An Unwelcome Embrace – Adverse Pulmonary-Aortic Interactions in Pulmonary Hypertension

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Vascular remodeling in pulmonary hypertension (PH) causes increased ventricular afterload, resulting in right ventricular (RV) failure and high mortality.[1] Afterload is the mechanical impedance imposed by the arterial tree, against which the ventricle must work to eject blood. Despite the tendency to conflate afterload with blood pressure, it cannot be reduced to a single number or variable. Instead it is more appropriately defined in terms of pressure-flow relations. [2, 3]

Afterload is divided into several steady and pulsatile components including vascular resistance, total arterial compliance, characteristic impedance, and wave reflections. Each of these has been shown to be abnormal in the pulmonary circulation in PH resulting in increased RV afterload.[4-8] However, abnormalities of the systemic vasculature that result in increased left ventricular (LV) afterload have been relatively understudied in PH.

In this issue of circulation imaging, Schäfer *et al*.[9] (*editorial team to correct reference*) demonstrate elevated proximal aortic pulse wave velocity and other metrics of local aortic stiffness in children with pulmonary hypertension. This elevation was strongly associated with the degree of dilatation of the main and branch pulmonary arteries, suggesting that the aortic root is mechanically constrained by the 'embrace' of the PAs.

In addition, the authors noted a modest correlation between aortic 'relative area change' RAC: ($[Area_{max}-Area_{min}]/Area_{max}$) and the MPA:Aorta ratio with decreased LVEF. They went on to suggest that increased aortic stiffness due to pulmonary arterial constraint resulted in LV dysfunction in this patient group. This is an intriguing hypothesis and we believe that it is worth exploring the mechanisms by which this could occur.

When the LV ejects, it must accelerate blood into the aorta, overcoming a combination of inertance and vessel compliance. This is the characteristic impedance (Z_c) of the vessel and Z_c governs ventricular load in early systole. The Z_c is directly related to pulse wave velocity (c) by:

$$Z_c = \rho\, c/A_d \qquad \textit{Equation 1}$$

Where A_d is vessel diastolic area and ρ is blood density. As can be seen from equation 1, ventricular load in early systole is increased in vessels with smaller areas and elevated pulse wave velocity.[10] Therefore, Schäfer et al's results imply increased aortic Z_c in pediatric PH patients and increased LV afterload. However, elevated Z_z occurs in a range of conditions, including normal aging and, at this degree of elevation, would not be expected to be associated with impaired LV function. Indeed, diastolic aortic area was not different between the groups and pulse wave velocity was not associated with LVEF, suggesting that it may not a prime candidate for the association.

Given there was no evidence of increased systemic vascular resistance or total aortic compliance between PH patients and controls, alternative causes of LV dysfunction must be sought. The other element of afterload that is often neglected is wave reflections. Several types of wave reflections occur in the systemic vasculature and can be identified by wave intensity analysis in the time domain.[11] Backwards compression waves (BCW), which decelerate flow and increase pressure, increase LV afterload and have been associated with heart failure events in adults.[12] In addition, we have recently shown that BCW's arising in the repaired aortic arch, are an important determinant of LV hypertrophy following coarctation repair.[13] Reflections arise in the vasculature at areas of impedance mismatch (e.g. branches, changes in wall stiffness or calibre). In this study, the locally increased stiffness and reduced aortic expansion at the level of PA branches is a likely area of impedance mismatch. Therefore, it is possible that pediatric PH patients have increased BCW's, which increases LV afterload and results in myocardial dysfunction.[14] Evaluation of this hypothesis would be challenging; requiring simultaneous measurement of pressure and flow in the proximal aortic root. Alternatively, a non-invasive approach using PCMR area and flow data may be possible, but the close proximity of the reflecting site would require high temporal resolution approaches that may not be generally available.[7]

Of course, pulmonary artery size does increase with worsening PH, and other causes of LV dysfunction – collinear with RAC and MPA:Ao ratio – but operating via non-

afterload related mechanisms are possible. Alternative explanations might include adverse ventricular-ventricular interactions or reduced myocardial perfusion due to increased right atrial pressure or coronary compression. Larger studies are required to ascertain if these factors are also important.

In conclusion, PCMR imaging provides an excellent opportunity to assess both pulmonary and systemic vascular hemodynamics. The RV in PH has been shown to negatively impact the function of the LV through ventricular interactions.[15] However, the observation of adverse PA and aortic interaction is intriguing and may explain some of the symptomatic consequences of PH in children.

Conflict of Interest Disclosures

None.

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