Understanding Complex Pulmonary Hypertension through Advanced Hemodynamics

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Disclosures

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- Consultant: Actelion, Bayer, Gilead Sciences, United Therapeutics
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Objectives

At the conclusion of this activity, the participant will be able to:

- Describe the basics of hemodynamics obtained through right heart catheterization
- Explain through patient case example(s) how:
  - exercise right heart catheterization provides better understanding of etiology of multifactorial pulmonary hypertension
  - continuous hemodynamics provides valuable information on prognosis and response to pulmonary hypertension therapy
  - hemodynamics helps guide initial treatment approach and palliative care in severe pulmonary hypertension
- Demonstrate through video and photos how cardiopulmonary evaluation tools are used in conjunction with right heart catheterization to better understand complex hemodynamics
Current PH Classification

• Group 1: PAH
• Group 2: PH due to left heart disease
• Group 3: PH due to lung disease and/or hypoxia
• Group 4: CTEPH
• Group 5: PH with unclear multifactorial mechanisms

• Hemodynamic definition of PAH
  – PAPm ≥ 25 mmHg
  – PCWP ≤ 15 mmHg
  – PVR > 3 WU

• **Phenotype** is the observable characteristics of an individual determined by the genetic makeup and environmental influences

**Is this current classification system sufficient?**
Hemodynamics... The Basics

• Resting Right Heart Catheterization
  – Indications
    • Diagnosis of PH
    • Assessment of disease severity
    • Assessment of response to PH therapy
    • Congenital heart disease
    • Valvular heart disease
Obtaining Resting Hemodynamics
Advanced Hemodynamics

• Beyond the basics of resting RHC
• Uses:
  – Determine PH phenotype and individualized therapy
  – Better evaluate complex patients who are not clearly Group I
• Tools that we use at our institution:
  – Provocative testing
  – Invasive Cardiopulmonary Exercise Test
  – Continuous hemodynamics
Provocative Testing for PH Phenotyping

• 100% FiO2
  – Assess for hypoxic vasoconstriction and intracardiac shunt

• Vasodilator challenge
  – Test for acute vasoreactivity
  – Uncover left heart disease

• Volume challenge
  – Uncover left heart disease
  – Especially useful in patients with borderline PCWP
Case 1: Invasive CPET for Multifactorial Disease

• Patient Profile
  – 75 year old male
  – 60 year, 2ppd smoking history
  – Evaluation for back surgery
  – History of essential HTN
  – Minimal symptoms other than post-exertional fatigue (which he attributed to chronic pain)
Initial Evaluation

PFTs

- FVC 96%
- FEV1 74%
- Ratio 55%

Echocardiogram

- TLC 120%
- RV 136%
- DLCO 51%
Resting Hemodynamics (pretreatment)

<table>
<thead>
<tr>
<th>Sept 2013</th>
<th>Rest</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP</td>
<td>85/35/53</td>
</tr>
<tr>
<td>PCWP</td>
<td>18</td>
</tr>
<tr>
<td>RA</td>
<td>11</td>
</tr>
<tr>
<td>CO/CI</td>
<td>3.14/1.74</td>
</tr>
<tr>
<td>PVR</td>
<td>11.1 WU</td>
</tr>
</tbody>
</table>

Invasive CPET: Exercise RHC + Cardiopulmonary exercise test (CPET)

+ Infused Prostacyclin and PDE5 + Diuresis
Obtaining Exercise Hemodynamics

Setting the Pace in the PH Race | Through Education, Research and Advocacy
Hemodynamic Response to Exercise

<table>
<thead>
<tr>
<th>Normal</th>
<th>PAH</th>
<th>PVH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **PAP**
  - Rest: Normal
  - Exercise: PAH > Normal > PVH

- **CO**
  - Rest: Normal
  - Exercise: PAH < PVH < Normal

- **PCWP**
  - Rest: PAH < Normal < PVH
  - Exercise: PAH < Normal < PVH

- **PVR**
  - Rest: Normal
  - Exercise: PAH > PVH > Normal
**Exercise Data (invasive CPET)**
(infused prostacyclin + PDE5)

**March 2014**

<table>
<thead>
<tr>
<th>Rest</th>
<th>Pre-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP</td>
<td>61/13/36</td>
</tr>
<tr>
<td>PCWP</td>
<td>9</td>
</tr>
<tr>
<td>RA</td>
<td>3</td>
</tr>
<tr>
<td>CO</td>
<td>4.63</td>
</tr>
<tr>
<td>PVR</td>
<td>5.8</td>
</tr>
</tbody>
</table>

