Advanced Non-Invasive Imaging: Ventricular-vascular coupling unit in pediatric pulmonary arterial hypertension

Uyen T Truong, MD
Pediatric Cardiology and Radiology
Children’s Hospital Colorado, Aurora, Colorado

3rd European Conference on Neonatal and Paediatric Pulmonary Vascular Disease
October 13, 2017
Disclosure

• I have nothing to disclose
Background

• VVC describes the interaction between the heart and the vasculature to maintain adequate cardiac output in face of altering afterload.
  ▪ The ventricular reserve capacity to respond to increasing demand.

• This is conventionally determined by measurements obtained during catheterization.
Pressure-Volume Loop

Components:
- Arterial elastance ($E_a$)
- End-systolic elastance ($E_{es}$)
Ventricular vascular coupling ratio

- $E_a$: “Arterial Elastance”
  - Larger values $\rightarrow$ Greater afterload
  - Combined measure of resistive and compliant afterload

- $E_{es}$: “End-Systolic Elastance”; “Maximal Elastance”
  - Larger values $\rightarrow$ Greater contractility
  - Load independent measure of ventricular contractility

- $E_a / E_{es}$: Ventricular-Vascular Coupling Ratio (VVCR)

- Although $E_{es} / E_a$ can also be used
Estimation of VVC

Single beat (VVCR_s)

MRI (VVCR_m)

Breeman et al. In submission.
Why the need for non-invasively derived VVC in children?

- VVCR$_S$ is an independent predictor of progression of the World Health Organization (WHO) functional class.
- No exposure to ionizing radiation
- Reproducibility/Serial examination
- Avoidance of catheter instrumentation (O'Bryne et al. 2016)
  - Risk of catastrophic events in pediatric PAH is 3.3%
  - Increases with decreasing age
- Avoidance of anesthesia in cooperative patients
Right ventriculo-arterial coupling in pulmonary hypertension: a magnetic resonance study

Sanz et al. Heart 2012

- Estimated VVCR by a combination of catheterization/CMR data and by CMR data alone correlated with disease severity in adults with PAH.

- By pure CMR data (under the assumption PCWP is normal), this readily simplifies to

\[
VVCR \approx \frac{\text{stroke volume}}{\text{end systolic volume}}
\]
VVCR by Cardiac MRI

Figure 2  Correlations between the ratio of effective pulmonary arterial elastance to right ventricular maximal systolic elastance ($E_e/E_{max}$) and (A) right ventricular ejection fraction (RVEF), (B) mean pulmonary artery pressure (mPAP) and (C) pulmonary vascular resistance index (PVRI).

Sanz et al. 238 Heart 2012
Ventricular vascular coupling ratio in pediatric PAH

Fig. 3 Scatterplot showing a positive linear relationship between ventricular vascular coupling ratio obtained by MRI compared to that obtained by single beat method

$r = 0.79, p <0.0001$

Truong et al. JCMR. 2015
### Multicenter data: CHCO and Groningen

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis, years</td>
<td>9.0 (3.7 – 14.0)</td>
</tr>
<tr>
<td>Age at CMR study, years</td>
<td>13.6 (11.1 – 16.8)</td>
</tr>
<tr>
<td>Time between diagnosis and enrollment, months</td>
<td>46 (0.3 – 111.3)</td>
</tr>
<tr>
<td>Female</td>
<td>16 (59)</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>iPAH/hPAH</td>
<td>18 (66.7)</td>
</tr>
<tr>
<td>PAH-CHD, repaired</td>
<td>5 (18.5)</td>
</tr>
<tr>
<td>APAH-other</td>
<td>4 (14.8)</td>
</tr>
<tr>
<td><strong>WHO</strong></td>
<td></td>
</tr>
<tr>
<td>I - II</td>
<td>13 (59)</td>
</tr>
<tr>
<td>III - IV</td>
<td>9 (41)</td>
</tr>
<tr>
<td><strong>Deceased</strong></td>
<td>1 (3.7)</td>
</tr>
<tr>
<td><strong>Intravenous medication</strong></td>
<td></td>
</tr>
<tr>
<td>Prostacyclin pathway agonists</td>
<td>9 (33.3)</td>
</tr>
<tr>
<td>PDE5-inhibitors</td>
<td>1 (3.7)</td>
</tr>
<tr>
<td><strong>Atrial septostomy</strong></td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Lung transplantation</strong></td>
<td>1 (3.7)</td>
</tr>
<tr>
<td><strong>Days between CMR and catheterization</strong></td>
<td>1 (1 – 2)</td>
</tr>
<tr>
<td>mPAP, mmHg</td>
<td>27 40 (28 – 55)</td>
</tr>
<tr>
<td>PVRI, Wood units × m²</td>
<td>27 7.6 (4.1 – 12)</td>
</tr>
</tbody>
</table>
Multicenter data: Correlation

