IMAGING IN PULMONARY HYPERTENSION
AND COR PULMONALE

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Lecture Outline

- Definition of Pulmonary Hypertension and Cor Pulmonale
  - Epidemiology and Pathophysiology
  - Definition and Classification

- Echo imaging in Pulmonary Hypertension and Cor Pulmonale
  - Aim of imaging
  - Guidelines
  - Imaging parameters to guide prognosis and treatment
  - Other imaging modality for PHT

- CONCLUSION
Definition of
PULMONARY HYPERTENSION and
COR PULMONALE

- Epidemiology and Pathophysiology
- Definition and Classification
Prevalence of Pulmonary Hypertension

1. **Group 1 (PAH)**
   - In Europe (ESC 2015 guidelines), PAH prevalence and incidence are estimated to be **15-60 and 5-10 cases per million adults respectively**.
   - Half have iPAH, heritable or drug induced PAH.
   - In Associated PAH, highest prevalence is in the Connective Tissue Disease groups, mainly in patients with systemic sclerosis.

2. **Group 2 (PH due to LHD)**
   - 60% of HF due to impaired systolic function and 70% of HFPEF.
   - All patients with severe MV disease and 65% in those with severe AS (EHJ 2012;33:2451)

3. **Group 4 (CTEPH)**
   - Spanish 2013 PH Registry: CTEPH prevalence and incidence were **3.2 and 0.9 cases per million**.
   - Prevalence of 0.5-2% has been reported in survivors of acute PE (Pengo et al NEJM, 2004;350;2257)
   - International CTEPH Registry: **31.9% of CTEPH patients have associated thrombophilic disorders** (lupus anticoagulant/antiphospholipid antibodies, protein S and C deficiency, activated protein C resistance including factor V Leiden mutation, prothrombin gene mutation, antithrombin III deficiency and elevated factor VIII) and **3.4% had history of splenectomy.**
APAH, pulmonary arterial hypertension associated with other diseases or causes, in this case anorexigen; CHD-PH, congenital heart disease-associated pulmonary hypertension; CTD-PH, connective tissue disease-associated pulmonary hypertension; HIV-PH, human immunodeficiency virus-associated pulmonary hypertension; IPAH, idiopathic pulmonary arterial hypertension; PAH, pulmonary arterial hypertension; PPHTN, portopulmonary hypertension

Adapted from Peacock et al. Eur Respir J. 2007;30:104-109
Pathology of PAH

Muscular pulmonary artery from a PH patient

Intimal Proliferation
Adventitial Proliferation
Medial Hypertrophy

PATHOLOGICAL FEATURES OF PULMONARY ARTERIAL HYPERTENSION

• Medial hypertrophy

• Intimal thickening

• Complex lesions

• **Plexiform lesions** (black arrow)
  • Focal proliferation of endothelium, smooth muscle cells and extracellular matrix
Cor Pulmonale is **Right Heart Dysfunction** (dilatation, hypertrophy, systolic and diastolic impairment) due to the effects of **pulmonary hypertension specifically** associated with diseases of the chest/lung/airway components:

- Lung tissue (e.g. COPD, interstitial lung disease, etc)
- Pulmonary vasculature (e.g. iPAH, CTEPH)
- Upper airway obstruction (e.g. OSA)
- Chest wall restriction (e.g. kyphoscoliosis)

Right heart disease due to left-sided heart disease (Grp 2) or congenital heart disease (Grp 1.4.4) is **NOT** considered Cor Pulmonale.

Using the above definition, Cor Pulmonale is caused by some Group 1 diseases (Grp 1 but not Grp 1.4.4), Group 3 (lung), Group 4 (CTEPH) and Group 5 (Miscellaneous Grp e.g. sarcoidosis).

Focus on imaging in Pulmonary Hypertension and not just Cor Pulmonale.
Previously classified into 2 types (old classification)
- PRIMARY PULMONARY HYPERTENSION (PPHT)
- SECONDARY PULMONARY HYPERTENSION
  - Depends on presence or absence of identifiable causes
  - PPHT diagnosis of exclusion

In 1998 – 2nd World Symposium on PAH, ‘Evian Classification’ a new clinical based classification proposed to individualize different categories of PHT

In 2003 - in Venice, 3rd World Symposium on PAH, modifications to Evian Classification

2008 – Dana Point Update (4th World symposium on PAH), further modifications

2013 – Latest update in NICE (5th World Symposium on PAH)

2015 – ESC Guidelines on the diagnosis and treatment of Pulmonary Hypertension
PULMONARY HYPERTENSION DEFINITION:

• PATHOPHYSIOLOGICAL

- Increase in mean PAP ≥ 25 mmHg at rest assessed by RHC

- PAH is characterised by pre-capillary PH and PVR>3 WU in the absence of other causes of pre-capillary PH such as due to lung disease, CTEPH, etc

- No data to suggest this entity ‘PH on exercise’
**2015 ESC/ERS Guidelines for the diagnosis and treatment of Pulmonary Hypertension**