**CPET**

<table>
<thead>
<tr>
<th>VO2 max</th>
<th>65% predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing Reserve</td>
<td>26% (normal &gt; 40%)</td>
</tr>
</tbody>
</table>

**55 W**

**70 W**

**100 W**
Treatment Adjusted

- Weaned off prostacyclin
- Increased dose of PDE5
- Increased therapy for COPD
- Stopped smoking
Repeat Exercise Data (after treatment adjustment)

<table>
<thead>
<tr>
<th>RHC</th>
<th>Max Exercise 100W (prior RHC)</th>
<th>Max Exercise 75W</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP</td>
<td>113/33/68</td>
<td>122/50/75</td>
</tr>
<tr>
<td>PCWP</td>
<td>16</td>
<td>14</td>
</tr>
<tr>
<td>RA</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>CO</td>
<td>9.4</td>
<td>7.6</td>
</tr>
<tr>
<td>PVR</td>
<td>5.53</td>
<td>8</td>
</tr>
</tbody>
</table>

**CPET**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2 max</td>
<td>48% (was 65%)</td>
</tr>
<tr>
<td>Breathing Reserve</td>
<td>39% (was 26%)</td>
</tr>
</tbody>
</table>

How do we best treat this patient? Is he group 1? Group 3? Unique phenotype?
Follow up

• Ongoing care for 2+ years
• Further treatment adjustments
  – ERA therapy trialed
  – Hospitalized for pulmonary congestion
    • Left heart disease?
• Echo and symptoms stable on monotherapy
Invasive CPET is a useful tool in evaluating patients with characteristics of Group 1 and Group 3.

Advanced hemodynamics helped us to individualize treatment for the patient.
Case 2: End Stage PH: To Treat or Not to Treat?

- Patient profile
  - 55 year old female
  - Past medical history
    - Mitral valve replacement (1999)
    - OSA (treated with CPAP)
    - Hx of DVT/PE
- Presented with recurrent fluid overload and end-stage symptoms
Echocardiogram
### Hemodynamic Data

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>Room Air</th>
<th>Nitric 80 PPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA</td>
<td>79/31/50</td>
<td>74/26/46</td>
</tr>
<tr>
<td>PCWP</td>
<td>18</td>
<td>23</td>
</tr>
<tr>
<td>CO (CI)</td>
<td>3.09 (1.96)</td>
<td>3.86 (2.5)</td>
</tr>
<tr>
<td>PVR</td>
<td>10 WU</td>
<td>6 WU</td>
</tr>
</tbody>
</table>

Conflicting Data:
Echo favors classic severe PAH
RHC favors left heart disease-associated PH
VQ Scan
Continuous Hemodynamic Data

Parameter

6 hours 12 hours 18 hours 24 hours

PAP
CO
PCWP
Prostacyclin

IV Diuresis

15mmHg

Time Since Initiation of Prostacycllin
Chest Xray

Pre-therapy

Post-therapy
Treatment Options

• Vasodilator therapy
  – Worsened left heart disease, pulmonary congestion

• Treatment for left heart disease
  – Too high risk for surgery due to PH
  – Mitral valve gradients not high enough to warrant valve replacement

• PTE surgery
  – Patient too weak and cachectic
  – Patient preference/goals of care

• Palliative care and hospice was chosen
End of Life with PAH

• Study findings
  – 2/3 of PAH patients die in hospital, with 90% of deaths related to PAH
  – Barriers to death at home
    • Hospice and high cost of continuing PAH meds for palliative care
    • SOB hard to manage at home

• Lack of a palliative care model in PH community

Pearls

- Hemodynamics led us down the path to palliative care
- We learned the importance of counseling patients on end of life
  - The success of PAH medications have made it harder to have discussions about end of life
- Continuous hemodynamics are limited to observing acute changes in physiology. However, we can’t change a patient’s phenotype.
Case 3: Treatment Resistant PAH: A Unique Phenotype?

