Differential Diagnosis for Patients with Pulmonary Hypertension

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Pulmonary hypertension (PH) is an increase of blood pressure in the pulmonary artery, pulmonary vein, or pulmonary capillaries, together known as the lung vasculature, leading to shortness of breath, dizziness, fainting, leg swelling and other symptoms. PH is a complex, multidisciplinary disorder. Pulmonary arterial hypertension (PAH) is a syndrome resulting from restricted flow through the pulmonary arterial circulation resulting in increased pulmonary vascular resistance and ultimately in right heart failure. PH and PAH are not synonymous, PAH is a category of PH. Traditionally, the diagnostic imaging work-up of PH comprised mainly echocardiography, invasive right heart catheterization, and ventilation/perfusion scintigraphy. Due to technical advances, multidetector row computed tomography (CT) and magnetic resonance imaging (MRI) have become important investigations in the evaluation of patients with suspected PH. CT and MRI are well suited for a comprehensive morphological and functional assessment of patients with PH. Each modality has its strengths and limitations and different techniques may be used at different stages of diagnostic investigation and frequently complement each other.

1. Doppler Echocardiography

In patients in whom there is a clinical suspicion of PAH, the diagnosis should be screened with a Doppler Echocardiogram. Doppler Echocardiogram not only helps establish the diagnosis but can delineate the etiology and offer prognostic information as well. Doppler Echocardiograms can detect valvular heart disease, left ventricular dysfunction, and intracardiac shunts. In order to estimate a right ventricular systolic pressure by echocardiogram, tricuspid regurgitation (TR) jet must be present. In the absence of the ability to provide a quantitative assessment of right sided pressures using the TR jet, the presence of certain qualitative signs including RA and RV enlargement and septal bowing or flattening can prove helpful in the diagnosis of pulmonary hypertension. However, Doppler-derived pressure estimation in PH may be inaccurate in the individual patient and PH cannot be reliably defined by a cut-off value of Doppler-derived PA systolic pressure. Consequently, estimation of PAP based on Doppler transthoracic echocardiography measurements is not suitable for screening for mild, asymptomatic PH. However, in the absence of other potential etiologies of PH, such as left heart disease or advanced lung disease, an estimated RV systolic pressure of greater than 40 mm Hg generally warrants further evaluation in the patient with unexplained dyspnea.

2. Electrocardiogram (ECG)

ECG should also be performed in patients with suspected PAH; though not specific for PAH, typical findings on ECG include right ventricular strain, right ventricular hypertrophy, and right axis deviation.

3. Blood tests

Routine biochemistry, hematology, and thyroid function tests are required in all patients, as well as a number of

other essential blood tests. Serological testing is important to detect underlying CTD, HIV, and hepatitis. Systemic sclerosis is the most important CTD to exclude because this condition has a high prevalence of PAH. Anti-centromere antibodies are typically positive in limited scleroderma. In SLE, anti-cardiolipin antibodies may be found. Thrombophilia screening including anti-phospholipid antibodies, lupus anticoagulant, and anti-cardiolipin antibodies should be performed in CTEPH. Up to 2% of individuals with liver disease will manifest PAH and therefore liver function tests and hepatitis serology should be examined if clinical abnormalities are noted. Thyroid disease is commonly seen in PAH and should always be considered, especially if abrupt changes in the clinical course occur.

4. Abdominal ultrasound scan

Liver cirrhosis and/or portal hypertension can be reliably excluded by the use of abdominal ultrasound. The use of contrast agents and the addition of a colour-Doppler examination may improve the accuracy of the diagnosis. Portal hypertension can be confirmed by the detection of an increased gradient between free and occluded (wedge) hepatic vein pressure at the time of RHC.

5. Chest Radiography

Chest X-ray may support the diagnosis of PAH or may lead to the diagnosis of other underlying diseases. The main findings on chest radiograph in patients with PAH were enlarged hilar and pulmonary arterial shadows. Enlargement of the right ventricle, suggested by filling of the retrosternal space on lateral chest radiographs, is also consistent with PAH. Except in the case of accompanying parenchymal lung disease, the lungs on chest x-ray are typically clear in PAH. In PAH patients with late-stage disease, ascites with pleural effusions may be seen on chest x-ray.

6. Ventilation/perfusion scan

Ventilation/perfusion scan should be performed in all patients with PAH; a normal V/Q scan rules out thromboembolism but an abnormal one warrants further testing with pulmonary angiography.

7. Chest CT

The role of Chest CT angiography in excluding the diagnosis of CTEPH is currently under study, but CT scans of the chest may be useful in other ways as they can assess for the presence or absence of parenchymal lung diseases such as pulmonary fibrosis or emphysema.