### Table 3: Haemodynamic definitions of pulmonary hypertension

<table>
<thead>
<tr>
<th>Definition</th>
<th>Characteristics</th>
<th>Clinical group(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH</td>
<td>( PAP_m \geq 25 \text{ mmHg} )</td>
<td>All</td>
</tr>
<tr>
<td>Pre-capillary PH</td>
<td>( PAP_m \geq 25 \text{ mmHg} ) ( \text{PAWP} \leq 15 \text{ mmHg} )</td>
<td>1. Pulmonary arterial hypertension \ 3. PH due to lung diseases \ 4. Chronic thromboembolic PH \ 5. PH with unclear and/or multifactorial mechanisms</td>
</tr>
<tr>
<td>Post-capillary PH</td>
<td>( PAP_m \geq 25 \text{ mmHg} ) ( \text{PAWP} &gt; 15 \text{ mmHg} )</td>
<td>2. PH due to left heart disease \ 5. PH with unclear and/or multifactorial mechanisms</td>
</tr>
<tr>
<td>Isolated post-capillary PH (Ipc-PH)</td>
<td>DPG &lt; 7 \text{ mmHg} and/or \ PVR \leq 3 \text{ WU} ( ^c )</td>
<td></td>
</tr>
<tr>
<td>Combined post-capillary and pre-capillary PH (Cpc-PH)</td>
<td>DPG \geq 7 \text{ mmHg} and/or \ PVR \geq 3 \text{ WU} ( ^c )</td>
<td></td>
</tr>
</tbody>
</table>

### Table 5: Important pathophysiological and clinical definitions

1. Pulmonary hypertension (PH) is a haemodynamic and pathophysiological condition defined as an increase in mean pulmonary arterial pressure \( \geq 25 \text{ mmHg} \) at rest as assessed by right heart catheterization (Table 3). PH can be found in multiple clinical conditions (Table 4).

2. Pulmonary arterial hypertension (PAH, group 1) is a clinical condition characterized by the presence of pre-capillary PH (Table 3) and pulmonary vascular resistance \( >3 \text{ Wood units} \), in the absence of other causes of pre-capillary PH such as PH due to lung diseases, chronic thromboembolic PH, or other rare diseases (Table 4). PAH includes different forms that share a similar clinical picture and virtually identical pathological changes of the lung microcirculation (Table 4).

3. There is no sufficient data to support the definition of ‘PH on exercise’. 

Galie et al. EHW ESC Guidelines Aug 2015
### Comprehensive clinical classification of pulmonary hypertension (updated from Simonneau et al.\textsuperscript{5})

<table>
<thead>
<tr>
<th>Category</th>
<th>Subcategories</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Pulmonary arterial hypertension</strong></td>
<td>1.1 Idiopathic, 1.2 Heritable (1.2.1 BMPR2 mutation, 1.2.2 Other mutations), 1.3 Drugs and toxins induced, 1.4 Associated with: (1.4.1 Connective tissue disease, 1.4.2 Human immunodeficiency virus (HIV) infection, 1.4.3 Portal hypertension, 1.4.4 Congenital heart disease (Table 6), 1.4.5 Schistosomiasis)</td>
</tr>
<tr>
<td><strong>1’. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosi</strong></td>
<td>1’.1 Idiopathic, 1’.2 Heritable (1’.2.1 ELF2AK4 mutation, 1’.2.2 Other mutations), 1’.3 Drugs, toxins and radiation induced, 1’.4 Associated with: (1’.4.1 Connective tissue disease, 1’.4.2 HIV infection)</td>
</tr>
<tr>
<td><strong>1’’. Persistent pulmonary hypertension of the newborn</strong></td>
<td></td>
</tr>
<tr>
<td><strong>2. Pulmonary hypertension due to left heart disease</strong></td>
<td>2.1 Left ventricular systolic dysfunction, 2.2 Left ventricular diastolic dysfunction, 2.3 Valvular disease, 2.4 Congenital / acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies, 2.5 Congenital / acquired pulmonary veins stenosis</td>
</tr>
</tbody>
</table>

### 3. Pulmonary hypertension due to lung diseases and/or hypoxia

- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental lung diseases (Web Table III)

### 4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions

- 4.1 Chronic thromboembolic pulmonary hypertension
- 4.2 Other pulmonary artery obstructions (4.2.1 Angiosarcoma, 4.2.2 Other intravascular tumors, 4.2.3 Arteritis, 4.2.4 Congenital pulmonary arteries stenoses, 4.2.5 Parasites (hydatidosis))

### 5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
- 5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: pulmonary tumoral thrombotic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension
GROUP 1 AND GROUP 1’, 1”

Group 1: Pulmonary Arterial Hypertension

1.1 Idiopathic PAH
1.2 Heritable PAH
1.3 Drug and toxin induced
1.4 Associated with
   1.4.1 Connective tissue disease
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis

Group 1’: Pulmonary veno-occlusive disease and / or pulmonary capillary haemangiomatosis

Group 1”: Persistent PH of the newborn (PPHN)
Group 1: Pulmonary Arterial Hypertension

1.4 Associated with

1.4.1 Connective tissue disease

1.4.2 HIV infection

1.4.3 Portal hypertension

1.4.4 Congenital heart diseases

1.4.5 Schistosomiasis
1.4.1 Connective Tissue Disease
- The prevalence of PAH is well established only in scleroderma, and rate of occurrence is estimated between 7% and 12%.
- The prognosis for patients with PAH associated with scleroderma remains poor and worse compared to other PAH subgroups. The 1-year mortality rate in patients with idiopathic PAH is approximately 15% (31) versus 30% in PAH-associated with scleroderma.
- Scleroderma patients with a mean pulmonary artery pressure (PAP) between 21 and 24 mm Hg are at high risk for the development of overt PH within 3 years and should be closely followed.
- Some data to suggest that in scleroderma, early diagnosis and early intervention may improve long-term outcome.

