PAH Diagnostic Strategy, Disease Severity, and Risk of Death

PAH Definition and Classification

The European Society of Cardiology (ESC) and the European Respiratory Society (ERS) jointly released updated guidelines (ESC/ERS Guidelines) for the diagnosis and treatment of pulmonary hypertension (PH) (Humbert, Kovacs et al. 2022). These updated guidelines included changes to the hemodynamic definition of PH, a revised cut-off level for pulmonary vascular resistance (PVR), and a definition of exercise PH.

- **Definition**. Patients with PAH are hemodynamically characterized by pre-capillary PH in the absence of other causes of pre-capillary PH. Hemodynamic characteristics include mean pulmonary arterial pressure (mPAP), pulmonary arterial wedge pressure (PAWP), and pulmonary vascular resistance (PVR)
- **Revised cut-off level for PVR**. Cut-off levels for PVR are as follows:
    - Pre-capillary PH and combined post- and pre-capillary PH: > 2 Wood units (WU) [1]
    - Isolated post-capillary pulmonary hypertension (IpcPH): ≤ 2 WU
- **Definition of exercise PH**. Exercise PH is defined by an mPAP/cardiac output (CO) slope > 3 mmHg/L/min between rest and exercise

Diagnostic Strategy Summary

The ESC/ERS Guidelines diagnostic strategy encompasses 13 recommendations in three categories: echocardiography, imaging, and other diagnostic tests.

Echocardiography. The strategy begins by recommending echocardiography as the first-line, non-invasive, diagnostic investigation in suspected PH. From the results of that investigation, an echocardiographic probability of PH is assigned based on an abnormal velocity of tricuspid regurgitation (TRV) and the presence of other echocardiographic signs suggestive of PH. Notably, the current threshold for TRV of > 2.8 m/s for echocardiographic probability of PH, as per the updated hemodynamic definition, is maintained. Further testing should then be considered in the clinical context based on the probability of PH by echocardiography, i.e., symptoms and risk factors or associated conditions for PAH/chronic thromboembolic pulmonary hypertension (CTEPH). In the case of symptomatic patients with intermediate echocardiographic probability of PH, cardiopulmonary exercise tests (CPET) may be considered to further determine the likelihood of PH.

Imaging. For patients with unexplained PH, ventilation/perfusion or perfusion lung scan is recommended to assess for CTEPH. Likewise, CT pulmonary angiography is recommended in the work-up of patients with suspected CTEPH. In all patients with PAH, routine biochemistry as well as hematology, human immunodeficiency virus (HIV) testing, and thyroid function tests are recommended

[1] For pre-capillary PH, hemodynamics are mPAP > 20 mmHg, PAWP ≤ 15 mmHg, and PVR > 2 WU. For Combined post- and pre-capillary PH, hemodynamics are mPAP > 20 mmHg, PAWP > 15 mmHg, and PVR > 2 WU.

to identify associated conditions. Abdominal ultrasound is recommended for the screening of portal hypertension, while chest computed tomography (CT) should be considered in all patients with PH. Finally, as part of the work-up of patients with CTEPH, digital subtraction angiography should be considered.

Other diagnostic tests. Pulmonary function tests with lung diffusion capacity for carbon monoxide (DLCO) are recommended during the initial evaluation of patients with PH. However, open or thorascopic lung biopsy is not recommended in patients with PAH.

Disease Severity and Risk Summary

The ESC/ERS Guidelines provide five recommendations for evaluating the disease severity and risk of death in patients with PAH. First, disease severity in patients should be evaluated with PAH with a panel of data derived from clinical assessment, exercise tests, biochemical markers, echocardiography, and hemodynamic evaluations. Achieving and maintaining a low-risk profile on optimized medical therapy is recommended as a treatment goal in patients with PAH.

Risk stratification varies between time of diagnosis and during follow-up. At time of diagnosis, a three-strata model (low, intermediate, and high risk) is recommended and should consider all available data, including hemodynamics. A four-strata model is used at follow-up (low, intermediate–low, intermediate–high, and high risk). Classification in this model is based on WHO functional class, six-minute walk test (6MWD), and brain natriuretic peptide/N-terminal pro-brain natriuretic peptide (BNP/NT-proBNP).

Finally, the optimization of therapy should be considered on an individual bases in some PAH etiologies and patients with comorbidities, with the understanding that a low-risk profile is not always achievable.

References

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