Accuracy of echocardiography in pulmonary hypertension: thinking outside of the box beyond the Achilles' heel of right atrial pressure estimation

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If a theory is falsified (in the usual sense), it is proven false; if it is falsified (in the technical sense), it may still be true.

Imre Lakatos [1]

Echocardiography is a powerful screening tool in patients with suspected pulmonary hypertension (PH) and may be used to infer the diagnosis [2].

Echocardiographic estimation of pulmonary artery systolic pressure (PASP) is traditionally performed by adding right atrial pressure (RAP) obtained through the inferior vena cava (IVC) size and dynamics (i.e., collapsibility) to the continuous wave Doppler measurement of peak tricuspid regurgitation velocity (TRV). This method was described almost thirty years ago and is still recommended, though progressively refined, in the guidelines of the international Societies of echocardiography [3, 4]. Although several attempts have been made to develop alternative reliable non-invasive methods (e.g. Doppler-derived acceleration rate of right ventricular early filling) for evaluating RAP, the real Achilles' heel of the echocardiographic formula for PASP estimation, they have not gained widespread use [5]. Given the inaccuracies of RAP estimation and other potential technical pitfalls, guidelines for the diagnosis and treatment of PH recommend using the TRV (and not the PASP) as the main variable for assigning PH probability [2].

In the current issue of the *International Journal of Cardiovascular Imaging*, Venkateshvaran and colleagues investigated the accuracy of transthoracic echocardiography to estimate pulmonary artery (PA) pressures contained in a dual-centre database of PH referrals [6]. Four hundred and nineteen consecutive patients with unexplained dyspnea referred for right heart catheterization (RHC) were included in the study. The main findings of the study can be summarized as follows: (1) echocardiography accurately represents PA pressures for population studies but may be misleading for individual diagnosis owing to its modest precision and frequent misclassification; (2) recommended echocardiographic estimates of RAP_{mean} are often falsely elevated, and the incorporation of these estimates to calculate PA pressures results in relatively high bias with RHC; (3) the recommended 2.8 m/s cut-off for intermediate-probability PH misclassifies one in three subjects, whereas raising the cut-off to 3.4 m/s results in a drop in sensitivity, thereby warranting re-evaluation of these recommended values [6].

Previous studies have already shown that echocardiography may not accurately quantify PA pressures in individual patients. In a study of patients with and without systemic sclerosis-associated pulmonary hypertension Maukerjee et al. found that echocardiographically estimated tricuspid gradient showed a moderate positive correlation (r^2 0.44, $p < 0.005$) with both mean pulmonary pressure and invasively determined tricuspid gradient [7]. In the study by Venkateshvaran et al. echocardiography showed a better performance, with a strong correlation between PASP estimated by echocardiography and RHC (r 0.86, $p < 0.001$) [6].

From a clinical perspective the main question is why are the echocardiographic results not as accurate in individual patients. It is reasonable to hypothesize that the variables whose impact proves to be diluted in large cohorts might play a pivotal role in individual patients. These variables include: (1) technical issues (e.g., correct Doppler alignment, uncertainty in the assignment of the maximum

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Factors influencing the echocardiographic assessment of pulmonary artery pressures

Fig. 1 Factors influencing the echocardiographic assessment of pulmonary artery pressures: a complex puzzle

velocity of the regurgitant signal especially in presence of weak TR signals) [6, 7]; (2) pathophysiological factors (not only RAP as pointed out in the study by Venkateshvaran et al. but also rhythm disturbances [e.g., atrial fibrillation], conduction disturbances [e.g. left bundle branch block causing atrio-ventricular, intraventricular and interventricular dyssynchrony], cardiac implantable electronic devices [i.e. pacemaker/ICD leads], right ventricular function, vasculo-arterial coupling, left side heart/valvular diseases, loading conditions, systemic disease states) [8, 9]. The aforementioned factors not only influence TR flow but also velocities and pressures/gradients (Fig. 1). As pointed out by Venkateshvaran and colleagues, “a diagnostic algorithm that combines hemodynamic information with structural indices of right-heart structure and function may vastly improve accuracy of non-invasive PH estimation for individual cases and needs to be explored” [6].

As previously stated, several factors may limit the accuracy of non-invasive (indirect) assessment of PA pressures. However, RHC is a technically demanding procedure that requires attention to avoid gross errors (e.g. the zero point should be mid-thoracic, the point of reading pressure tracings should be at end of normal expiration, the operator should be aware of the factors preventing correct interpretation of pressure tracings such as diuretic use, chronic obstructive pulmonary disease, AF, high v-wave, thorax

deformities, abdominal obesity, etc.) [10]. Moreover, although RHC is considered the gold standard technique for diagnosis, a direct comparison between hemodynamic and imaging tests raises another question; are they truly looking at the same biological phenomenon (beyond the different perspective) or is it a case of comparing apples and oranges? Perhaps, the focus should be greater on the correlation between the results of the diagnostic test (whatever may be) and its prognostic and therapeutic impact, rather than on crude numerical results.

The Venkateshvaran et al. study includes a clinical message that goes beyond the performance analysis of a single diagnostic technique, and it seems to emphasize the importance of patient profiling with a tailored approach in PH. The concept of precision or personalized medicine should be applied not only to treatments but also to diagnostic tests.

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Declarations

Conflict of interest The authors have no conflicts of interest to declare.

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