Pulmonary Hypertension: Review of the New WHO Classification

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The authors of this presentation have no relevant financial disclosures
Introduction

• Pulmonary hypertension refers to a spectrum of diseases that leads to abnormal elevation of the pulmonary arterial pressure
• Typically has an insidious clinical onset with varying severity
• May progress to right sided heart failure/cor pulmonale and death
• The etiology is complex and multifactorial
• The World Health Organization (WHO) has attempted to classify this broad disease based on the expanding understanding of the mechanism and pathophysiology
• The 5th World Symposium in Nice, France 2013, provided the most recent modification of this classification
Objectives

• To review the proposed underlying mechanisms leading to pulmonary hypertension in the context of the different WHO categories
• Emphasis will be placed on imaging characteristics which may help to elucidate the underlying mechanism and pathophysiology
Pulmonary Hypertension

• Pulmonary artery pressure is a function of flow and resistance within the pulmonary vascular system

• Pulmonary hypertension occurs due to:
  – Increased flow
  – Pulmonary arterial vasoconstriction
  – Small pulmonary vessel structural changes or destruction

Courtesy of Casey Storck RT
Pulmonary Hypertension

- Includes both pulmonary arterial and venous hypertension
  - difficult to clinically distinguish and may overlap
- Pulmonary arterial hypertension = mean pulmonary artery pressure ≥ 25 mm Hg at rest
- Elevated pulmonary venous pressure = pulmonary capillary wedge pressure is ≥ 18 mm Hg

Pulmonary Hypertension (PH)

- Enlargement of the MPA is highly suggestive of PH
- Initial study showed that a size of $\geq 2.9$ cm has a 87% sensitivity and 89% specificity
  - However, absolute measures are not completely reliable, as PA pressure and size depend on the BMI, gender and age
- Other studies have demonstrated that a PA/Aortic ratio $>1$ is a more accurate indicator

- 48 year old female with PH. CT demonstrates an enlarged main pulmonary artery measuring 6.6 cm
- MPA should be measured at its widest point, within 3 cm of the bifurcation

<table>
<thead>
<tr>
<th>Group</th>
<th>Subcategory</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Pulmonary Arterial Hypertension (Includes all causes that lead to structural narrowing of the pulmonary vessels)</td>
</tr>
<tr>
<td></td>
<td>• 1.1 Idiopathic PAH</td>
</tr>
<tr>
<td></td>
<td>• 1.2 Heritable PAH</td>
</tr>
<tr>
<td></td>
<td>• 1.3 Drug and toxin induced PAH</td>
</tr>
<tr>
<td></td>
<td>• 1.4 PAH associated with: Connective tissue diseases, HIV, Portal hypertension, Congenital heart disease, Schistosomiasis</td>
</tr>
<tr>
<td></td>
<td>• 1‘ Pulmonary veno-occlusive disease and/or Pulmonary capillary hemangiomatosis</td>
</tr>
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<td></td>
<td>• 1” Persistent pulmonary hypertension of the newborn</td>
</tr>
<tr>
<td>II</td>
<td>Pulmonary Hypertension due to left sided heart disease</td>
</tr>
<tr>
<td></td>
<td>• 2.1 LV Systolic dysfunction</td>
</tr>
<tr>
<td></td>
<td>• 2.2 LV Diastolic dysfunction</td>
</tr>
<tr>
<td></td>
<td>• 2.3 Valvular Disease</td>
</tr>
<tr>
<td></td>
<td>• 2.4 Congenital/acquired left heart inflow/outflow tract obstruction and Congenital cardiomyopathies</td>
</tr>
<tr>
<td>III</td>
<td>Pulmonary Hypertension related to lung disease or hypoxia</td>
</tr>
<tr>
<td></td>
<td>• 3.1 Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td></td>
<td>• 3.2 Interstitial lung disease</td>
</tr>
<tr>
<td></td>
<td>• 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern</td>
</tr>
<tr>
<td></td>
<td>• 3.4 Sleep breathing disorders</td>
</tr>
<tr>
<td></td>
<td>• 3.5 Alveolar hypoventilation disorders</td>
</tr>
<tr>
<td></td>
<td>• 3.6 Chronic high altitude exposure</td>
</tr>
<tr>
<td></td>
<td>• 3.7 Developmental lung disease</td>
</tr>
<tr>
<td>IV</td>
<td>Chronic Thromboembolic Pulmonary Hypertension</td>
</tr>
<tr>
<td>V</td>
<td>Pulmonary Hypertension related to multifactorial mechanisms</td>
</tr>
<tr>
<td></td>
<td>• 5.1 Hematologic disorders</td>
</tr>
<tr>
<td></td>
<td>• 5.2 Systemic Disorders: Sarcoidosis, Pulmonary histiocytosis, Lymphangioleiomyomatosis</td>
</tr>
<tr>
<td></td>
<td>• 5.3 Metabolic disorders: Glycogen storage disorders, Gaucher disease</td>
</tr>
<tr>
<td></td>
<td>• 5.4 Other: Fibrosing Mediastinitis, Tumoral calcinosi, Renal failure</td>
</tr>
</tbody>
</table>