• Patient profile
  – 70 year old female
  – Progressive severe dyspnea for 8 years without clear etiology or beneficial treatment
  – Mild upper lobe emphysema
    • Normal PFTs except DLCO 24%
    • Without symptoms or past improvement on inhaler therapy
  – Significant hypoxemia with exertion not well explained
Initial Evaluation: Echocardiogram
### Hemodynamic Data

#### Feb 2014

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP</td>
<td>73/26/45</td>
</tr>
<tr>
<td>PCWP</td>
<td>3</td>
</tr>
<tr>
<td>RV</td>
<td>68/0.12</td>
</tr>
<tr>
<td>RA</td>
<td>10</td>
</tr>
<tr>
<td>CO/Cl</td>
<td>2.87/1.66</td>
</tr>
<tr>
<td>PVR</td>
<td>14.5</td>
</tr>
<tr>
<td>SV</td>
<td>37 ml</td>
</tr>
</tbody>
</table>

#### April 2014

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP</td>
<td>75/38/48</td>
</tr>
<tr>
<td>PCWP</td>
<td>13</td>
</tr>
<tr>
<td>RV</td>
<td>73/0.9</td>
</tr>
<tr>
<td>RA</td>
<td>5</td>
</tr>
<tr>
<td>CO/Cl</td>
<td>3.25/1.91</td>
</tr>
<tr>
<td>PVR</td>
<td>10.7</td>
</tr>
<tr>
<td>SV</td>
<td>38 ml</td>
</tr>
</tbody>
</table>

+ Infused Prostacyclin

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*Setting the Pace in the PH Race | Through Education, Research and Advocacy*
## Hemodynamic Data

### 9/2014 Resting

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>PAP</td>
<td>70/28/46</td>
</tr>
<tr>
<td>PCWP</td>
<td>8</td>
</tr>
<tr>
<td>RV</td>
<td>68/0, 9</td>
</tr>
<tr>
<td>RA</td>
<td>6</td>
</tr>
<tr>
<td>CO</td>
<td>4.31</td>
</tr>
<tr>
<td>PVR</td>
<td>8.81</td>
</tr>
<tr>
<td>SV</td>
<td>51 ml</td>
</tr>
</tbody>
</table>

**+ ERA**

**+ PDE5**
Cardiac MRI
Functional Data

*All walk tests performed on 4L O2*
Re-evaluation of Underlying Lung Disease

- HRCT scan and PFTs repeated
  - stable
Is Hypoxemia Her Limiting Factor?

• Possible causes for worsening hypoxemia
  – Intracardiac shunt
    • Due to PFO
  – Intrapulmonary shunt
    • Due to VQ mismatch
Invasive CPET+ Intracardiac Ultrasound + Bubble study
# Hemodynamic Data

<table>
<thead>
<tr>
<th>April 2015</th>
<th>Resting 4L</th>
<th>100% FiO2</th>
<th>Exercise 40% FiO2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PAP</strong></td>
<td>76/30/53</td>
<td>77/37/53</td>
<td>82/43/55</td>
</tr>
<tr>
<td><strong>PCWP</strong></td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td><strong>RV</strong></td>
<td>77/18</td>
<td>75/17</td>
<td></td>
</tr>
<tr>
<td><strong>RA</strong></td>
<td>10</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td><strong>CO</strong></td>
<td>4.40</td>
<td>5.32</td>
<td>5.45</td>
</tr>
<tr>
<td><strong>PVR index</strong></td>
<td>26.09</td>
<td>17.68</td>
<td></td>
</tr>
<tr>
<td><strong>Shunt</strong></td>
<td>21%</td>
<td>13%</td>
<td>11%</td>
</tr>
<tr>
<td><strong>Desaturation</strong></td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Bubble study</strong></td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

Prostacyclin + ERA + PDE5
Conclusions

• Cause of hypoxemia with exertion
  – Likely severely worsened VQ mismatch with exertion OR positional PFO (not present when supine)
  – Combination of emphysema and PAH
    • Patient report of improvement in SOB with prednisone burst

• Treatment changes to optimize VQ matching
  – Increase therapy for emphysema
  – Decrease or change therapy for PAH
Pearls

• Patients with parenchymal lung disease in addition to PH can have severe VQ mismatch on vasodilator therapy

• Medications have complex effects in patients with mixed phenotypes
Conclusions

• Understanding complex patients often requires thinking out of the box
  – Tailoring therapy to a specific phenotypes
  – Advanced testing + looking beyond the current WHO classification

• Advanced hemodynamics are useful in properly phenotyping complex disease
  – But at what cost to the patient?
  – Use to better understand and manage patients rather than propagation of the diagnostic modality itself
Thank you!!!!

Dr. Franz Rischard
Dr. Steve Knoper
Dr. Ankit Desai
Margaret Debose, RN
Marcia Cerise, RN
MICU nurses
Cath lab nurses
Obtaining CME/CE Credit

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