Aortic Wall Shear Stress and Left Ventricular Systolic Performance are Reduced in Pediatric Patients with Pulmonary Arterial Hypertension

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Introduction

- Pediatric Pulmonary Arterial Hypertension (PAH) is associated with progressive pulmonary vascular resistance resulting in higher afterload and mechanical stress on the right ventricle which has been associated with reduced vascular wall shear stress (WSS) and stiffening.
- Adult PAH studies suggest that ventricular interdependency has been associated with reduced left ventricular (LV) mechanical efficiency and worse prognosis. The effect of the LV performance and systemic flow hemodynamic forces in pediatric population has not yet been investigated.
- Vascular systemic wall shear stress (WSS) is a primary flow hemodynamic factor influencing the mechanotransduction and behavior of endothelial cells. Low and oscillatory shear has been correlated with the development of atherosclerosis, thrombosis, endothelial thickening, and smooth muscle cell proliferation.
- Goal: To investigate WSS and oscillatory shear index (OSI), both known to be responsible for mechanotransduction in vascular tissue, simultaneously with the LV function in large cohort of pediatric PAH patients.

Methods

- Forty pediatric patients with PAH and 25 age matched controls prospectively underwent phase-contrast magnetic resonance imaging (PC-MRI) along with standard cardiac magnetic resonance evaluation.
- Tissue and phase data sets were segmented in parallel using the freely available Segment® software and converted into custom made Matlab program to compute flow hemodynamic metrics. The WSS was computed as product of kinematic shear rate and patient specific dynamic viscosity. The OSI was computed using standard formula (2).

\[
WSS = \mu(\bar{H}) \frac{du}{dy} 
\]

\[
OSI = 0.5 \left(1 - \frac{\tau_{WSS,dt}}{\tau_{WSS,tau}}\right) 
\]

The evaluation plane for the flow hemodynamic analysis was placed at the level of sinotubular junction in the ascending aorta and ten centimeters below aortic isthmus in descending aorta. Vessel strain was measured by means of relative area change defined as the difference between maximum and minimum area values divided by maximum value

\[
RAC = \frac{(Area_{max}-Area_{min})}{Area_{max}} \times 100\% 
\]

Table 1. Demographic and Basic Hemodynamic Parameters

<table>
<thead>
<tr>
<th>Control (n = 25)</th>
<th>PAH (n = 40)</th>
<th>PAH (n = 40)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>11.4 ± 3.9</td>
<td>11.4 ± 3.9</td>
</tr>
<tr>
<td>Max (mmHg)</td>
<td>12.4 ± 3.4</td>
<td>12.4 ± 3.4</td>
</tr>
<tr>
<td>P value</td>
<td>0.457</td>
<td>0.457</td>
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</tbody>
</table>

Table 2. CMR Derived Hemodynamic Measurements

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Control (n = 25)</th>
<th>PAH (n = 40)</th>
<th>PAH (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WSS (dyn/cm²)</td>
<td>6.8 ± 3.5</td>
<td>10.5 ± 3.4</td>
<td>10.5 ± 3.4</td>
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<tr>
<td>OSI (%)</td>
<td>0.53 ± 0.03</td>
<td>0.43 ± 0.06</td>
<td>0.43 ± 0.06</td>
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<tr>
<td>OSI (%)</td>
<td>126 ± 26</td>
<td>115 ± 38</td>
<td>115 ± 38</td>
</tr>
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</table>

Results

- PAH children exhibited significantly reduced WSS and OSI than normal controls.
- PAH patients had lower systemic WSS and OSI compared to control group.

Discussion

- Parallel stiffening of the systemic vasculature in pediatric PAH population with associated reduced WSS and LVEF may further elevate mechanical stress on both ventricles and accelerate disease progression.
- We speculate that the vascular mechanical and flow characterization in large systemic arteries could provide important insights to progressive pathogenesis in a pediatric PAH population.
- Significantly altered flow hemodynamic parameters WSS and OSI can play major in development of stiffness in large systemic vessels.
- Future studies will focus on correlating the flow hemodynamic forces to vascular inflammatory and remodeling markers, as well as outcomes.
- The non-invasive evaluation of WSS via PC-MRI may be an important serial marker to investigate the vascular remodeling in the progression of pediatric PAH and possible therapeutic targets.

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