# Hepatopulmonary Syndrome and Portopulmonary Hypertension - Full Clinical Guideline

Reference no.: CG-T/2013/202

**Hepatopulmonary Syndrome (HPS)** is characterised by abnormal arterial oxygenation secondary to intra-pulmonary vascular dilatations in patients with liver disease. Approximately 25% of patients with HPS will have **Platypnoea*** (SOB on moving from supine to sitting position) and/or **Orthodeoxia*** (hypoxia (> 5% decrease in Pa02) on moving from supine to sitting position). Clubbing may be present

*The dilated pulmonary capillaries where the shunting occurs are predominantly situated in the lung bases which might account for the gravitational pooling of blood when upright. Platypnoea and Orthodeoxia only seen in 25% of patients with HPS

**Screening:** Pulse oximetry - $O_2$ sats < 96% should trigger Arterial blood gas sampling

**Criteria for diagnosis:**
1. *Defect in oxygenation*: Partial pressure of Oxygen ($PaO_2$) < 10.6 kPa or Alveolar- arterial oxygen gradient [P(A-a) $O_2$] ≥ 2 kPa on room air
2. *Pulmonary vascular dilatation*†: Abnormal contrast transthoracic echocardiogram - delayed appearance of microbubbles in left heart 3 or more cardiac cycles after seen in right heart
3. *Liver disease*: Portal hypertension with or without cirrhosis

† A $^{99}$Tc macroaggretated albumin (MAA) lung brain scan can help clarify the contribution of HPS related hypoxia in patients with co-existent cardiopulmonary disease

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| **Severity:** | **Mild:** | P(A-a) $O_2$ > 2 kPa*, $PaO_2$ ≥ 10.6 kPa |
| | **Moderate:** | P(A-a) $O_2$ > 2 kPa, $PaO_2$ ≥ 8 to < 10.6 kPa |
| | **Severe:** | P(A-a) $O_2$ > 2 kPa, $PaO_2$ ≥ 6.6 to < 8 kPa |
| | **Very Severe:** | P(A-a) $O_2$ > 2 kPa, $PaO_2$ < 6.6 kPa |

* P(A-a) $O_2$ values can be easily obtained from online calculators and apps, for example: http://www.mdcalc.com/a-a-o2-gradient/

**Management:**
Oxygen therapy is frequently needed to address hypoxia. There is no specific therapy for HPS other than liver transplantation. Portal decompression with TIPSS is of uncertain benefit.

**Portopulmonary hypertension (PPH)** is pulmonary hypertension in the setting of portal hypertension. It is found in approximately 5% of patients with end-stage liver disease assessed for liver transplantation. The pathophysiology is incompletely understood but may relate to local pulmonary release of vascoconstrictors in the presence of systemic vasodilatation. The predominant symptom is SOBOE, but patients may also complain of fatigue, palpitations, chest pain and syncope (late sign with poor prognosis).

**Diagnosis:** Echocardiograophy is the initial investigation. The systolic pulmonary artery pressure (PAP) is usually reported. To convert to the mean multiply by 0.61. A systolic PAP of < 30mmHg has a 100% NPV, but only 59% PPV. To confirm a diagnosis of PPH right heart catheter studies are required. It is also important to exclude other causes of pulmonary hypertension such as thromboembolic and intrinsic lung disease.

**Criteria for diagnosis on right heart catheter study in setting of portal hypertension:**

- Mean pulmonary artery pressure—MPAP > 25 mmHg at rest
- Pulmonary vascular resistance—PVR > 240 dynes s cm−5
- Pulmonary artery occlusion pressure— PAOP < 15mmHg or transpulmonary gradient—TPG > 12 mmHg where TPG = MPAP − PAOP

**Severity:**
Portopulmonary hypertension is classified as mild (25-34 mmHg), moderate (35-44 mmHg), or severe (> 45 mmHg), though a better indicator of severe disease may a decrease in cardiac output (increased in mild/ moderate disease).

**Management:**
PPH may be reversible with liver transplantation in patients with mild to moderate disease. Post transplant mortality is increased in PPH - approximately 40% in patients with mean PAP > 35 mm Hg and 70%-100% in those > 45 mm Hg.

Patients who have a mean PAP < 35 mm Hg and pulmonary vascular resistance < 240 dynes/sec/cm$^5$ can proceed to transplantation, whereas those with a mean PAP > 35 mm Hg and pulmonary vascular resistance > 240 dynes/sec/cm$^5$ should be treated before transplantation to see whether adequate reduction of pulmonary artery pressure can be achieved. Of patients transplanted with pulmonary hypertension, most can stop their intravascular therapy within 6-12 months of transplantation.

The aim of medical treatment is to achieve pulmonary vasodilatation without systemic hypotension. Patients should be referred to the Pulmonary Hypertension clinic at the Royal Hallamshire hospital, Sheffield. Calcium channel blockers should be avoided and beta-blockers should be minimised or stopped. Treatment options include prostacyclin analogues (e.g epoprostenol), endothelin-receptor antagonists (e.g Bosentan) and phosphodiesterase-5 inhibitors such as sildenafil.

**Further reading:**
International liver transplantation society practice guidelines: Diagnosis and Management of Hepatopulmonary Syndrome and Portopulmonary Hypertension. Transplantation 2016.

## Documentation Controls

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