**EDITORIAL**

# Classification and Management of Pulmonary Hypertension.

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Pulmonary arterial hypertension (PAH) is a disease characterized by progressive resistance to flow across the pulmonary vascular bed, resulting in death from progressive right heart failure[1]. According to the most recent consensus conference, pulmonary hypertension (PH) is categorized into five main groups. Group 1: PAH (Idiopathic, Hereditary, Drug induced, Associated with other diseases, Veno occlusive Disease); Group 2: PH associated with left sided heart diseases; Group 3: PH associated with chronic hypoxic lung diseases; Group 4: PH due to chronic thromboembolic disease; and Group 5: miscellaneous diseases of multifactorial or unclear origin, a variety of rare and not well characterized disorders[1]. Establishing diagnosis of PH is of utmost importance as this provides basis for making decision on management. During the 4th World Symposium (2008) on PH held in USA, new thresholds for mPAP (mean Pulmonary Artery Pressure) were introduced. An mPAP <21 mm Hg was defined as normal, from 21-25 mm Hg was categorized as borderline, and an mPAP >25 mm Hg was designated as manifest PH. The exercise induced pulmonary hypertension was removed from the definition [1].

The therapy of pulmonary hypertension (PH) has changed substantially in the last 10 to 15 years. Historical survival of patients with idiopathic PH prior to availability of the pulmonary hypertension specific medications was dismal with the median life expectancy of only 2.8 years from the time of diagnosis [2]. Current PAH specific medications, including prostanoids, endothelin receptor antagonists (ERA), and phosphodiesterase 5 inhibitors (PDE5i) have substancially changed the quality of life and survival of patients diagnosed with pulmonary arterial hypertension [3, 4].

**DIAGNOSTIC WORK-UP FOR PULMONARY ARTERIAL HYPERTENSION:**

As PH is not a disease rather a hemodynamic state, the signs and symptoms are non-specific and include dyspnea, chest pain, fatigue, dizziness, syncope and abdominal distension. The examination may reveal loud second heart sound, left parasternal heave, murmur of tricuspid regurgitation, ascites, and peripheral edema. The exanimation may also provide the clues of the etiology of pulmonary hypertension.

Once clinical suspicion arises screening with basic diagnostic workup is required. To start with, Doppler study with Echocardiography is more desirable than right heart catheterization. ECG may show evidence of right ventricular hypertrophy or strain, such as right axis deviation, T wave inversion in the anterior leads, persistent S wave, right bundle branch block, and Right atrial enlargement like p-pulmonale. Chest radiograph X-ray may show enlargement of central pulmonary vessels, pruning of peripheral blood vessels, enlargement of right ventricle and right atrium. It may also give clues to the etiology of pulmonary hypertension. Pulmonary function test may reveal the presence of obstructive or restrictive lung disease contributing to the development of pulmonary hypertension (Group 3). In PAH a mild restrictive pattern and a reduction in diffusion capacity can be seen. Laboratory tests can help to identify the etiology of pulmonary hypertension and include complete blood count, liver function tests, thyroid function tests, connective tissue serologies and HIV test.

Ventilation/perfusion lung scan or contrast enhanced CT may reveal Perfusion abnormalities which will help exclude the chronic thromboembolic pulmonary hypertension (group 4).

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**ECHOCARDIOGRAPHY**

Trans thoracic echocardiography is an excellent screening tool for patients suspected of having pulmonary hypertension. Echocardiography can provide several important findings including presence of valvular heart disease, left ventricular systolic or diastolic dysfunction, congenital heart defects and estimation of right ventricular systolic pressure. A right ventricular systolic pressure of >40mmHg generally warrants further evaluation in a patient with unexplained dyspnea. Echocardiography has its own limitations and false positive reporting in high output states like severe anemia, AV shunting, hyperthyroidism hepatopulmonary syndrome and left heart failure may be recognized.

**RIGHT HEART CATHETERIZATION:**

The right heart catheterization remains the gold standard for confirming the diagnosis of pulmonary arterial hypertension. According to the new guidelines, the diagnosis of PH requires an elevated mPAP >25 mm Hg, and a vascular resistance of more than 3 Wood units, in the presence of a normal PCWP (<15 mm Hg). A vasoreactivity testing is recommended for IPAH and some patients with Associated PAH. A positive vasoreactive response was defined as a drop in mPAP of >10 mm Hg, a reduction below an absolute value of 40 mm Hg, with preserved or increased cardiac output during administration of a short acting vasodilator such as inhaled NO or intravenous adenosine. Only 5-10% of patients are vasoreactive and are candidates for long term calcium channel blocker therapy.

**TREATMENT OF PAH:**

General treatment: includes anticoagulation for IPAH (level of evidence A) and associated PAH (level of evidence B), diuretics, oxygen and life style modification.

Specific therapy for PAH: Long term calcium channel blockers are indicated for the 5-10% responders to the vasoreactivity testing. For the non-responders the specific pulmonary hypertension medications like endothelin receptor antagonists, phosphodiesterase inhibitors and prostanoids should be prescribed [3,4].

The approved compounds in endothelin receptor group include bosentan and ambrisentan, both are potentially hepatotoxic. Regular monitoring of aminotransferases every 4 weeks is required. The starting dose of bosentan in adult is 62.5 mg twice daily and the target dose for bosentin is 125 mg twice daily, for ambrisentan the dose is 5-10 mg daily[6]. The approved compounds in phosphodiesterase group include sildenafil at a dose 20 mg three times daily and tadalafil with target dose 40 mg once daily. The approved compounds in prostanoid group include inhaled iloprost starting with 2.5 mg 6-9 times daily with a special nebulizer. The maximum dose is 5 mg 6-9 times daily. The intravenous epoprostenol is titrated in the dose of 2-20ng/kg/minute. The patients require a permanent indwelling intravenous catheter. The treprostenol is available in subcutaneous or intravenous form the dose is titrated from 1.25ng/kg/min up to a maximum of 40ng/kg/min. Atrial septostomy is a temporizing measure for selected patients with right heart failure due to PAH. If all medical therapy fails the patient should be referred for lung or heart-lung transplantation [5]. The patients with thromboembolic pulmonary hypertension (Group 4) should be considered for thromboendarterectomy.

A six minute walk test is an important marker of prognosis and is a useful tool to assess the response to therapy. A walking distance of <320meters is associated with poor outcome and a walking distance of >380 meters following 3 months of IV epoprostenol correlates with improved survival.

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