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Point/Counterpoint

Advanced Imaging Tools Rather Than Hemodynamics Should Be the Primary Approach for Diagnosing, Following, and Managing Pulmonary Arterial Hypertension

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See article by Maron, pages 515-520 of this issue.

ABSTRACT

Pulmonary hypertension (PH) is currently defined based on invasive measurements: a resting pulmonary artery pressure ≥ 25 mm Hg. For pulmonary arterial hypertension, a pulmonary arterial wedge pressure ≤ 15 mm Hg and pulmonary vascular resistance > 3 Wood units are also required. Thus, right heart catheterization is inevitable at present. However, the diagnosis, follow-up, and management of PH by noninvasive techniques is progressing. Significant advances have been achieved in the imaging of pulmonary vascular disease and the right ventricle. We review the current sensitivities and specificities of noninvasive imaging of PH and discuss its role and future potential to replace hemodynamics as the primary approach to screening, diagnosing, and following/managing PH.

RÉSUMÉ

L'hypertension pulmonaire (HP) est actuellement définie selon des méthodes effractives de mesure : une pression artérielle pulmonaire ≥ 25 mm Hg au repos. Pour définir l'hypertension artérielle pulmonaire, une pression artérielle pulmonaire d'occlusion ≤ 15 mm Hg et une résistance vasculaire pulmonaire > 3 unités Wood sont également requises. Par conséquent, le cathétérisme cardiaque droit est inévitable pour le moment. Malgré cela, le diagnostic, le suivi et la prise en charge de l'HP par des techniques non effractives évoluent. L'imagerie des maladies vasculaires pulmonaires et du ventricule droit a connu d'importants progrès. Nous passons en revue la sensibilité et la spécificité actuelles de l'imagerie non effractive de l'HP, et discutons de ses rôles et de son potentiel futur de remplacement de l'hémodynamique comme principale approche en matière de dépistage, de diagnostic, de prise en charge/suivi de l'HP.

Pulmonary arterial hypertension (PAH) is an orphan condition with high morbidity and mortality. Despite increased awareness of pulmonary hypertension (PH), data indicate that the majority of patients are still diagnosed in late stages of the disease. A higher World Health Organization functional class is associated with poorer median survival, illustrating the importance of early diagnosis. In this article, we were asked to defend the value of noninvasive imaging in the diagnosis and follow-up of PH. Although we agree that at this point, invasive assessment remains essential, in the long term it is hoped that noninvasive methods will eliminate the need for invasive assessment. Our original mandate was to discuss PAH; however, because this is a rare condition with relatively little information available, we have broadened our approach to include PH in general.

Limitations of Invasive Assessment

Invasive hemodynamic assessment by right heart catheterization is relatively safe but has technical limitations

At the Nice 5th World Symposium on PH, right heart catheterization (RHC) was confirmed as essential for the diagnostic workup of PH to assess the severity of the disease and to perform a vasoreactivity test.[1-3] However, RHC is associated with rare, albeit serious, procedure-related complications, including death. In an analysis of 7218 RHC procedures performed in experienced PH centres, 76 serious adverse events, including 4 fatalities, were observed. The most common serious adverse events were supraventricular and ventricular tachycardia, vagal reactions, and systemic hypotension.[4] Although RHC is relatively safe, reports of complications do appear, even in expert centres.[5]

Data acquisition during RHC requires resting supine patients. There is no standard operating procedure for

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Table 1. Noninvasive imaging to screen for PH

First author	Technique	Number of patients	Study population/cause	Functional parameter/variable	Screening for PH	
					Sensitivity (95% CI), %	Specificity (95% CI), %
Denton et al.[24]	TTE	33	CTD (SSc)	sPAP	90	75
Parent et al.[25]	TTE	385	Sickle cell disease	Tricuspid regurgitation jet velocity	100	80
Rajaram et al.[26]	TTE	81	CTD	Tricuspid gradient	86	82
Wang et al.[27]	TTE	123	CHD	sPAP	89	84
Kuriyama et al.[28]	CT	23	Suspected PH	MPAD	69	100
Perez-Enguix et al.[29]	CT	71	Candidates for LTX	MPAD	66	86
Rajaram et al.[26]	CT	81	CTD	Ventricular mass index	85	82
Stevens et al.[30]	MRI	100	Suspected PH	PVR	92.5	85.2
Rajaram et al.[26]	MRI	81	CTD	RV mass index	85	82

