Clinical Science Working Group 6:
Diagnosis & Assessment of PAH

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A. Should we include PVR at rest in the definition of PH and how do we define and handle "borderline" PH?

B. What should be the upper limit of the PCWP, and what are the roles of fluid challenge and exercise hemodynamics in the identification of HFpEF patients?

C. How do we diagnose PAH in its early stages (including screening programs for high-risk populations)?

D. Which are most useful clinically - prognostic factors measured at baseline or prognostic factors that change with therapy?

Proposal: To use WU instead of dynes

Textbox: Harmonization of PVR units

While PAP is always given as mmHg, various units are used for PVR, most frequently dyn·s·cm^{-5} and Wood units (mmHg/l•min). Consistency would be useful and the working group suggests using Wood units (WU), which can be directly derived from PAP and CO measurements without the arbitrary multiplication with the factor 80. The use of SI units is not endorsed, as they are not commonly being used for hemodynamics in clinical practice.

# Proposal: To use PAWP rather than PCWP or PAOP

Textbox: PAWP/PAOP/PCWP - Harmonization of terminology

The term pulmonary capillary wedge pressure (PCWP) is widely used in the medical literature. In order to measure this pressure, balloon occlusion occurs in the pulmonary arteries and the obtained value is not equal to the pulmonary capillary pressure in non-occluded areas. Thus, the term PCWP is misleading. Better terms are pulmonary artery occlusion pressure (PAOP) and pulmonary artery wedge pressure (PAWP). The working group prefers the latter term as the short versions "wedge" and "wedge pressure" are well established in daily clinical practice, even in non English-speaking countries.

Revised diagnostic algorithm

Figure I Modified diagnostic algorithm
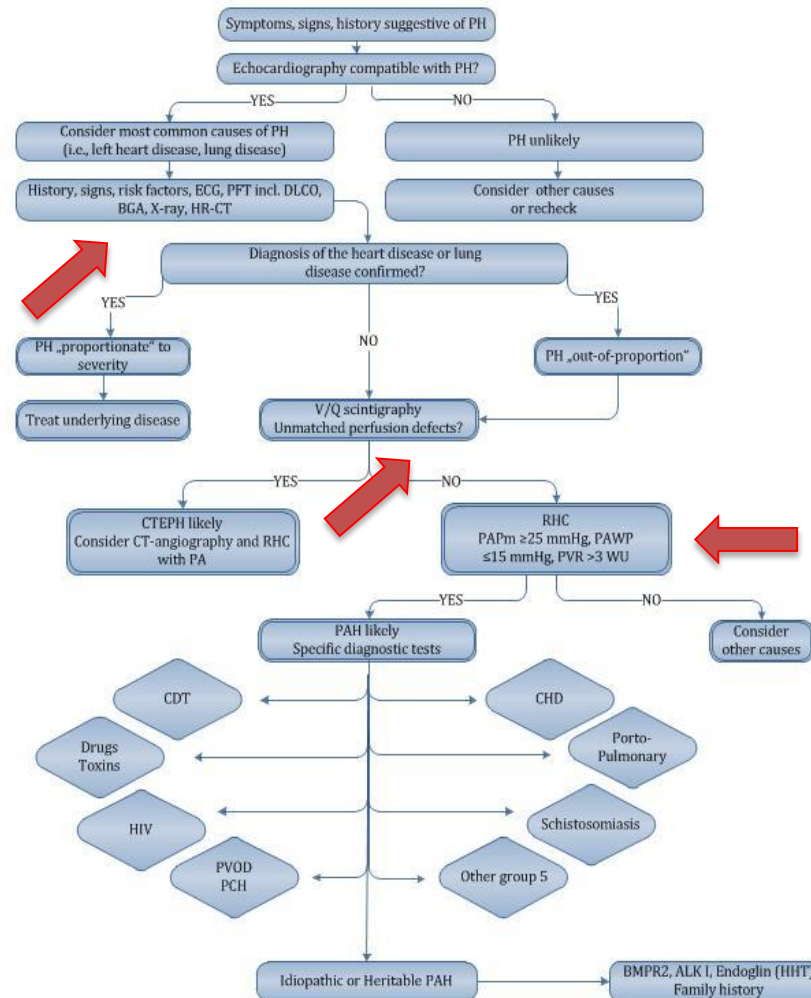
A1: Should we include PVR?

