

## PULMONARY HYPERTENSION

### Introduction

Pulmonary arterial hypertension is technically defined as a *mean* pulmonary artery pressure of **greater** than:

**25 mm Hg** at rest

*Or*

**30 mm Hg** with exercise

as recorded during right heart catheterisation.

It can be primary or it can be due to secondary causes.

**Its presence usually portends a poor prognosis.**

### Pathology

The main causes of pulmonary arterial hypertension include:

1. Idiopathic (previously known as Primary):
  - Essentially this means pulmonary hypertension of unknown cause.
2. Familial
3. Secondary causes:

This is pulmonary hypertension due to a known pathology, which may include:

- Recurrent pulmonary emboli
- Chronic lung disease:
  - ♥ Asthma
  - ♥ COPD
  - ♥ Pulmonary fibrosis (of any cause)

- ♥ Obstructive sleep apnoea
- ♥ Chronic exposure to high altitude.
- **Chronic heart disease:**
  - ♥ Left sided valvular heart disease.
  - ♥ Uncorrected congenital heart disease with left to right shunting, (Eisenmenger's Syndrome):
    - ♥♥ ASDs
    - ♥♥ VSDs
    - ♥♥ Patent Ductus Arteriosus
- **Severe kyphoscoliosis.**

### Complications

- Chronic hypoxia, from right heart failure
- Arrhythmias
- Polycythaemia (haemoglobin level > 170 g/L)

### Clinical Features

#### Clinical examination signs of pulmonary hypertension:

The classically described signs of pulmonary hypertension include: <sup>4</sup>

1. General inspection:
  - In severe disease there may be obvious:
    - Tachypnoea
    - Cyanosis (peripheral and/ or central)
2. Pulse:
  - In severe disease the pulse will be of low volume.
3. JVP:
  - A prominent "a" wave may be seen, due to forceful atrial contraction.

4. Cardiac auscultation:

Heart sounds:

- There may be a loud S2, (this is due to a loud pulmonary component of the second heart sound)
- There may be an S4

Murmurs:

- There may be a pulmonary ejection systolic flow murmur.
- There may be a diastolic pulmonary regurgitation murmur, if there is significant dilation of the pulmonary artery.

5. Apex beat:

- There may be a palpable right ventricular heave
- There may be a palpable second heart sound

6. Cor pulmonale:

- In late cases of severe disease there may be signs of right heart failure.

*Functional assessment of the patient with Pulmonary Hypertension:*

Functional assessment is required to provide prognostic information and also to assess suitability for specific pulmonary hypertension therapies.

The World Health Organization (WHO) functional classification should be used and is shown in the table below:

WHO functional class	Symptoms
Class I	Minimal symptoms (dyspnoea, chest pain, fatigue, presyncope) that do not limit physical activity
Class II	Symptoms resulting in a slight limitation of physical activity
Class III	Symptoms resulting in marked limitation of physical activity
Class IV	Symptoms resulting in the inability to carry out physical activity

## Investigations

### Blood tests

Depending on the nature of the presentation, the following may be considered:

1. FBE
2. CRP
3. U&Es/ glucose
4. ABGs

### ECG

Electrocardiographic features seen in pulmonary hypertension include:

1. Sinus tachycardia
2. Non-specific signs of right heart strain/ hypertrophy:
  - P pulmonale
  - RBBB pattern
  - Dominant R waves in early chest leads
  - Right axis deviation.

3. Arrhythmias:

The following are common: <sup>4</sup>

- Atrial Fibrillation
- Multifocal atrial tachycardia

### CXR

This is useful as an initial screen for lung disease, in particular interstitial lung disease (pulmonary fibrosis) or COPD

It is also useful for assessment of the cardiac silhouette, as a possible indicator of cardiac disease:

*Indirect indicators of right ventricular disease include:*

- Right ventricular dilatation, (on A-P or lateral views)
  - ♥ Right ventricular enlargement however may be difficult to detect because of lung hyperinflation.
- Enlarged proximal pulmonary arteries with peripheral "pruning".

### CT Scan

High resolution CT scan is required to assist in diagnosing the nature and extent of causative lung pathology.

### Echocardiography

Transthoracic echocardiography is the best initial non-invasive method of assessing pulmonary hypertension but image quality may be reduced by lung hyperinflation. Trans-oesophageal echocardiography may be required.

It measures the **peak pulmonary artery pressure** rather than the mean pressure.

An elevation of *peak* pulmonary artery pressure of greater than **40 mm Hg** indicates pulmonary hypertension.

Right ventricular dilation and abnormal septal motion are also indicators of pulmonary hypertension.

The severity of pulmonary hypertension may however be overestimated by echocardiography, especially in high cardiac output states, and cardiac catheterisation is required to confirm the diagnosis before prescribing specific therapies for pulmonary hypertension.

### Cardiac catheterisation:

Pulmonary hypertension is technically defined as a *mean* pulmonary artery pressure of greater than **25 mm Hg at rest or 30 mm Hg with exercise**, recorded during right heart catheterisation.

Cardiac catheterisation is therefore considered to be the "gold standard" investigation required to make a definitive diagnosis.

It is also useful for ruling out co-existent coronary artery disease.

