



Enriching Research in Pulmonary Vascular Medicine

Embracing the Potential of
**YOUNG
INVESTIGATORS**

2015 ABSTRACT

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MATCH-uPP – MRI and catheterization hemodynamics in pediatric pulmonary hypertension.

INTRODUCTION:

Prognosis in childhood pulmonary hypertension (PH) remains poor. Research efforts in pediatrics are complicated by the disease's multifactorial nature and potential risks posed on pediatric subjects. The single, standard diagnostic measure is pulmonary vascular resistance. However, this is only one of many factors predictive of mortality and does not reflect ventricular dysfunction.

BACKGROUND:

Pediatric PH is a rare disorder, and the body of research in children is grossly insufficient. Management in children is extrapolated from evidence-based literature in adults and experiences of clinicians. Adult PH management relies on serial cardiac catheterization to obtain hemodynamic data. However, when applied to children, catheterization exposes them to repeated anesthesia, radiation, and adverse risks associated with catheter manipulations. As a result, there is an increased risk of resuscitation, vascular injury, cancer development, thromboembolic events, and death in an already high-risk group. Recently, the FDA excluded catheterization as an end-point in clinical trials in children with PH, further restricting research efforts.

The pathophysiology of PH involves elevated pulmonary pressures, vascular resistance, and vascular stiffness resulting in alterations in wall shear stress (WSS) and the ventricular vascular coupling ratio (VVCR). WSS is a marker of vascular function and a mechanical stimulus of downstream signaling in the endothelium. Previously, we showed that magnetic resonance imaging (MRI)-derived WSS in the proximal pulmonary arteries is significantly lower in children with PH compared to normotensive children, and believe that WSS is key to vascular adaptation in PH. We also believe that VVCR plays an important role in the disease. VVCR describes the response of the ventricle to a changing afterload to maintain adequate cardiac output; the breakdown of this relationship leads to right ventricular failure. Recently, work in adults shows that VVCR can be derived by MRI, whereas VVCR has been conventionally determined only by catheterization. We propose that MRI-derived WSS and VVCR could replace the gold standard, invasively derived hemodynamic data. Success in this study has the potential of shifting the paradigm of pediatric PH care towards a safer, noninvasive monitoring modality and significantly improving quality of life in children with PH. Furthermore, it will add a powerful tool to move pediatric research efforts ahead, particularly in clinical trials.

HYPOTHESIS AND OBJECTIVES:

A complex set of factors contributes to the pathophysiology of PH and can be thought of as two major components—vascular and ventricular adaptations. In this study, we aim to compare vascular and cardiac parameters derived from MRIs in children with PH with hemodynamic markers derived from cardiac catheterization.

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AIM 1 (VASCULAR INDICES):

Determine the ability of non-invasively derived proximal WSS to predict the gold standard, invasively derived hemodynamic data. WSS changes have been associated with changes in both resistance and stiffness in an adult population, thus measuring this important component of vascular adaptation by a non-invasive means is important in the care of children with PH. Of the imaging techniques for determining WSS, MRI is the most accurate because of the higher spatial resolution of the arterial wall compared to ultrasound and compared to computed tomography set at the same voxel size. Moreover, MRI, unlike CT, avoids radiation exposure.

Hypothesis: WSS in children with PH correlates with PVR, mPAP, pulmonary capillary wedge pressure (PCWP), transpulmonary gradient (difference between mPAP and PCWP), and right ventricular end-diastolic pressure as determined by cardiac catheterization.

AIM 2 (VASCULAR AND VENTRICULAR INDEX):

Determine the ability of non-invasively derived myocardial structure and function to predict the gold standard, invasively derived hemodynamic data.

Hypothesis 2: WCR determined by MRI correlates with hemodynamic data, including PVR, mPAP, PCWP, transpulmonary gradient, right ventricular end-diastolic pressure, cardiac output, and reference-standard single beat method using pressure tracings obtained by catheterization.

AIM 3 (CLINICAL OUTCOMES):

Determine relationship between MRI findings and standard clinical outcomes, including echocardiographic findings, biomarkers, 6-minute walk test, and exercise test.