Clinical Classification of Patients with Pulmonary Hypertension in Rural Minnesota

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Rural Medicine

- In MN, over 25% of the population live in rural communities (over 1.38 million people)
- Different demographics, socioeconomic pressures than urban communities
- Lack of access to specialist physicians:
  - 30/100,000 specialists vs. 263/100,000 specialists

Pulmonary Hypertension (PH)

- Increased pressures in pulmonary vasculature
  - Remodeling, right heart failure and death
- Symptoms: shortness of breath, fatigue, chest pain, dizziness, syncope
  - Not unique to PH
- Treatment depends on PH classification

[Image of normal and pulmonary hypertension lung structures]

https://dovemed-prod-k8s.s3.amazonaws.com/media/images/shutterstock_116410816.width-750.png
PH diagnosis

- Pulmonary function test, 6 minute walking test, Ventilation perfusion scan
- Echocardiogram (screening)
  - Estimated right ventricular systolic pressure (RVSP) ≥50 mmHg from tricuspid regurgitant velocity
  - Non-invasive
• Right Heart Catheterization (RHC) (diagnostic)
  • Gold-standard, high accuracy
  • Definition: mPAP ≥20 mmHg (2018 WSPH)

https://www.pcipedia.org/images/thumb/6/64/RightHeart_Waveforms_Fig1.svg/1599px-RightHeart_Waveforms_Fig1.svg.png
Group 1: Pulmonary Arterial Hypertension (PAH)

RISK FACTORS AND ASSOCIATED CONDITIONS
- Collagen Vascular Disease
- Congenital Heart Disease
- Portal Hypertension
- HIV Infection
- Drugs and Toxins
- Pregnancy

SUSCEPTIBILITY
- Abnormal BMPR2 Gene
- Other Genetic Factors

VASCULAR INJURY
- Endothelial Dysfunction
  - Nitric Oxide Synthase
  - Prostacyclin Production
  - Thromboxane Production
  - Endothelin 1 Production

Vascular Smooth Muscle Dysfunction
- Impaired Voltage-Gated Potassium Channel (Kv1.5)
- Smooth Muscle Hyper trophy
- Early Intimal Proliferation

DISEASE PROGRESSION
- Loss of Response to Short-Acting Vasodilator Trial
- Adventitial and Intimal Proliferation
- In situ Thrombosis
- Plexiform Lesion
- Advanced Vascular Lesion

NORMAL
REVERSIBLE DISEASE
IRREVERSIBLE DISEASE

Objectives

1. Compare clinical characteristics between patients with group 1 PH and those in non-group 1 PH
2. Compare risks of 2 year mortality in group 1 vs non-group 1 PH
3. Estimate the prevalence of PAH in rural MN

https://icon-library.net/icon/bullseye-icon-png-2.html
Methods

• Retrospective review of patients with suspected PH between 1/1/2010 and 3/31/20.

• Inclusion criteria
  • ≥18 years old with suspected PH seen at MHI outreach sites (Baxter/Crosby/Aitkin)
  • Screening echo
  • Diagnostic RHC
PH Groups

- Total: n=229
- Group 1: PAH
  - 56 (24%)
- Group 1*: combined pre- and post-capillary PH
  - 41 (18%)
- Non-group 1: groups 2 – 5
  - 132 (58%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Pulmonary Arterial Hypertension</td>
</tr>
<tr>
<td>Group 2</td>
<td>PH from left-sided heart disease</td>
</tr>
<tr>
<td>Group 3</td>
<td>PH from chronic hypoxic lung disease</td>
</tr>
<tr>
<td>Group 4</td>
<td>PH from chronic blood clots</td>
</tr>
<tr>
<td>Group 5</td>
<td>Unclear multifactorial mechanisms (sarcoidosis, hematological disorders, etc)</td>
</tr>
<tr>
<td></td>
<td>All pts (n=229)</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td><strong>Male (%)</strong></td>
<td>123 (54)</td>
</tr>
<tr>
<td><strong>BMI @ first consult Mean ± SD</strong></td>
<td>32±8.9</td>
</tr>
<tr>
<td><strong>Living (%)</strong></td>
<td>184 (80)</td>
</tr>
<tr>
<td><strong>Age at RHC Mean ± SD</strong></td>
<td>72.2±11.9</td>
</tr>
<tr>
<td><strong>Sleep Apnea (%)</strong></td>
<td>96 (42)</td>
</tr>
<tr>
<td><strong>Diabetes mellitus (%)</strong></td>
<td>69 (30)</td>
</tr>
<tr>
<td><strong>Hypertension (%)</strong></td>
<td>161 (70)</td>
</tr>
<tr>
<td><strong>Coronary artery disease (%)</strong></td>
<td>101 (44)</td>
</tr>
<tr>
<td><strong>Atrial fibrillation (%)</strong></td>
<td>111 (48)</td>
</tr>
<tr>
<td><strong>Supraventricular tachycardia (%)</strong></td>
<td>15 (7)</td>
</tr>
<tr>
<td><strong>Liver dysfunction (%)</strong></td>
<td>12 (5)</td>
</tr>
<tr>
<td><strong>Connective tissue disease (%)</strong></td>
<td>6 (3)</td>
</tr>
</tbody>
</table>