# Radiographic Classification

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>PRE CAPILLARY</th>
<th>LUNG RELATED</th>
<th>POST CAPILLARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>PULMONARY VESSELS PRIMARILY INVOLVED</td>
<td>ARTERIAL</td>
<td>ARTERIAL</td>
<td>VENOUS</td>
</tr>
<tr>
<td>ADDITIONAL IMAGING FINDINGS</td>
<td>PRUNED PERIPHERAL PULMONARY VESSELS, MOSAIC ATTENUATION</td>
<td>LUNG PARENCHYMAL DISEASE</td>
<td>EVIDENCE OF PULMONARY VENOUS HTN – septal lines, ground glass opacities, pleural effusions</td>
</tr>
<tr>
<td>EXAMPLES</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Idiopathic PAH</td>
<td>• COPD</td>
<td>• Left ventricular failure</td>
</tr>
<tr>
<td></td>
<td>• Familial PAH</td>
<td>• ILD</td>
<td>• LV inflow or outflow obstruction</td>
</tr>
<tr>
<td></td>
<td>• Drug-related</td>
<td>• Sleep Apnea</td>
<td>• Pulmonary venoocclusive disease</td>
</tr>
<tr>
<td></td>
<td>• L to R cardiac shunt</td>
<td>• Developmental lung disease</td>
<td>• Mediastinal fibrosis</td>
</tr>
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Radiographic Classification – Pre Capillary

- Enlargement of the central pulmonary arteries
- Pruning of the peripheral pulmonary vessels
- Mosaic attenuation
  - Inhomogeneous lung opacity representing the presence of differential parenchymal perfusion

CT demonstrates a mosaic attenuation with prominent central vessels. More lucent portions of the lungs represent area of decreased perfusion. Subtle paucity of vessels within these regions represent peripheral pruning.

Radiographic Classification – Lung Related

- PH is commonly seen in patients with chronic pulmonary disease
- Findings are similar to the pre capillary form with superimposed lung parenchymal disease

CT chest in a patient with Idiopathic Pulmonary Fibrosis (IPF), found to also have PH – likely a sequelae of chronic lung disease.
Radiographic Classification – Post Capillary

- Pulmonary Venous Hypertension
  - Interlobular septal thickening
  - Subpleural thickening
  - Ground glass opacities
  - Pleural effusion

Chest radiograph demonstrates an enlarged MPA with interlobular septal thickening and mild ground glass opacity in the right lung.

Additional Radiographic Findings in PH

**ANGIOCENTRIC GROUND-GLASS NODULES**
Represent cholesterol granuloma formation as a result of repeated pulmonary hemorrhage

**CORKSCREW SHAPED VESSELS**
Caused by the increased flow within the dilated central pulmonary arteries

Group I - Idiopathic/Heritable PAH (IPAH)

- Pulmonary arterial hypertension
  - no clinically discernible cause
  - normal pulmonary arterial wedge pressure
  - no evidence of left-to-right shunt
- 3:1 female to male ratio
- Mean survival of 2.8 years w/o treatment
- Heritable PAH is similar to the idiopathic form
  - Familial predilection
  - Not well understood
  - Bone morphogenetic protein receptor type II (BMPR2) mutation in over half of patients

Group I – IPAH Pathophysiology

- A proliferative vasculopathy of the distal pulmonary arteries
- Proposed mechanism is:
  - prolonged vasoconstriction due to endothelial dysfunction causing decreased synthesis of endothelium-derived vasodilators
  - leads to structural changes
- Structural changes include intimal proliferation and medial hypertrophy
- Leads to laminar fibrosis and in situ thrombosis
- Pulmonary veins are usually unaffected
- Can be classified in the Pre Capillary Classification Radiographic Scheme

Photomicrograph demonstrates a muscular pulmonary artery narrowed by medial hypertrophy and obstructed by intravascular thrombus.

Group I - Pulmonary Veno-occlusive Disease (PVOD)/Pulmonary Capillary Hemangiomatosis (PCH)

- Rare idiopathic disorders
- Caused by a widespread vascular obstructive process, either in the pulmonary venules/small veins (PVOD) or the alveolar capillary bed (PCH)
- Unclear if these are two distinct entities or varied expression of a single disorder
- Commonly occur in tandem
- Occurs in young adults with a 2:1 Male to Female ratio
- PVOD may have a pre- or post capillary radiographic appearance
- However, in PCH a precapillary appearance is the dominant feature

Group I – PVOD/PCH

Pulmonary Veno-occlusive Disease:
Small veins/venules (red) become occluded, leading to dilatation of the capillary network, lymphatic (yellow) engorgement, and interlobular septal thickening.