8. Pulmonary Function Test (PFT)

PFT and arterial blood gas should be performed in all patients; in patients with systemic sclerosis, regular PFT with measurements of diffusing capacity may aid in the early detection of PAH. An assessment of functional status using a 6-minute walk test should be performed in all patients with PAH.

9. Cardiac magnetic resonance imaging

Cardiac MRI provides a direct evaluation of RV size, morphology, and function, and allows non-invasive assessment of blood flow including stroke volume, CO, distensibility of PA, and RV mass. Cardiac MR data may be used to evaluate right heart haemodynamics particularly for follow-up purposes. A decreased stroke volume, an increased RV end-diastolic volume, and a decreased LV end-diastolic volume measured at baseline are associated with a poor prognosis. Among the triad of prognostic signs, increased RV end-diastolic volume may be the most appropriate marker of progressive RV failure in the follow-up.

10. Right Heart Catheterization

RHC is the gold standard for the diagnosis of PAH. It aids in the diagnosis by excluding other etiologies such as left heart disease and provides important prognostic information for patients with PAH. The following variables must be recorded during RHC: PAP (systolic, diastolic, and mean), right atrial pressure, PWP, and RV pressure. Cardiac output must be measured in triplicate preferably by thermodilution or by the Fick method. Superior vena cava, PA, and systemic arterial blood oxygen saturations should also be determined. These measurements are needed for the calculation of PVR. Adequate recording of PWP is required for the differential diagnosis of PH. Vasodilator testing using short-acting agents such as adenosine, inhaled nitric oxide, or epoprostenol should be performed during cardiac catheterization to identify the small subset of patients who may benefit from long-term therapy with calcium channel blockers.

11. Diagnostic algorithm

The diagnostic algorithm is shown in following Figure. The diagnostic process starts with the identification of the more common clinical groups of PH (group 2—left heart disease and group 3—lung diseases), then distinguishes group 4—CTEPH and finally makes the diagnosis and recognizes the different types in group 1—PAH and the rarer conditions in group 5.

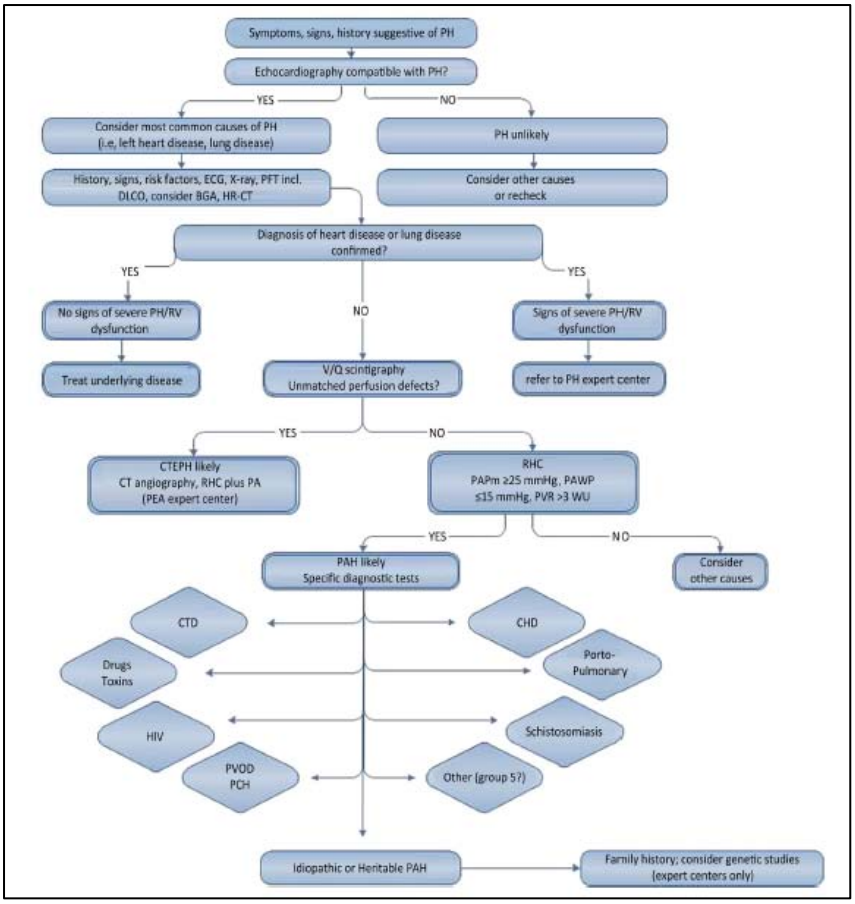

Figure. Diagnostic Algorithm for the differential diagnosis of PH (Hoeper MM, et al. J Am Coll Cardiol 2013)

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