Introduction

- Pulmonary Hypertension (PH) has historically been defined by a mean pulmonary artery pressure (mPAP) ≥ 25 mmHg.
- Precapillary PH, a subgroup of PH that benefits from targeted therapies, has been defined by a mPAP ≥ 25 mmHg, a pulmonary capillary wedge pressure (PCWP) of ≤ 15 mmHg, and a pulmonary vascular resistance (PVR) of ≥ 3 Wood Units (WU).1
- In 2018, the 6th World Symposium on Pulmonary Hypertension (6WSPH), proposed a lower diagnostic threshold for precapillary PH: mPAP >20, PCWP ≤ 15, PVR ≥ 3 WU.2
- This definition was based on a meta-analysis of 882 healthy subjects from 47 studies, showing the average mPAP of healthy individuals to be 14.0, ± 3.3 mmHg, as measured at sea level.3
- Controversy has arisen around whether or not to treat patients that have been "recategorized" as having precapillary PH, as the clinical significance of a mPAP of 20-24 mmHg is unknown.
- A concern that has not been addressed is the generalizability of this definition to patients at altitude, as elevation has well-known effects on mPAP.4,5

Methods

- Data including mPAP, PCWP, and PVR, as well as age, BMI, and gender were collected were automatically abstracted from the EMR for all patients undergoing right heart catheterization for any indication at the University of Colorado Hospital between the years of 2015 and 2017.
- Municipal information was used to calculate the mean elevation of patients’ home counties based on zip code.
- All patients with a mPAP > 20 mmHg were included in the analysis.
- This population was categorized according to the ERS definition, then re-categorized according to the 6WSPH Definition.
- Number and proportion of PH diagnoses were recorded, and significant differences determined by 1-sample proportions test with continuity correction, with significance set at .05.

Pulmonary Hypertension Definitions

<table>
<thead>
<tr>
<th>PH Category</th>
<th>ERS Definition (mmHg)</th>
<th>6WSPH Definition (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-capillary PH</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>mPAP &gt; 20, PCWP ≤ 15 &amp; PVR ≥ 3</td>
</tr>
<tr>
<td>Combined PH</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>mPAP &gt; 20, PCWP ≤ 15 &amp; PVR ≥ 3</td>
</tr>
<tr>
<td>Post-capillary PH</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>mPAP &gt; 20, PCWP ≤ 15 &amp; PVR ≥ 3</td>
</tr>
<tr>
<td>Other PH</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
</tr>
</tbody>
</table>

Definitions used to categorize patients1,2

Figure adapted from Yang et al., demonstrating the effects of increased elevation on mPAP.

- Our study examined whether the 6WSPH definition of PH would result in a significant increase in PH diagnosis and precapillary PH in Denver.

Results

Diagnoses of Pulmonary Hypertension by Definition

<table>
<thead>
<tr>
<th>Category</th>
<th>No PH</th>
<th>Other PH</th>
<th>Postcapillary PH</th>
<th>Combined PH</th>
<th>Precapillary PH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of Population</td>
<td>63%</td>
<td>8%</td>
<td>4%</td>
<td>28%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Changes in PH Diagnosis Following 6WSPH Recategorization

<table>
<thead>
<tr>
<th>PH Category</th>
<th>ERS Definition</th>
<th>6WSPH Definition</th>
<th>Change in Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-capillary PH</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>mPAP &gt; 20, PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>-31%</td>
</tr>
<tr>
<td>Combined PH</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>mPAP &gt; 20, PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>-4%</td>
</tr>
<tr>
<td>Post-capillary PH</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>mPAP &gt; 20, PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>-24%</td>
</tr>
<tr>
<td>Other PH</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>mPAP ≥ 25 &amp; PCWP ≤ 15 &amp; PVR ≥ 3</td>
<td>-4%</td>
</tr>
<tr>
<td>No PH</td>
<td>286</td>
<td>286</td>
<td>0%</td>
</tr>
</tbody>
</table>

Using the 6WSPH definition resulted in a statistically significant increase in the proportion of patients diagnosed with precapillary PH and Other PH, as well as an increase of 17% in patients diagnosed with PH increased overall.

Discussion

- The results of this study suggest that use of the 6WSPH definition result in an increase in the diagnosis of PH overall, with a particular increase in the diagnosis of precapillary PH.
- This study builds on prior cohort studies examining the effects of the new definition on different populations.
- The increase in PH by 17% was higher in this cohort than in other similar studies in Sao Paolo (2%), Giessen (6%), and Turkey (9.8%), all of which are lower in elevation than Denver, CO. This may suggest that patients living at altitude have a higher baseline mPAP than those at sea level, limiting the generalizability of the 6WSPH definition.
- The significant increase in precapillary PH of 6% is consistent with another Turkish cohort study showing a greater-than-expected increase in precapillary PH after application of the 6WSPH.4

Future Directions

- Clinical significance of mPAP 20 - 24 remains unclear, prospective data on the impact of PH treatment in this population is lacking.
- Several studies have shown that borderline mPAP values are associated with poor prognosis.6,7
- No causative link has been established
- An important question is whether any link between morbidity and mPAP is observed at altitude.
- A future study is planned to follow this cohort from 2017 - 2021, evaluating trends in mortality and development of PH or associated diagnoses, and any association with baseline mPAP.6

References