Pulmonary Capillary Hemangiomatosis:
Discrete area of capillary proliferation without changes within the pulmonary veins or interlobular septum.

Group I – PVOD/PCH

Pulmonary Veno-occlusive Disease: Evidence of sepal lines and subtle groundglass nodules.

Pulmonary Capillary Hemangiomatosis: Groundglass nodules with peripheral vascular pruning. No significant interlobular septal thickening demonstrated.

Group I – Congenital Heart Disease

- Systemic to Pulmonary Shunt
  - Atrial Septal Defect
  - Ventricular Septal Defect
  - Patent Ductus Arteriosus
  - Eisenmenger syndrome
  - Total or Partial Anomalous Pulmonary Venous Return

- Caused by a large increase in pulmonary arterial blood flow

44 year old with a secundum type ASD (black arrow). Chest CT reveals enlargement of main pulmonary artery with right sided heart enlargement.

Group II – PH due to Left Heart Dysfunction

- Backup of flow into the pulmonary venous system raising venous pressure and eventually arterial pressure
- May be caused by:
  - restriction of flow into (pulmonary vein stenosis) or through the left atrium (mitral valve disease)
  - or to due to poor flow into (diastolic dysfunction) or through the left ventricle (systolic dysfunction or aortic valve disease)

Patient with prolonged mitral stenosis (black arrow) demonstrates evidence of venous pulmonary HTN with septal lines.

Group II - Pathophysiology

- Related to pulmonary venous hypertension
- Left sided heart failure causes increased pulmonary venous pressure and vascular smooth muscle remodeling including:
  - thickening of the pulmonary capillary basal lamina causing subsequent interstitial edema and proliferation of the connective tissue around the alveoli
- Capillary congestion causes distention of the lymphatics and increased vascular resistance
- Leads to compensatory pulmonary arterial hypertension to drive pulmonary flow
- Can be included in the Post Capillary Classification Radiographic Scheme

Photomicrograph demonstrates venous dilatation with venous arterialization caused by medial hypertrophy of the pulmonary vein.

Group III – Related to underlying Lung Disease

- Caused by multiple factors
  - Hypoxic induced vasoconstriction
  - Mechanical stress due to the hyper-inflated lungs
  - Destruction of the pulmonary capillaries by emphysema/fibrosis

54 year old female with sarcoidosis. CT chest demonstrates upper lobe predominant fibrosis related to end stage sarcoidosis. The MPA was enlarged and the patient was found to have PH, due to the underlying lung disease.
Group IV - Chronic Thromboembolic Disease

- Chronic emboli tightly adhere to the medial layer of the artery, replacing the normal intima and causing stenosis/obstruction
- Mechanical obstruction leads to decrease in the cross-sectional area and increased resistance within the pulmonary arteries
- Can be considered in the Pre Capillary Classification Radiographic Scheme

CT PE study demonstrates enlarged MPA due to large chronic pulmonary emboli. Organization of the thrombi with its eccentric location and internal calcification (arrows) prove its chronicity.

Group IV - Chronic Thromboembolic Disease (CTEPH)

Additional Image Findings:

**Mosaic Attenuation:**
Reflecting geographic variation in blood flow

**Enlarged Bronchial Arteries:**
Due to the development of systemic–pulmonary anastomoses, to maintain pulmonary blood flow

Group V – Related to Multifactorial Mechanisms

• Related to different underlying systemic disease
• Causal relationship either multifactorial and/or not well understood

Mediastinal Fibrosis: Coronal oblique CT reconstructions reveal constriction of the pulmonary venous drainage into the left atrium, causing post capillary pulmonary hypertension with septal lines (black arrows). Pre capillary hypertension is also evident with MPA dilatation.

Right Ventricular Changes

- Increased pulmonary arterial pressure
- RV pressure overload
- Myocardial remodeling with RV hypertrophy
- RV dilatation, increased wall stress and dysfunction
- RV failure and Cor Pulmonale

Cor Pulmonale: RV Strain and Hypertrophy

COR PULMONALE
• Anterior Free Wall RV > 6 mm
• Dilatation of RV chamber (RV/LV > 1)
• Septal flattening or curve reversal
• Regurgitant flow: Pulmonary & tricuspid valves

MRI demonstrates a dilated RV with free wall thickening and delayed hyperenhancement at the RV insertion points (arrows) related to RV strain.

WHO Classification -- Radiological Flowsheet

- Enlarged MPA
  - No other abnormalities
    - IPAH
      - GROUP I
    - Congenital Heart Disease
      - GROUP I
    - Left Sided Dysfunction
      - GROUP II
  - Heart
  - Lungs
    - Underlying Lung Disease
      - GROUP III
  - Pulmonary Vasculature
    - CTEPH
      - GROUP IV
  - Variable Involvement / Systemic Disease
    - GROUP V

References


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