1.4.2 HIV infection
- 0.5% HIV patients develop iPAH, no relationship to CD4 count or viral load.
- Before the era of highly active antiretroviral therapy (HAART) and the development of specific PAH drugs, the prognosis for HIV-PAH was extremely poor, with a mortality rate of 50% in 1 year.
- The advent of HAART and the wide use of PAH therapies in HIV patients have improved their prognosis, and the current survival rate at 5 years in the French cohort is more than 70%.
- Interestingly, approximately 20% of these cases experience a normalization of hemodynamic parameters after several years of treatment.

1.4.3 Portal hypertension
- Hemodynamic studies have shown that PAH is confirmed in 2% to 6% of patients with portal hypertension, porto-pulmonary hypertension (POPH) and the risk of developing POPH is independent of the severity of the liver disease.
- Long-term prognosis is related to the severity of cirrhosis and to cardiac function.

1.4.4 Congenital heart disease
1.4.5 Schistosomiasis
**ESC/ERS recommendations for PAH associated with connective tissue disease 2016**

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>In patients with PAH associated with CTD, the same treatment algorithm as for patients with IPAH is recommended</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Resting echocardiography is recommended as a screening test in asymptomatic patients with SSc, followed by annual screening with echocardiography, DLSO and biomarkers</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>RHC is recommended in all cases of suspected PAH associated with CTD</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Oral anticoagulation may be considered on an individual basis and in the presence of thrombophilic predisposition</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

GROUP 2: PULMONARY VENOUS HYPERTENSION, DUE TO LEFT HEART DISEASE

2.1 Left ventricular systolic dysfunction

2.2 Left ventricular diastolic dysfunction

2.3 Valvular disease

2.4 Congenital / acquired left heart inflow / outflow tract obstruction and congenital cardiomyopathies

2.5 Congenital / Acquired pulmonary vein stenosis
Table 30  Examples of key factors suggestive of group 2 pulmonary hypertension

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Echocardiography</th>
<th>Other features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65 years</td>
<td>Structural left heart abnormality</td>
<td>ECG</td>
</tr>
<tr>
<td></td>
<td>• Disease of left heart valves</td>
<td>• LVH and/or LAH</td>
</tr>
<tr>
<td></td>
<td>• LA enlargement (&gt;4.2 cm)</td>
<td>• AF/Afib</td>
</tr>
<tr>
<td></td>
<td>• Bowing of the IAS to the right</td>
<td>• LBBB</td>
</tr>
<tr>
<td></td>
<td>• LV dysfunction</td>
<td>• Presence of Q waves</td>
</tr>
<tr>
<td></td>
<td>• Concentric LV hypertrophy and/or increased LV mass</td>
<td></td>
</tr>
<tr>
<td>Symptoms of left heart failure</td>
<td>Doppler indices of increased filling pressures</td>
<td>Other imaging</td>
</tr>
<tr>
<td></td>
<td>• Increased E/e’</td>
<td>• Kerley B lines</td>
</tr>
<tr>
<td></td>
<td>• &gt;Type 2–3 mitral flow abnormality</td>
<td>• Pleural effusion</td>
</tr>
<tr>
<td>Features of metabolic syndrome</td>
<td>Absence of</td>
<td>• Pulmonary oedema</td>
</tr>
<tr>
<td></td>
<td>• RV dysfunction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Mid systolic notching of the PA flow</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pericardial effusion</td>
<td></td>
</tr>
<tr>
<td>History of heart disease (past or current)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistent atrial fibrillation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
GROUP 3: DUE TO CHRONIC LUNG DISEASE/HYPOXIA

3.1 Chronic obstructive pulmonary disease

3.2 Interstitial lung disease

3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern

3.4 Sleep-disordered breathing

3.5 Alveolar hypoventilation disorders

3.6 Chronic exposure to high altitude

3.7 Developmental lung diseases
### Table 32: Haemodynamic classification of pulmonary hypertension due to lung disease

<table>
<thead>
<tr>
<th>Terminology</th>
<th>Haemodynamics (right heart catheterization)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD/IPF/CPFE without PH</td>
<td>PAPm &lt; 25 mmHg</td>
</tr>
<tr>
<td>COPD/IPF/CPFE with PH</td>
<td>PAPm ≥ 25 mmHg</td>
</tr>
<tr>
<td>COPD/IPF/CPFE with severe PH</td>
<td>PAPm &gt; 35 mmHg, or PAPm ≥ 25 mmHg in the presence of a low cardiac output (CI &lt; 2.5 L/min, not explained by other causes)</td>
</tr>
</tbody>
</table>

CI = cardiac index; COPD = chronic obstructive pulmonary disease; CPFE = combined pulmonary fibrosis and emphysema; IPF = idiopathic pulmonary fibrosis; PAP = pulmonary artery pressure; PAPm = mean pulmonary arterial pressure; PH = pulmonary hypertension.
GROUP 4:

