Invasive and Noninvasive Evaluation for the Diagnosis of Pulmonary Hypertension

How to Use and How to Combine Them

Michele D'Alto, MD, PhD, FESC[a,*,1],
Giovanni Maria Di Marco, MD[a],
Antonello D'Andrea, MD, PhD[a], Paola Argiento, MD, PhD[a],
Emanuele Romeo, MD, PhD[a], Francesco Ferrara, MD, PhD[b,c],
Bouchra Lamia, MD, MPH, PhD[d,e], Stefano Ghio, MD[f],
Lawrence G. Rudski, MD[g]

KEYWORDS

• Pulmonary hypertension • Heart catheterization • Echocardiography • Invasive • Noninvasive

KEY POINTS

- Diagnosis of pulmonary hypertension may be challenging.
- Right heart catheterization is the gold standard for the diagnosis of pulmonary hypertension.
- A combined invasive and noninvasive evaluation has been shown to be crucial for a complete diagnostic and therapeutic management.

INTRODUCTION

Pulmonary hypertension (PH) is a pathophysiologic condition defined hemodynamically as having an increase in mean pulmonary artery pressure (mPAP) $\geq$25 mm Hg assessed at rest by right-heart catheterization (RHC).[1] PH is considered precapillary when pulmonary artery wedge pressure (PAWP) is $\leq$15 mm Hg and postcapillary when PAWP is >15 mm Hg.[1]

The most common form of PH is postcapillary PH, due to left heart diseases. By comparison, pulmonary arterial hypertension (PAH), a rare and devastating disease, is characterized by the presence of precapillary PH and a pulmonary vascular resistance >3 Wood units, in the absence of other

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[a] Department of Cardiology, Università degli Studi della Campania Luigi Vanvitelli, Monaldi Hospital, Piazzale E. Ruggieri, 1, Naples 80131, Italy; [b] Heart Department, Cardiology Division, Cava de' Tirreni and Amalfi Coast Hospital, University of Salerno, Fisciano, Italy; [c] Department of Cardiology, Cava de' Tirreni Hospital, University Hospital Ruggi d'Aragona, Salerno, Italy; [d] Normandie University, UNIROUEN, EA 3830, Rouen University Hospital, Department of Pulmonology and Critical Care F 76000, Rouen, France; [e] Department of Pulmonology, Le Havre Hospital, F 76600 Le Havre, France; [f] Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, piazza Golgi 1, Pavia 27100, Italy; [g] Azrieli Heart Center, Jewish General Hospital, McGill University, Montreal, Quebec, Canada

[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

* Corresponding author.

E-mail address: mic.dalto@tin.it

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causes of precapillary PH.[1] The differential diagnosis between these 2 forms of PH may be challenging even if invasive data are available.

This review points out the importance of combining invasive and noninvasive evaluation for reaching a definitive differential diagnosis of PH, considering the strengths and weaknesses of each diagnostic tool.

RIGHT HEART CATHETERIZATION: PITFALLS AND CAVEATS

RHC represents the gold standard for measuring pulmonary hemodynamics and is considered mandatory to confirm the diagnosis of PH.[1]

Although performing RHC, a correct "zero level" (ZL) is pivotal because it represents the ideal starting point for all measurements. In fact, each pressure measured during RHC represents the difference between the pressure at the chosen ZL and the pressure in the chamber (or vessel) where the fluid-filled catheter tip is located, assuming there is no obstruction and no significant flow within the catheter.[2,3]

A wrong ZL setting represents one of the most common mistakes and confounding factors in clinical practice. Over time, the ZL has been recommended to be set at the level of the right atrium, or at the level of the tricuspid valve, or 5 cm below the anterior thorax surface, based on the concept of the "hydrostatic indifferent point," representing the location in the circulatory system at which gravitational pressure factors caused by changes in body position do not much affect the pressure measurements.[2–4] Recently, it has been proposed as a standardized reference point named "phlebostatic axis"[5] and would correspond to the level of the left atrium in the supine position in most of the patients. This point may be easily set at the midthoracic level, as shown by Kovacs and colleagues[6] and then suggested by current European guidelines on PH.[1]

A wrong ZL set is of clinical relevance in the diagnostic process. For example, a wrong ZL set 5 cm above or 5 cm below the midthoracic level leads to an underestimation or an overestimation, respectively, of all pressures of about 4 mm Hg. A mistake in ZL may be of crucial importance in particular in defining the real value of the PAWP for differentiating precapillary from postcapillary PH.

PAWP is the pressure measured by wedging a pulmonary catheter with an inflated balloon into a small pulmonary arterial branch. In common practice, it is recorded as the mean of 3 to 5 measurements determined at the end of normal expiration. In the authors' opinion, averaging pulmonary vascular pressures over several respiratory cycles may be preferable, in particular for patients with dynamic hyperinflation states such as severe chronic obstructive pulmonary disease.[5] However, this issue is still unsolved and needs further evidence. As a quality control method, it is mandatory to consider that PAWP must be equal or lower than diastolic PAP; PAWP tracing must be similar to atrial pressure tracing (a wave and v wave); respirophasic swings should be visible; and catheter position must be stable at fluoroscopic control.[7] Moreover, to confirm a correct measurement in the case of uncertainty, aspiration from the distal lumen of the catheter should be possible and O_2 saturation in occluding position should be the same as systemic blood (>94%).[7] There has been a long debate on increasing or lowering the PAWP threshold from 15 to 18[8] or 12 mm Hg,[9] respectively, in clinical practice for distinguishing precapillary from postcapillary PH. Nevertheless, using the threshold of 18 mm Hg, some patients with heart failure with preserved ejection fraction (HFpEF) may be misclassified as PAH patients. On the contrary, lowering the PAWP threshold to 12 mm Hg from one side could decrease the likelihood of falsely labeling patients with PH due to HFpEF on optimal therapy as PAH, from the other side it could also increase the missing diagnosis of PAH.[10] Based on the above consideration, it has been considered appropriate thus far to maintain the threshold of 15 mm Hg of PAWP to distinguish between precapillary and postcapillary PH.[1]

Another crucial point is represented by the assessment of cardiac output (CO), performed by either the Fick method or by thermodilution. The latter is the most used in clinical practice, except for patients affected by congenital heart disease (CHD), where the Fick method is mandatory.

The gold standards for pressure and blood flow measurement of the pulmonary circulation are the high-fidelity micromanometer-tipped catheters and the direct Fick method, respectively. The fluid-filled flow-directed thermodilution catheters as compared with the gold standard have demonstrated to be accurate, although with a lack of precision of $\pm$ 1 L/min for CO and $\pm$ 10 mm Hg for pulmonary vascular pressures.[5,11–16] Nevertheless, errors on "accurate" but "not-precise" measurements can be limited by repetition and averaging the observed values. Consequently, it is recommended to average 3 to 5 thermodilution CO measurements rejecting the values with a variation greater than 10%.