Pulmonary hypertension: Using CMR for early detection

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Disclosures

- Discuss off label use of Gd MRI contrast agent

- Discuss emerging research related to velocity transfer function
  
  (Co-Inventor; The University of Alabama at Birmingham and Auburn University co-own the patent. Arcus-Med, LLC, has the exclusive rights. H. Gupta is a major stakeholder in Arcus-Med, LLC.)
How do you assess RV function and remodeling

- A) 2D transthoracic echocardiography
- B) 3D transthoracic echocardiography
- C) Cardiac MRI
- D) Cardiac CT
How important is quantification of Right Ventricular Volumes and EF in Pulmonary Hypertension

- A) Not important
- B) Somewhat useful
- C) Very important
Outline

- Definition and Physiology
- Prognosis
- PA Pressure Estimation
- Emerging Research
  - Velocity transfer function
RV and LV Architecture

**Right Ventricle**
- 2 Layers
  - Circumferential Superficial Fibers
  - Longitudinal Deep Fibers

**Left Ventricle**
- 3 Layers
  - Helical Arrangement of the layers

Right ventricle

- Volume Pump: operates at lower pressures

Ho and Nihoyannopoulos. Heart 2006
**PH Hemodynamic Definition**

<table>
<thead>
<tr>
<th>Definition</th>
<th>Characteristics</th>
<th>Clinical group(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH</td>
<td>PAPm ≥25 mmHg</td>
<td>All</td>
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</table>
| Pre-capillary PH                                | PAPm ≥25 mmHg, PAWP ≤15 mmHg | 1. Pulmonary arterial hypertension  
3. PH due to lung diseases  
4. Chronic thromboembolic PH  
5. PH with unclear and/or multifactorial mechanisms |
| Post-capillary PH                               | PAPm ≥25 mmHg, PAWP >15 mmHg | 2. PH due to left heart disease  
5. PH with unclear and/or multifactorial mechanisms |
| Isolated post-capillary PH (Ipc-PH)             | DPG <7 mmHg and/or PVR ≤3 WUc   |                                                                                 |
| Combined post-capillary and pre-capillary PH (Cpc-PH) | DPG ≥7 mmHg and/or PVR >3 WUc    |                                                                                 |

DPG = diastolic pressure gradient (diastolic PAP – mean PAWP)

Pressure Volume Relationship in PH

Pressure Volume Loops in different stages:
- normal (blue), PH (green), RV failure (purple)
- Ees: end-systolic elastance; Ea: arterial elastance

Noordegraaf et al Eur Respir J 2019
RV-LV Interaction in PAH

**RV**
- RV Hypertrophy
- Altered Shape
- Myocardial Fibrosis
- Dysynchrony

**IVS**
- Flattening
- Myocardial Fibrosis
- Dysynchrony

**LV**
- Compressed
- Possible LV Atrophy
- Dysynchrony
RV, LV Myocardial Strains in PAH

Normal

PAH
RV-LV Asynchrony in PHTN

Delayed time from R wave to peak shortening for RV regions in comparison with LV wall

Vonk-Noordegraaf A et al Chest 2005:128
CMR Prognostic Parameters

(A) SVI > 25 mL/m²
SVI ≤ 25 mL/m²

P = 0.009

(B) RV mass index < 59 g/m²
RV mass index ≥ 59 g/m²

P = 0.059

(C) RVEDVI < 84 mL/m²
RVEDVI ≥ 84 mL/m²

P = 0.011

(D) LVEDVI > 40 mL/m²
LVEDVI ≤ 40 mL/m²

P = 0.016

van Wolferen S A et al. Eur Heart J 2007
After PAH-targeted therapy, RV function can deteriorate despite a reduction in PVR.

Loss of RV function is associated with a poor outcome.
RV-arterial coupling (Ees/Ea) by Volume Method in PAH

Brewis et al Int J Cardiol 2016
CMR Prognostic Parameters: COMPASS-3 Study

Baseline parameters for clinical worsening and/or decline.

Benza et al Pulm Circ. 2018
COMPASS-3: Results

Predicted Probability of Clinical Worsening and/or Clinical Decline

Predicted Probability

Change from Baseline to Week 16 in PVR (Woods Units)

RVEDV/LVEDV ratio
1
2
3
4
5

Benza et al Pulm Circ. 2018
Conclusion 1

- CMR provides accurate and comprehensive assessment of
  - LV- RV function
  - LV-RV interaction

- Important for initial and serial quantitative assessment
  - Accuracy and reproducibility
  - Prognosis
Echocardiography for estimating PA pressure

- Echo PA systolic pressure
  - Estimate RA pressure
  - TR: may be absent
  - Severe TR: under or overestimate mPAP
  - Moderate agreement with that measured with RHC
  - Wide 95% limits of agreement
    - +38.8 to −40.0 mm Hg
    - +14.1 to −18.1 mmHg

- Meta-analysis shows modest diagnostic accuracy for PH
  - Sensitivity of 83% and a Specificity of 72%

- Acoustic window limitations in severe lung disease

CMR PA Pressure estimation

- Independent cardiac MRI predictors of mean pulmonary arterial pressure (mPAP)
  - Interventricular septal angle
  - Ventricular mass index
    - RV mass/LV mass
  - Black blood slow flow score

CMR PA Pressure estimation

◊ CMR mPAP:
  • Model 1: \(-179 + \log_e \text{interventricular septal angle} \times 42.7 + \log_{10} \text{ventricular mass index (right ventricular mass/left ventricular mass)} \times 7.57 + \text{black blood slow flow score} \times 3.39\)
  • Model 2: \(-231.423 + \log_e \text{interventricular septal angle} \times 53.8 + \log_{10} \text{ventricular mass index (right ventricular mass/left ventricular mass)} \times 8.708 + \text{diastolic pulmonary artery area} \times 0.009\)

◊ mPAP at least 25 mm
  • Sensitivity 93%
  • Specificity 79%
  • PPV 96%  NPV 67%

Emerging techniques: Pulmonary Impedance

- **PAH**
  - Conventional definition based on increased PAP and PVR
  - Assumes
    - Non-elastic PA conduits
    - Static and non-pulsatile pressure-volume relationship
  - PAs are highly distensible
    - Pulsatile energy losses up to 2.5 times systemic circulation

- **Pulmonary impedance**
  - Opposition to Pulsatile flow due to wave reflection
  - More accurate measure of afterload
  - Accounts for the viscoelastic properties of the vessel and pulse wave reflections
  - Better predictor of outcomes than PVR
PA impedance

- Earliest physiological manifestation of PA remodeling
  - ↓ PA compliance
  - ↑ PA stiffness
  - ↑ PA impedance

- PA impedance not routinely measured
  - invasive PA catheterization
  - simultaneous PA flow
Velocity Transfer Function: Non-invasive PA Impedance

Figure 2. The velocity transfer function (VTF) and impedance curves. VTF (A) and invasive impedance (B) curves averaged for subjects with low pulmonary vascular resistance (PVR; <2.5 Wood units [WUs]; black), and subjects with high PVR (≥2.5 WUs; red).

Gupta et al Journal of the American Heart Association. 2018;7
Velocity Transfer Function: Non-invasive PA Impedance

ROC for discrimination of low vs high pulmonary vascular resistance

Gupta et al. Journal of the American Heart Association. 2018;7
Conclusions

♦ CMR can comprehensively measure:
  • RV and LV Function
  • RV-PA interaction
  • PA flow

♦ Diagnostic and Prognostic Information