- Chronic Thrombo-embolic Pulmonary Hypertension (CTEPH)
- Other pulmonary artery obstructions
GROUP 5: UNCLEAR MULTIFACTORIAL MECHANISMS

5.1 Hematologic disorders
5.2 Systemic disorders
5.3 Metabolic disorders
5.4 Others
5. Pulmonary Hypertension of Unclear Multifactorial Mechanisms

5.1 Hematologic disorders:
- Chronic hemolytic anemia
- Myeloproliferative disorders
- Splenectomy

5.2 Systemic disorders:
- Sarcoidosis
- Pulmonary histiocytosis,
- Lymphangioleiomyomatosis

5.3 Metabolic disorders:
- Glycogen storage disease
- Gaucher disease
- Thyroid disorders

5.4 Others:
- Tumoral obstruction
- Fibrosing mediastinitis
- Chronic renal failure (with or without dialysis)
- Segmental pulmonary hypertension
Echo imaging in Pulmonary Hypertension and Cor Pulmonale

- Aim of echo imaging
- Guidelines – echo in the diagnosis of PHT
- Imaging parameters to guide prognosis and treatment
- Other imaging modality for PHT
AIM OF ECHO IMAGING IN PULMONARY HYPERTENSION
AIM of echo imaging in PHT

- **TTE** is a very useful **non-invasive screening tool** for PHT

- **Diagnosis**, cause, severity and progression of PHT

- **Estimate pulmonary artery systolic pressure** from Doppler pattern of tricuspid (TR) and pulmonary regurgitant (PR) jet
  - \( \text{PASP} = \text{RVSP} \) if no RVOT/PA obstruction
  - \( \text{RVSP} = 4 (Vtr)^2 + \text{RAP} \)

- **Assess Left Ventricular and Right Ventricular** size and function

- **Assess heart valves** – TR and PR, Mitral stenosis

- Associated congenital heart disease if any

- **Pericardial Effusion**
GUIDELINES: ECHO IN THE DIAGNOSIS OF PULMONARY HYPERTENSION
2015 ESC/ERS Guidelines for the diagnosis and treatment of Pulmonary Hypertension

**Figure 1** Diagnostic algorithm.

- **Symptoms, signs, history suggestive of PH**
  - **Echocardiographic probability of PH (Table 8)**
    - High or intermediate
    - Low
  - Consider left heart disease and lung diseases by symptoms, signs, risk factors, ECG, PFT+DLCO, chest radiograph and HRCT, arterial blood gases (Table 9)
  - Diagnosis of left heart disease or lung diseases confirmed?
    - Yes
    - No
  - Signs of severe PH/RV dysfunction
    - No signs of severe PH/RV dysfunction
      - Treat underlying disease
    - Yes
      - V/Q scan
        - Mismatched perfusion defects?
          - Yes
            - Refer to PH expert centre
          - No
            - RHC (Table 10)
              - mPAP >25 mmHg, PAWP ≤15 mmHg, PVR >3 Wood units
              - CTEPH possible:
                - CT pulmonary angiography, RHC +/- Pulmonary Angiography
              - Refer to PH expert centre
            - PAH likely
              - Specific diagnostic tests
                - CTD
                - Drugs - Toxin
                - HIV
                - Heritable PVOD/PCH
                - Idiopathic PVOD/PCH
                - Idiopathic PAH
                - Heritable PAH
              - Consider other causes
                - Group 5
2015 ESC Guidelines on Echo probability of PHT

Table 8A  Echocardiographic probability of pulmonary hypertension in symptomatic patients with a suspicion of pulmonary hypertension

<table>
<thead>
<tr>
<th>Peak tricuspid regurgitation velocity (m/s)</th>
<th>Presence of other echo 'PH signs'</th>
<th>Echocardiographic probability of pulmonary hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2.8 or not measurable</td>
<td>No</td>
<td>Low</td>
</tr>
<tr>
<td>≤2.8 or not measurable</td>
<td>Yes</td>
<td>Intermediate</td>
</tr>
<tr>
<td>2.9–3.4</td>
<td>No</td>
<td>High</td>
</tr>
<tr>
<td>2.9–3.4</td>
<td>Yes</td>
<td>High</td>
</tr>
<tr>
<td>&gt;3.4</td>
<td>Not required</td>
<td>High</td>
</tr>
</tbody>
</table>

4 x 2.8 x 2.8 + 3 = 31.4 + 3 = 34 mmHg

4 x 2.9 x 2.9 + 3 = 33.6 + 3 = 37 mmHg

4 x 3.4 x 3.4 + 3 = 46.2 + 3 = 49 mmHg

4 x 3.5 x 3.5 +3 = 49.0 + 3 = 52 mmHg

Table 8B  Echocardiographic signs suggesting pulmonary hypertension used to assess the probability of pulmonary hypertension in addition to tricuspid regurgitation velocity measurement in Table 8A

A: The ventricles
- Right ventricle/left ventricle basal diameter ratio >1.0
- Right ventricular outflow Doppler acceleration time <105 msec and/or midsystolic notching
- Early diastolic pulmonary regurgitation velocity >2.2 m/sec
- Right atrial area (end-systole) >18 cm²

B: Pulmonary artery
- Inferior vena cava diameter >21 mm with decreased inspiratory collapse (<50 % with a sniff or <20 % with quiet inspiration)

C: Inferior vena cava and right atrium

PA = pulmonary artery.