### Management

The diagnosis of pulmonary hypertension necessitates an evaluation of the underlying aetiology to correct reversible causes where possible.

Thereafter, management involves:

- An assessment of functional status.
- Disease severity.
- The role of general and specific pharmacological agents.

With respect to ED presentations of patients with pulmonary hypertension, issues will include:

1. Immediate resuscitation
2. Investigation and management of any underlying precipitating factors
3. Review of medications directed toward the pulmonary hypertension itself
4. Assessment of the patient's functional status and ability to cope at home, and hence the need for admission to hospital.

#### *Immediate resuscitation*

**Oxygen therapy** should be administered if it provides symptomatic relief.

Hypoxaemia can worsen pulmonary arterial hypertension, and oxygen should be used if the patient has hypoxaemia.

Long term, continuous (>15 hour /day) oxygen therapy to treat chronic hypoxaemia prolongs survival of patients with COPD, presumably by reducing pulmonary hypertension.<sup>4</sup>

#### *Investigation and management of any underlying precipitating factors*

Precipitating factors should be sought and treated as indicated, in particular consider the possibilities of:

- Sepsis
- Acute coronary syndrome
- Pulmonary embolism
- Bacterial endocarditis, especially in cases of known valvular heart disease.

#### *Review of medications directed toward the pulmonary hypertension itself.*

Medications used in the treatment of patients with pulmonary hypertension will depend on the underlying pathology and the severity of the disease as well as any specific contraindications a patient may have.

In *general terms* the following medications are used: <sup>1,4</sup>

1. Diuretics:

- Should be used if there is right heart failure, particularly if oedema is present.
- Diuretics may reduce right ventricular filling pressure and oedema, but excessive volume depletion must be avoided. Volume status can be monitored by measuring serum creatinine and urea levels.
- Diuretics may cause metabolic alkalosis resulting in suppression of ventilatory drive.

2. Digoxin:

- This is often prescribed in the presence of right heart failure or a low cardiac output, (although data concerning its efficacy in this setting are lacking).
- In general digoxin is **not specifically** indicated in the treatment of cor pulmonale and may increase the risk of arrhythmia when hypoxaemia is present.<sup>4</sup>
- It **may** be used to control the **rate** of chronic atrial fibrillation.<sup>4</sup>

3. Calcium channel blockers:

In general vasodilators (hydralazine, nitrates, nifedipine, verapamil, diltiazem, angiotensin-converting enzyme inhibitors) do **not** produce **sustained** relief of pulmonary hypertension in patients with COPD. <sup>4</sup> In fact they can worsen oxygenation (by increasing blood flow through poorly ventilated lung) and result in systemic hypotension. <sup>4</sup>

Only a small proportion of patients with pulmonary arterial hypertension may benefit from these. A cautious trial may be used in patients with severe or persistent pulmonary hypertension not responsive to home oxygen therapy. <sup>4</sup> A trial of calcium channel blockade is worthwhile in these patients, but should be **discontinued** if there is no clinical improvement. <sup>1</sup>

Verapamil should **not** be used because of its significant negative inotropic effects.

The following agents may be used:

- Amlodipine
- Diltiazem

- Felodipine
- Lercanidipine
- Nifedipine

**See latest Cardiovascular Therapeutic Guidelines for full prescribing details.**

4. Specific pulmonary arterial hypertension therapies:

There are now three classes of drugs with evidence of efficacy in pulmonary arterial hypertension from randomized controlled trials. These are: <sup>1</sup>

- Endothelin receptor antagonists
- Prostanoid analogues
- Phosphodiesterase type 5 (PDE5) inhibitors.

These drugs may only be prescribed through Section 100 of the Pharmaceutical Benefits Scheme (PBS) if specific criteria are met, and only through designated prescribing centres. These agents are prescribed by specialist cardiologists or respiratory physicians.

Extensive clinical and laboratory testing, including right heart catheterisation, is required, as is referral to a pulmonary hypertension unit at a designated prescribing centre.

The combination of these specific therapies may confer additional benefit.

5. Anticoagulation:

Pulmonary arterial and arteriolar thrombosis can complicate pulmonary hypertension and worsen its severity.

There is evidence that anticoagulant therapy improves outcome, particularly in idiopathic pulmonary arterial hypertension, but overall this evidence is not strong.

Nonetheless, anticoagulation with warfarin is usually recommended if the risk of bleeding is low.

Use warfarin, with a target INR of 2 to 3.

*Assessment of the patient's functional status and ability to cope at home*

This is also obviously an important consideration in any patient with pulmonary hypertension who presents to the ED

Hospital admission will often be required on this basis alone, even if an obvious precipitating event cannot be found.

References

1. Cardiovascular Therapeutic Guidelines, 5th ed 2008.
2. McLaughlin VV, McGoon MD. Pulmonary arterial hypertension. *Circulation* 2006; 114(13):1417-31.
3. Talley NJ, O'Conner S: *Medicine, the examination series* 6<sup>th</sup> ed 2010, p.91-97.
4. The COPD-X Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease 2011. Australian Lung Foundation & The Thoracic Society of Australia & New Zealand.

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Reviewed November 2011.