Working group recommendations on PVR:

- In order to avoid the use of various units, PVR should be given in Wood units (WU).

- PVR should not become part of the definition of PH or PAH.

  - But, measurement of CO, and calculation of PVR is a very important part of the diagnostic evaluation

    - High-flow states (such as portopulmonary hypertension, shunts, and sickle cell anemia) differ in terms of treatment approach

A2: Should we add the term „borderline PH"?

Working group recommendations:

- The general definition of PH should remain unchanged: PH is defined by a PAPm ≥25 mmHg at rest measured by right heart catheterization.

- Patients with scleroderma and PAPm 21-24 should be followed closely for the possible development of PH

B1: Maintain PAWP at 15 mmHg?

Working group recommendations for PAWP at rest

- The working group does not recommend lowering the threshold to 12 mmHg in clinical practice.

- The cut-off for pre-capillary PH should remain at ≤15 mmHg as this has been used in almost all clinical trials generating evidence for the safety and efficacy of PAH-targeted therapies in patients fulfilling these criteria.

- Sponsors of PAH trials may decide to use a PAWP ≤12 mmHg as cut-off in order to decrease the likelihood of including patients with HFpEF.

- Invasive hemodynamics need to be placed in clinical and echocardiographic context with regard to probability of existence of HFpEF.

B2: Role of fluid challenge and exercise hemodynamics to uncover HFpEF

Working group recommendation on fluid challenge:

- Fluid challenge may be useful in identifying occult HFpEF patients but this technique requires meticulous evaluation and standardization before its use in clinical practice can be recommended.

Working group recommendations on exercise-induced PH

- Due to the lack of a suitable definition, an exercise criterion for PH should not be re-introduced at the present time.

- Further studies are needed to define which levels of exercise-induced elevations in PAPm and PVR have prognostic and therapeutic implications.

Detection of SSc-Associated PAH:

- Screening of SSc patients without clinical signs and symptoms of pulmonary hypertension should include a 2-step approach using:

  - clinical assessment for the presence of telangiectasia, anti-nuclear-antibodies, PFT and DLCO measurements, ECG, biomarkers (NT-proBNP and uric acid) in the initial stage
  - followed by echocardiography and consideration of right heart catheterization in patients with abnormal findings (at-risk population).

D. Prognostic factors at baseline and during follow-up

Working group recommendations on baseline and follow-up assessments

- A comprehensive evaluation of "biomarkers" should be performed at baseline, i.e. at the time of diagnosis prior to initiation of targeted therapy (including at least a full hemodynamic assessment, echocardiography, functional class, 6MWD, BNP/NT-proBNP; cardiopulmonary exercise testing and cardiac MRI should be considered, where available).

- The first re-assessment of stable patients should be performed no later than 8-12 weeks after initiation of therapy.

- Re-assessments should include at least the evaluation of functional class, 6MWD and BNP/NT-proBNP measurements; CPET and cardiac MRI may provide valuable additional information.

- Frequent reassessments in 8-12 weekly intervals should be continued as long as the patient does not reach the treatment goals.

- When all clinical and hemodynamic treatment goals have been reached, reassessment of at least functional class, 6MWD and BNP/NT-proBNP should be performed every 3-6 months or whenever clinically indicated.

- Follow-up hemodynamics should be obtained whenever therapeutic consequences are to be expected and it is highly recommended 3-6 months after initiation of PAH therapy to determine whether hemodynamic treatment goals (i.e, CI $\geq$ 2.5 l/min/m^2, RAP < 8 mmHg, SvO$_2$ > 65%) are met.

- Most of the variables and treatment goals have mainly been studied in IPAH and their usefulness in other forms of PAH is unclear.