this study is that decreased LV torsion-rate directly compromises contractile function in the overloaded RV, which is accompanied by abnormal myocardial wall stress and biomarker expression.

### **SPECIFIC AIM 1:**

Identify the role of LV torsion-rate in PAH using tagged MRI imaging and hemodynamics: 1.1. Using tagged MRI, compare maximum LV torsion-rate between normotensive children (n = 15, recruited) and children with PAH (n = 10 expected recruitment). 1.2. Associate LV torsion-rate with RV contractility and function in PAH.

### **SPECIFIC AIM 2:**

Establish cause-and-effect between LV torsion-rate and: RV contractility and myocardial stress: 2.1. Develop a patient-specific mathematical model of the cardiopulmonary complex to compute myocardial wall stress for each patient. 2.2. Repeat Aim 2.1 for each PAH subject under normal LV torsion-rate, and compute change in RV contractility and wall stress.

### **SPECIFIC AIM 3:**

Measure serum NT-proBNP and identify circulating miRNAs that are associated with abnormal LV torsion-rate and myocardial wall stress (n = 10 patients; NT-proBNP and 765 miRNAs per patient will be measured).