**Table 1: Demographics**
### Table 1: Demographics cont’d

<table>
<thead>
<tr>
<th></th>
<th>All pts (n=229)</th>
<th>Group 1 (n=56)</th>
<th>Group 1* n=41</th>
<th>Non-group 1 (n=132)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCB (%)</td>
<td>79 (34)</td>
<td>20 (36)</td>
<td>14 (34)</td>
<td>45 (34)</td>
<td>0.961</td>
</tr>
<tr>
<td>Anticoag (%)</td>
<td>114 (50)</td>
<td>17 (31)</td>
<td>24 (59)</td>
<td>73 (55)</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td>Digoxin (%)</td>
<td>26 (11.4)</td>
<td>8 (14)</td>
<td>8 (20)</td>
<td>10 (8)</td>
<td>0.083</td>
</tr>
<tr>
<td>BNP median (IQR)</td>
<td>280.5 (137.5, 505.8)</td>
<td>316 (148, 801)</td>
<td>186.5 (112, 725.8)</td>
<td>287 (139.5, 443.5)</td>
<td>0.548</td>
</tr>
<tr>
<td>Pro-BNP median (IQR)</td>
<td>1730 (532, 3270)</td>
<td>1830 (330.5, 6710)</td>
<td>1690 (756.5, 4758.5)</td>
<td>1725 (541, 3015)</td>
<td>0.778</td>
</tr>
<tr>
<td>Troponin median (IQR)</td>
<td>0.037 (0.014, 0.20)</td>
<td>0.033 (0.012, 0.11)</td>
<td>0.033 (0.014, 0.179)</td>
<td>0.038 (0.016, 0.257)</td>
<td>0.48</td>
</tr>
<tr>
<td>Hemoglobin median (IQR)</td>
<td>12.95 (11.2, 14.2)</td>
<td>13.1 (11.3, 14.3)</td>
<td>12.2 (10.5, 13.1)</td>
<td>13.25 (11.25, 14.4)</td>
<td><strong>0.048</strong></td>
</tr>
<tr>
<td>Creatinine median (IQR)</td>
<td>1.06 (0.84, 1.4)</td>
<td>1 (0.74, 1.25)</td>
<td>1.23 (0.88, 1.60)</td>
<td>1.065 (0.858, 1.363)</td>
<td><strong>0.042</strong></td>
</tr>
</tbody>
</table>
### Table 2: Echo Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All pts (n=229)</th>
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<th>Non-group 1 (n=132)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVSP Mean ± SD</td>
<td>60.2±20.2</td>
<td>66.7±21.4</td>
<td>66.7±19.5</td>
<td>54.5±18.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mod/severe RA enlargement (%)</td>
<td>96 (42)</td>
<td>30 (53)</td>
<td>19 (46)</td>
<td>47 (36)</td>
<td>0.14</td>
</tr>
<tr>
<td>Mod/severe RV enlargement (%)</td>
<td>64 (28)</td>
<td>25 (45)</td>
<td>12 (29)</td>
<td>27 (20)</td>
<td>0.002</td>
</tr>
<tr>
<td>Mod-/severe RV dysfunction (%)</td>
<td>44 (19)</td>
<td>17 (30)</td>
<td>8 (19.5)</td>
<td>19 (14)</td>
<td>0.037</td>
</tr>
<tr>
<td>TAPSE Mean ± SD</td>
<td>19.8±7.2</td>
<td>19±7.5</td>
<td>17.6±6.4</td>
<td>20.8±7.3</td>
<td>0.112</td>
</tr>
<tr>
<td>Pericardial effusion (%)</td>
<td>34 (15)</td>
<td>10 (18)</td>
<td>4 (10)</td>
<td>20 (15)</td>
<td>0.523</td>
</tr>
<tr>
<td>LVEF Mean ± SD</td>
<td>58.8±12.0</td>
<td>62.4±9.8</td>
<td>59.4±11.9</td>
<td>57.0±12.6</td>
<td>0.026</td>
</tr>
<tr>
<td>Mod/severe LA enlargement (%)</td>
<td>102 (45)</td>
<td>16 (29)</td>
<td>26 (63)</td>
<td>60 (45)</td>
<td>0.002</td>
</tr>
<tr>
<td>E/e' median (IQR)</td>
<td>12 (9.0, 17.2)</td>
<td>10.3 (7.6, 13.2)</td>
<td>13.7 (11.0, 20.1)</td>
<td>11.9 (9.2, 17.7)</td>
<td>0.011</td>
</tr>
</tbody>
</table>
Table 3: RHC Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All pts (n=229)</th>
<th>Group 1 (n=56)</th>
<th>Group 1* n=41</th>
<th>Non-group 1 (n=132)</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAP Mean ± SD</td>
<td>11.0±5.5</td>
<td>8.6±5.0</td>
<td>13.2±5.0</td>
<td>11.2±5.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVSP Mean ± SD</td>
<td>57.6±18.5</td>
<td>65.8±21.2</td>
<td>68.9±14.1</td>
<td>50.8±15.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>mPAP Mean ± SD</td>
<td>36.6±11.6</td>
<td>41.3±14.2</td>
<td>44.0±7.5</td>
<td>32.3±9.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PAWP Mean ± SD</td>
<td>17.3±7.3</td>
<td>11.3±6.0</td>
<td>21.7±5.3</td>
<td>18.5±6.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Odds Ratios for having PAH