*Echocardiographic signs from at least two different categories (A/B/C) from the list should be present to alter the level of echocardiographic probability of pulmonary hypertension.
2015 ESC Guidelines on Echo probability of PHT

### Table 9: Diagnostic management suggested according to echocardiographic probability of pulmonary hypertension in patients with symptoms compatible with pulmonary hypertension, with or without risk factors for pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension

<table>
<thead>
<tr>
<th>Echocardiographic probability of PH</th>
<th>Without risk factors or associated condition for PAH or CTEPH&lt;sup&gt;4&lt;/sup&gt;</th>
<th>With risk factors or associated conditions for PAH or CTEPH&lt;sup&gt;5&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alternative diagnosis should be considered</td>
<td>IIa</td>
<td>Echo follow-up should be considered</td>
</tr>
<tr>
<td><strong>Intermediate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alternative diagnosis, echo follow-up, should be considered</td>
<td>IIa</td>
<td>Further assessment of PH including RHC should be considered&lt;sup&gt;6&lt;/sup&gt;</td>
</tr>
<tr>
<td>Further investigation of PH may be considered&lt;sup&gt;a&lt;/sup&gt;</td>
<td>IIb</td>
<td></td>
</tr>
<tr>
<td><strong>High</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Further investigation of PH (including RHC)&lt;sup&gt;c&lt;/sup&gt; is recommended</td>
<td>I</td>
<td>Further investigation of PH&lt;sup&gt;c&lt;/sup&gt; including RHC is recommended</td>
</tr>
</tbody>
</table>

CTEPH = chronic thromboembolic pulmonary hypertension; Echo = echocardiographic; PAH = pulmonary arterial hypertension; PH = pulmonary hypertension; RHC = right heart catheterization.

<sup>a</sup>Class of recommendation.

<sup>b</sup>Level of evidence.

<sup>c</sup>Reference(s) supporting recommendations.

<sup>d</sup>These recommendations do not apply to patients with diffuse parenchymal lung disease or left heart disease.

<sup>e</sup>Depending on the presence of risk factors for PH group 2, 3 or 5.

Further investigation strategy may differ depending on whether risk factors/associated conditions suggest higher probability of PAH or CTEPH – see diagnostic algorithm.
TR velocities and PASP

- Simplified Bernoulli equation
  \[ RVSP: 4 \ (TR \ V_{\text{max}})^2 + RA \ \text{pressure} \]
  \[ RVSP = PASP \text{ in the absence of RVOT / pulmonary valve obstruction} \]

- RA pressure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal (0-5 [3 mm Hg])</th>
<th>Intermediate (5-10 [8 mm Hg])</th>
<th>High (15 mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVC diameter</td>
<td>\leq 2.1 cm</td>
<td>\leq 2.1 cm</td>
<td>&gt;2.1 cm</td>
</tr>
<tr>
<td>Collapse with sniff</td>
<td>&gt;50%</td>
<td>&lt;50%</td>
<td>&gt;50%</td>
</tr>
</tbody>
</table>

- Use TR velocities for probability generation because any inaccuracies with RA pressure estimation can amplify errors

or < 20% on quiet inspiration
TR velocity to calculate PASP

Is this TR measurement correct?
Other ways to derive estimated pressures

- **PA Diastolic Pressure**
  
  $$\text{PADP: } 4 \text{ (End diastolic pulmonary regurgitation velocity)}^2 + \text{RA pressure}$$

- **Mean PAP (Masuyama)**
  
  $$\text{MPAP: } 4 \text{ (Early diastolic pulmonary regurgitation velocity)}^2 + \text{RA pressure}$$
Continuous-wave Doppler echocardiographic detection of pulmonary regurgitation and its application to noninvasive estimation of pulmonary artery pressure

TOHRU MASUYAMA, M.D., KAZUHISA KODAMA, M.D., AKIRA KITABATAKE, M.D., HIROSHI SATO, M.D., SHINSUKE NANTO, M.D., AND MICHITOSHI INOUE, M.D.

ABSTRACT Continuous-wave Doppler echocardiography was used to estimate pulmonary artery pressures by measuring pulmonary regurgitant flow velocity in 21 patients with pulmonary hypertension (mean pulmonary artery pressure ≥ 20 mm Hg) and 24 patients without pulmonary hypertension. The pulmonary regurgitant flow velocity patterns, characterized by a rapid rise in flow velocity immediately after closure of the pulmonary valve and a gradual deceleration until the next pulmonary valve opening, were successfully obtained in 18 of the 21 patients with pulmonary hypertension and in 13 of the 24 patients without pulmonary hypertension. As pulmonary artery pressure increased, pulmonary regurgitant flow velocity became higher; the pulmonary artery–to–right ventricular pressure gradient in diastole (PG) was estimated from the pulmonary regurgitant flow velocity (V) by means of the simplified Bernoulli equation (PG = 4V²). The Doppler-determined pressure gradient at end-diastole correlated well with the catheter measurement of the pressure gradient at end-diastole (r = .94, SEE = 3 mm Hg) and with pulmonary artery end-diastolic pressure (r = .92, SEE = 4 mm Hg). The peak of Doppler-determined pressure gradient during diastole correlated well with mean pulmonary artery pressure (r = .92, SEE = 3 mm Hg). Thus continuous-wave Doppler echocardiography was useful for noninvasive estimation of pulmonary artery pressures.