**PVR**
- \( r = -0.67 \)
- \( p < 0.01 \)

**Mean RAP**
- \( r = -0.46 \)
- \( p = 0.02 \)

**Cardiac index**
- \( r = 0.43 \)
- \( p = 0.02 \)

**WHO-FC**
- \( r = -0.7 \)
- \( p < 0.01 \)

**mPAP**
- \( r = -0.64 \)
- \( p < 0.01 \)

Breeman et al. *In submission.*
Limitations of MRI-derived VVCR

- Comparing $E_{es}$ from single beat and simplified approach
- Estimated $E_{es}$ underestimates true VVCR
- $V_0$ is not negligible

Trip et al. JHLT 2013
Looking beyond volume based ventricular vascular coupling

• Direct vascular visualization

• Myocardial deformation

• 4D flow MRI
Vascular-vascular interaction

Schafer et al. Circulation Imaging 2017
Ascending aorta in PH is stiff
MPA size and the relation to left ventricular function

![Graphs showing the relationship between MPA size and LV ejection fraction, and MPA size and LV VVR, with statistical significance indicated.]

- \( -8.830 \pm 3.012, p = 0.0005 \)
- \( 0.323 \pm 0.131, p = 0.0169 \)
Changing the Paradigm

![Diagram of interdependency between ventricular and vascular systems.](image-url)
Advantage of 4D Flow MRI

- Acquisition of comprehensive data set of blood flow through the region of interest
- Allows visualization and quantification of flow, as well as its derivation
- Allows retrospective placement of analysis plane.
4D and RV diastolic dysfunction

Vorticity in the Left Ventricle
MPA vorticity and PVR

- Multivariate regression using vorticity (MPA and RPA) along with cross sectional area predicts 94% of PVR variability

Kheyfets at al. JMRI 2016
Summary

• Ventricular vascular coupling is a critical concept in understanding the pathophysiology and prognosis of pediatric PAH

• Volume-only MRI approach
  ❖ Easy to derive
  ❖ Safe
  ❖ Reproducible/serial exam
  ❖ Underestimate true VVCR

• Novel techniques
  ❖ Myocardial deformation
  ❖ 4D Flow MRI
Acknowledgement

• Children's Hospital Colorado
  • Pediatric Cardiology
   • Dunbar Ivy MD
   • Kathleen Miller-Reed RN
   • Brian Fonseca MD
  • Pediatric Pulmonology
   • Steve Abman, MD
   • Donna Parker, RT
  • Pediatric Radiology
   • Lorna Browne, MD

• Grants
  • NIH NHLBI K23 KHL135352
  • NIH RO1 HL 114753
  • Colorado Clinical Translational Institute Pilot Grant CRS00000502
  • Research Institute Research Scholar Award
  • Actelion ENTELLIGENCE Award

• Bioengineering
  • University of Colorado
   • Michal Schafer MS
   • Jean Hertzberg, PhD
   • Vitaly Kheyfets PhD
   • Kendall Hunter PhD

• Northwestern
  • Alex Barker PhD

• University of Linkoping
  • Petter Dvverfeldt, PhD
  • Tino Ebbers, PhD

• ACtelion
  • Actelion ENTELLIGENCE Young Investigator Award

• National Jewish Health
  • Brent Renseler MD

• Colorado CTSA Grant UL1 TR001082

• Jayden Deluca Foundation
References


• Jone PN, Patel SS, Cassidy C, Ivy DD. Three-dimensional Echocardiography of Right Ventricular Function Correlates with Severity of Pediatric Pulmonary Hypertension. Congenital Heart Dis. 2016 Dec;11(6):562-569.