- Echo Pericardial Effusion
- Echo Mod/severe LAE
- Echo RVSP
- RHC mean PAP
- RHC PVR
- 6 Minute Walk distance
- CAD
- Afib/flutter
- Hypertension
- Age at RHC
- Male

Odds Ratios

0 0.5 1 1.5 2 2.5 3 3.5 4 4.5

Odds ratios
Kaplan-Meier survival estimates

Proportion Surviving

Time (years)

p=0.003

Number at risk
Age < 80 169
Age ≥ 80 58

Age < 80 146 126 112 103
Age ≥ 80 42 36 30 27
Kaplan-Meier survival estimates

Proportion Surviving

p=0.014

Time (years)

Number at risk

<table>
<thead>
<tr>
<th>Age Group</th>
<th>&lt;50 years</th>
<th>50-59 years</th>
<th>60-69 years</th>
<th>70-79 years</th>
<th>≥80 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 years</td>
<td>15</td>
<td>11</td>
<td>9</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>50-59 years</td>
<td>19</td>
<td>17</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>60-69 years</td>
<td>47</td>
<td>41</td>
<td>36</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>70-79 years</td>
<td>88</td>
<td>77</td>
<td>65</td>
<td>59</td>
<td>50</td>
</tr>
<tr>
<td>≥80 years</td>
<td>58</td>
<td>42</td>
<td>36</td>
<td>30</td>
<td>27</td>
</tr>
</tbody>
</table>
Kaplan-Meier survival estimates

Proportion Surviving

Time (years)

p=0.276

Number at risk
Group 1  55  44  38  33  30
Group 1* 41  37  32  26  24
Non-group 1 131 107 92 83 76

Legend:
- Blue: Group 1
- Red: Group 1*
- Green: Non-group 1
Prevalence of PH in Rural Minnesota

Aitkin County, MN
-PAH: 370/million
-Group 1*+2: 1543/million

Crow Wing County, MN
-PAH: 368/million
-Group 1*+2: 1360/million

Cass County, MN
-PAH: 560/million
-Group 1*+2: 420/million

Population:
- Aitkin County: 62,500
- Cass County: 28,567
- Crow Wing County: 16,202
Conclusions/Future direction

- Group 1 and Group 1* appear different at baseline
- Age may influence patient survival
- PH groups may have similar mortality
- Rural prevalence may be higher than literature
  - Socioeconomic pressures, older population

Future directions
- 5 year mortality for PH groups
Summer Highlights!

- Lunch and Learns
  - Dr. Hauser
  - Dr. Sengupta
  - Dr. Sharkey
- Continued mentoring
- Golfing, Minnehaha, Zoom, Skype, conference calls, etc.
• Future Plans
  • MHIF Gap year
    • Structural
    • EP/Prevention
    • IIR
  • Medical School?
Acknowledgements

• John and Susan Morrison

• MHIF staff and support team
  • Education team
  • IIR

• Archana and Ananya

• Dr. Eric Fenstad and Stephanie Ebnet
  • And all other mentors!
Questions?
<table>
<thead>
<tr>
<th>Odds Ratios - Group 1 vs Non-Group 1 + 1*</th>
<th>Odds of having Group 1 PH</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echo Mod/severe LAE</td>
<td>0.377 (0.195, 0.727)</td>
<td>0.004</td>
</tr>
<tr>
<td>RHC PVR</td>
<td>1.277 (1.157, 1.408)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CAD</td>
<td>0.52 (0.275, 0.982)</td>
<td>0.044</td>
</tr>
<tr>
<td>Afib/flutter</td>
<td>0.29 (0.149, 0.562)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at RHC</td>
<td>0.698 (0.945, 0.992)</td>
<td>0.01</td>
</tr>
<tr>
<td>Male</td>
<td>2.186 (1.158, 4.125)</td>
<td>0.016</td>
</tr>
</tbody>
</table>
Rural poverty/age

• Aitkin
  • 65+: 5060
  • Poverty: 13.7%

• Crow Wing
  • 65+: 13698
  • Poverty: 12.6%