Other ways to derive estimated PA pressures

Mahan’s formula

- Using pulmonary acceleration time by pulsed Doppler of pulmonary artery in systole
  - MPAP: 79 – (0.45 x acceleration time)  \(\Rightarrow\) AT > 120ms
  - MPAP: 90 – (0.62 x acceleration time)  \(\Rightarrow\) AT < 120ms
### Table 3: Doppler echocardiographic indices for the evaluation of patients with clinical suspicion of PH

<table>
<thead>
<tr>
<th>Key indices (cutoff)</th>
<th>Additional indices (cutoff)</th>
<th>Complementary indices (cutoff)</th>
<th>Research tools</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary hemodynamics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPAP = 4 × TRV² + RAP&lt;sup&gt;9-12&lt;/sup&gt; (TRV &gt; 2.8–2.9 msec: SPAP 36 mm Hg)</td>
<td>MPAP = TIV&lt;sub&gt;TR&lt;/sub&gt; + RAP&lt;sup&gt;13&lt;/sup&gt; (≥25 mm Hg)</td>
<td>AT&lt;sub&gt;RVOT&lt;/sub&gt; (&lt;100 msec)</td>
<td>PVCAP = SV/4 × (TRV² - PRV²)&lt;sup&gt;14&lt;/sup&gt; (&lt;0.8 mL/mm Hg predicts mortality in PAH patients)</td>
</tr>
<tr>
<td>RAP = IVC size and collapsibility&lt;sup&gt;16&lt;/sup&gt; (&gt;2.1 cm, collapse &lt; 50%: RAP 15 mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MPAP = 4 × PRV² + RAP&lt;sup&gt;17,18&lt;/sup&gt; (≥25 mm Hg)</td>
<td>MPAP = 0.61 × SPAP + 2 mm Hg&lt;sup&gt;11&lt;/sup&gt;</td>
<td>MPAP = 90 - 0.62 × AT&lt;sub&gt;RVOT&lt;/sub&gt;&lt;sup&gt;20&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>DPAP = 4 × (PRV ED)² + RAP</td>
<td></td>
<td>MPAP = 79 - 0.45 × AT&lt;sub&gt;RVOT&lt;/sub&gt;</td>
<td></td>
</tr>
<tr>
<td>PVR = TRV/IV&lt;sub&gt;RVOT&lt;/sub&gt; (cm) × 10 + 0.16&lt;sup&gt;21&lt;/sup&gt; (&gt;0.2: PVR &gt; 2 WU; &lt;0.15: normal PVR)</td>
<td>PVR = SPAP/(HR × TVI&lt;sub&gt;RVOT&lt;/sub&gt;)&lt;sup&gt;22&lt;/sup&gt; (&gt;0.076: indexed PVR &gt; 15 RU)</td>
<td>FVE&lt;sub&gt;RVOT&lt;/sub&gt;&lt;sup&gt;23&lt;/sup&gt; (midsystolic “notch”)</td>
<td></td>
</tr>
<tr>
<td>PCWP = 1.9 + 1.24 × E/E'&lt;sup&gt;24&lt;/sup&gt; (E/E' &gt; 15: PCWP &gt; 15 mm Hg)</td>
<td>LAVI&lt;sup&gt;25&lt;/sup&gt; (&gt;31 mL/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Impaired RV systolic function</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAPSE (&lt;16 mm)</td>
<td>Tei index: (IVRT + IVCT)/ET (&gt;0.40 by PW Doppler; &gt;0.55 by DTI)</td>
<td>3D RV EF (&lt;44%)</td>
<td></td>
</tr>
<tr>
<td>RV FAC (&lt;35%)</td>
<td>RV LPSS&lt;sup&gt;26&lt;/sup&gt; (≥-19%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S'-wave velocity by DTI &lt;10 cm/sec</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Pulmonary vascular resistance (PVR)

PRESSURE change = Flow X Resistance

• PVR distinguishes elevated pulmonary pressure due to high flow from that due to pulmonary vascular disease

• PVR can be estimated using the ratio of
  • \[ PVR \text{ (woods)} = \frac{TR \text{ max velocity (m/s)}}{RVOT \text{ VTI (in cm)}} \times \text{constant} \]
  This relationship is not reliable in patients with very high PVR, with measured PVR > 8 Wood units

• Normal PVR is <1.5 Wood units, significant PH is defined as a PVR > 3 Wood units
Resistance (PVR) = PA – LA Pressure difference / RV CO

Simplified Method to estimate / calculate PVR by Abbas et al using TR Vmax and RVOT VTI

TRV / TVI_{RVOT} = 2.78 / 11 = 0.253

PVR = TRV / TVI_{RVOT} x 10 = 2.53 WU
Table 8B  Echocardiographic signs suggesting pulmonary hypertension used to assess the probability of pulmonary hypertension in addition to tricuspid regurgitation velocity measurement in Table 8A