CHD, congenital heart disease; CT, computed tomography; CTD, connective tissue disease; LTX, lung transplantation; MPAD, main pulmonary artery diameter; MRI, magnetic resonance imaging; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RV, right ventricular; sPAP, systolic pulmonary artery pressure; SSc, systemic sclerosis/scleroderma; TTE, transthoracic echocardiography.

capturing hemodynamic changes that occur with an upright posture or with physical activity using RHC. In addition, hemodynamic measurements acquired by RHC are subject to intraindividual spontaneous variability and represent only a hemodynamic snapshot.[1,6]

Routine RHC relies on the use of fluid-filled catheters, which have an insufficient frequency response.[7] Standard Swan-Ganz catheter manometry systems used in clinical practice have a frequency response of 12 Hz, whereas a minimum of 50 Hz would be required for the assessment of instantaneous pressure signals.[7] Fluid-filled catheters require fast flushes to remove air bubbles in the monitoring system, which account for most of the variability compared with the true gold-standard high-fidelity micromanometer-tipped catheters.[7] In contrast to high-fidelity micromanometer-tipped catheter systems, fluid-filled catheter transducers have to be positioned at a "zero reference level," which is most accurately obtained at midthoracic level or at one third of the thoracic diameter below the anterior thorax surface.[8] A deviation of 1 cm of the transducer from zero level affects pressures by 0.78 mm Hg, thus leading to significantly different results if 2 different zero reference levels are used in a single patient.[8]

Currently used invasive cardiac output measurements estimate but do not measure true cardiac output

The gold standard for the assessment of cardiac output (CO) is the direct Fick method in which CO equals O_2 consumption divided by the difference between arterial and venous O_2 content. Although O_2 consumption can be measured accurately, that measurement is cumbersome, and many laboratories use standard tables for an assumed value instead of direct measurements. Such estimation may cause an error of as much as 40% in the assessment of CO.[9] Most laboratories now use thermodilution based on an indicator dilution methodology to measure CO.[10] When compared with the direct Fick method, thermodilution measurements show little bias, with a mean difference of 0.1 L/min and a confidence interval of 0.2 L/min, corresponding to excellent accuracy even in the presence of tricuspid regurgitation, but limits of agreement are $\pm$ 1 L/min, corresponding to moderate precision.[11]

Need for an integrated diagnostic approach

Clinically significant information is gained from RHC that helps guide decisions. A restrictive use of RHC may delay a timely diagnosis and treatment.[6] Still, the simple distinction between pre- and postcapillary PH is a task that often cannot even be achieved by invasive RHC. In particular, heart failure with preserved ejection fraction is commonly misdiagnosed as precapillary PH.[12-14] Unresolved issues are the assessment of precatheterization fluid status, standardization of fluid loading,[3,15,16] and mean pulmonary arterial wedge pressure measurements—end-expiratory or as pressure-time integral.[16,17] The interpretation of invasive hemodynamics is meaningless outside the context of the clinical picture, in particular echocardiography.[1,3] To manage the growing number of PH cases resulting from left heart disease (group 2 PH) and caused by lung disease/hypoxia (group 3 PH) in the general population, successful noninvasive diagnostic algorithms combining multiple parameters have been developed to avoid unnecessary RHC.[1,18]

Present Value of Noninvasive Techniques

Advanced imaging tools are useful for screening

Transthoracic Doppler echocardiography is the predominant screening modality in early stages of diagnosis to assess right ventricular (RV) structure and function, including the degree of ventricular remodelling as well as the derivation of RV systolic and diastolic pressures and analysis of contraction timing,[19-23] thus providing a reliable method for the early detection of PH, with a particularly high sensitivity and specificity in systemic sclerosis (Table 1). Recently, software programs for 2-dimensional (2D) strain analysis by speckle tracking have been applied to evaluate the right ventricle.[31] Furthermore, significant progress has been made in the use of knowledge-based reconstruction of 3D RV structure and function from 2D images.[32] Studies have suggested that 3D echocardiographic imaging of the right ventricle is feasible, and its results compare well with magnetic resonance imaging (MRI).[33,34]

Theoretically, imaging of the pulmonary vasculature should be more sensitive to screening because this is where disease starts; yet, the available methods do not appear to have reached adequate sensitivity and specificity for that purpose.[35]

Advanced imaging tools are useful for diagnosis

Any patient with unexplained PH should be evaluated for chronic thromboembolic PH (CTEPH). Diagnostic algorithms