<table>
<thead>
<tr>
<th>Category</th>
<th>Sign</th>
<th>Category</th>
<th>Sign</th>
<th>Category</th>
<th>Sign</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A: The ventricle</strong>a</td>
<td>Right ventricle/left ventricle basal diameter ratio &gt; 1.0</td>
<td><strong>B: Pulmonary artery</strong>a</td>
<td>Right ventricular outflow Doppler acceleration time &lt; 105 msec and/or midsystolic notching</td>
<td><strong>C: Inferior vena cava and right atrium</strong>a</td>
<td>Inferior cava diameter &gt; 21 mm with decreased inspiratory collapse (&lt; 50% with a sniff or &lt; 20% with quiet inspiration)</td>
</tr>
<tr>
<td></td>
<td>Flattening of the interventricular septum (left ventricular eccentricity index &gt; 1.1 in systole and/or diastole)</td>
<td></td>
<td>Early diastolic pulmonary regurgitation velocity &gt; 2.2 m/sec</td>
<td></td>
<td>Right atrial area (end-systole) &gt; 18 cm²</td>
</tr>
<tr>
<td></td>
<td>PA diameter &gt; 25 mm.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PA = pulmonary artery.

aEchocardiographic signs from at least two different categories (A/B/C) from the list should be present to alter the level of echocardiographic probability of pulmonary hypertension.
Echo signs suggestive of Pulmonary Hypertension

- Dilated Right Ventricle
- Dilated Right Atrium
- Flatted IVS
Echo signs suggesting likelihood of Pulmonary Hypertension

- Reduced LV size
- LV Eccentricity Index of > 1
  - Length/Width in ED and ES > 1
  - How to Measure?
    - Endocardium to Endocardium
LV Eccentricity index

Ratio between LV anteroposterior : septolateral dimension

- **Ratio > 1 is abnormal**

**Not so straight forward**

- Dimensions are an interaction between RV and LV pressure

- If patient has left side heart disease, there is interplay between systolic RV pressure overload and diastolic LV pressure overload
**LV Eccentricity Index**

Echo Report:
- Flattened septum in systole and diastole consistent with right ventricular pressure and volume overload
- LV eccentricity index (end diastole) is 1.96 and (endsystole) is 3.0
Echo signs suggesting likelihood of Pulmonary Hypertension

- Dilated Pulmonary Artery $> 25$ mm
  (avoid measuring in an oblique angle)

- Dilated PA can also be seen on suprasternal view
Echo signs suggesting likelihood of Pulmonary Hypertension

RVOT PW - Mid systolic notch

Short Acceleration Time
Signs Indicative of Pulmonary Hypertension

- Dilated and Plethoric Inferior Vena Cava
Example of patient with CTEPH:
LV Eccentricity Index at end diastole = 6.28/3.67 = 1.7

LV Eccentricity Index at end systole = 4.15/3.03 = 1.4
TAPSE = 1 (reduced)

TDI s wave = 4.7
PASP = 52 mmHg + RAP

Mean PAP = 32 mmHg + RAP
Short ACT of 66 ms with mid-systolic notch present

Dilated and plethoric IVC, estimated RAP at least 15 mmHg
ECHO IMAGING TO GUIDE
- PROGNOSIS AND
- TREATMENT IN PULMONARY HYPERTENSION
### 2015 ESC/ERS Guidelines for the diagnosis and treatment of Pulmonary Hypertension

**Follow up: For risk assessment**

1. RA size – RA area
2. Presence of Pericardial effusion

<table>
<thead>
<tr>
<th>Determinants of prognosis (estimated 1-year mortality)</th>
<th>Low risk &lt;5%</th>
<th>Intermediate risk 5–10%</th>
<th>High risk &gt;10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs of right heart failure</td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Progression of symptoms</td>
<td>No</td>
<td>Slow</td>
<td>Rapid</td>
</tr>
<tr>
<td>Syncope</td>
<td>No</td>
<td>Occasional syncope</td>
<td>Repeated syncope</td>
</tr>
<tr>
<td>WHO functional class</td>
<td>I, II</td>
<td>III</td>
<td>IV</td>
</tr>
<tr>
<td>6MWD</td>
<td>&gt;440 m</td>
<td>165–440 m</td>
<td>&lt;165 m</td>
</tr>
<tr>
<td>Cardiopulmonary exercise testing</td>
<td>Peak VO₂ &gt; 15 ml/min/kg (&gt;65% pred.)</td>
<td>Peak VO₂ 11–15 ml/min/kg (35–65% pred.)</td>
<td>Peak VO₂ &lt;11 ml/min/kg (&lt;35% pred.)</td>
</tr>
<tr>
<td></td>
<td>VE/VO₂ slope &lt;36</td>
<td>VE/VO₂ slope 36–44.9</td>
<td>VE/VO₂ ≥45</td>
</tr>
<tr>
<td>NT-proBNP plasma levels</td>
<td>BNP &lt;50 ng/l</td>
<td>BNP 50–300 ng/l</td>
<td>BNP &gt;300 ng/l</td>
</tr>
<tr>
<td></td>
<td>NT-proBNP &lt;300 ng/ml</td>
<td>NT-proBNP 300–1400 ng/ml</td>
<td>NT-proBNP &gt;1400 ng/ml</td>
</tr>
<tr>
<td>Imaging (echocardiography, CMR imaging)</td>
<td>RA area &lt;18 cm²</td>
<td>RA area 18–26 cm²</td>
<td>RA area &gt;26 cm²</td>
</tr>
<tr>
<td></td>
<td>No pericardial effusion</td>
<td>No or minimal, pericardial effusion</td>
<td>Pericardial effusion</td>
</tr>
<tr>
<td>Haemodynamics</td>
<td>RAP &lt;8 mmHg</td>
<td>RAP 8–14 mmHg</td>
<td>RAP &gt;14 mmHg</td>
</tr>
<tr>
<td></td>
<td>CI ≥2.5 l/min/m²</td>
<td>CI 2.0–2.4 l/min/m²</td>
<td>CI &lt;2.0 l/min/m²</td>
</tr>
<tr>
<td></td>
<td>SvO₂ &gt;65%</td>
<td>SvO₂ 60–65%</td>
<td>SvO₂ &lt;60%</td>
</tr>
</tbody>
</table>
How often to do serial echo in follow up of PH patients?

- At baseline
- 6-12 monthly if no change in PH therapy
- 3-4 monthly after change of PH therapy

### 2015 ESC/ERS Guidelines for the diagnosis and treatment of Pulmonary Hypertension

**Table 14** Suggested assessment and timing for the follow-up of patients with pulmonary arterial hypertension

<table>
<thead>
<tr>
<th>Test</th>
<th>At baseline</th>
<th>Every 3–6 months (^a)</th>
<th>Every 6–12 months (^a)</th>
<th>3–6 months after changes in therapy (^b)</th>
<th>In case of clinical worsening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical assessment and determination of functional class</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>ECG</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>6MWT/Borg dyspnoea score</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CPET</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Echo</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Basic lab (^b)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Extended lab (^c)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Blood gas analysis (^c)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Right heart catheterization</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

\(^a\) For patients with stable PAH.

\(^b\) For patients with new-onset PAH.

\(^c\) For patients with drug-induced PAH.
In reality, the survival of PH patients is determined by their **Right Ventricle Function** and hence serial assessment of RV function is mandatory in the echo follow up of PH patients.
PAH: a rapidly evolving disease

I Preclinical / No symptoms
II Symptomatic / Stable
III Progression / declining

Pulm pressure
Cardiac output
RV function
Therapeutic window

Level

Years
Months

Time
PH and RV Failure: The Downward Spiral

↑ RV EDP

- RV volume overload
- Tricuspid regurgitation
- High right-sided filling pressures
- Oedema; Organ congestion

HIGH PVR

- RV pressure overload
- RV dilatation
- Increased RV wall stress

Loss of RV-PA coupling

Reduced right coronary perfusion

RV ischaemia

Reduced RV output

HYPOTENSION

- Low aortic root pressure
- RCA perfusion limited to systole
- Compensatory tachycardia

Ongoing RV ischaemia

Ventricular interdependence

Reduction in overall CO

Other useful Imaging Modalities in PHT

- VQ scan
- CTPA / HRCT
- CMR
- PA Angiography
Other useful imaging modalities in PHT

1) Ventilation Perfusion Scan (to exclude CTEPH)

• Maybe entirely normal

• VQ mismatch from normally ventilated lung with decrease perfusion in small peripheral non-segmental pulmonary arteries

• VQ mismatch from chronic thromboembolic disease, the perfusion defects are more common in lobar and segmental pulmonary arteries

• Matched VQ defects in patients with parenchymal lung disease
VENTILATION

VQ SCAN

PERFUSION
2) Contrast enhanced CT / High Resolution CT

- Contrast enhanced spiral CT chest in patients with V/Q mismatch suggestive of thromboembolic disease
- Central pulmonary artery occlusion, recanalisation, stenosis
- High Resolution CT important for fine details of lung parenchyma
  - Diagnosis of interstitial lung disease, emphysema
  - Pulmonary veno-occlusive disease => central ground glass opacification and thickening of interlobular septa
  - Pulmonary capillary haemangiomatosi => thickening of interlobular septa, small centrilobular nodular opacities
- Presence of lymphadenopathy, pleural effusion, etc
CTPA of 45 year old lady with CTEPH
High Resolution CT showing advance interstitial lung disease with honeycomb appearance
Other useful imaging modalities in PHT

3) Cardiac Magnetic Resonance Imaging

- For both pathology and function of cardiovascular and pulmonary circulation

- Heart => RV and LV size and function, PA dilatation and thrombus, pulmonary and tricuspid regurgitation, shunts
OTHER IMAGING MODALITIES IN CTEPH: PA ANGIO

4) Pulmonary angiography

Selective LPA angiogram and balloon dilatation for CTEPH
CONCLUSION

- Echocardiography can help to categorize patients with suspected PH into low, intermediate or high probabilities of PHT by using parameters such as TR velocity and assessing the effect of pulmonary hypertension on the right heart such as IVC, RA, RV and PA using 2D and Doppler measurements.

- Some causes of PHT can be excluded by echocardiography such as Group 2 PH (due to left heart disease) and in patients with congenital heart defects and left to right shunting.

- Other imaging modalities (such as CT, VQ, CMR) are often required to classify PH patients into the appropriate PH Groups. This is essential as current PH therapies are mainly limited to patients in Group 1 and Group 4.

- It is important to follow up PH patients with serial echocardiograms every 6-12 monthly or after change in therapy or with worsening symptoms.

- Serial echocardiograms should include the assessment of pulmonary pressures, RV function and other prognostic markers such as RA size, presence of pericardial effusion, LV eccentricity index, etc.