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Clinical and Research Measurement Techniques of the Pulmonary Circulation: The Present and the Future

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ABSTRACT

There has been a lot of progress in measurement techniques of the pulmonary circulation in recent years, and this has required updating of basic physiological knowledge. Pulmonary artery pressures (PAP) are normally low and dependent on left atrial pressure (LAP) and cardiac output (CO). Therefore, defining the functional state of the pulmonary circulation for the detection of pulmonary vascular disease or evaluation of disease progression requires measurements of PAP, LAP and CO. Invasive measurements have lately improved by a better definition of zero leveling and of the effects of intrathoracic pressure changes, and understanding of the inherent limitations of fluid-filled thermodilution catheters. The effects of LAP and pulmonary flow on PAP in health and disease are now integrated in the hemodynamic diagnosis of pulmonary hypertension. Development of alternative noninvasive approaches is critically dependent on their potential to quantify pulmonary vascular pressures and CO. Doppler echocardiography and magnetic resonance imaging are coming close. Both approaches are performant for flow measurements, but pressures remain indirectly assessed from flow velocities and/or structural changes. Doppler echocardiography or magnetic resonance imaging has been shown to be accurate, allowing for valid population studies, but with insufficient precision for single number-derived clinical decision making.

Introduction: pulmonary artery pressures (PAP) and blood flow

A lot of effort has been devoted in recent years to the development of noninvasive measurement techniques of the pulmonary circulation. Most have relied on Doppler echocardiography or, more recently, magnetic resonance imaging (MRI). Both have focused either on the imaging of pulmonary vascular flow patterns, with integration of pressure gradients calculated maximum velocities of trans-valvular flow-velocities, or, alternatively on changes in right ventricular (RV) structure or function as indicators of changes in pulmonary vascular function.[1–3] Integration of newly available high quality signals to define pulmonary vascular function has required some revisiting of basic physiological concepts, which has also resulted in tightening of invasive procedure methodology.

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Abbreviations and Acronyms

Ca = pulmonary artery compliance

CTEPH = chronic thromboembolic pulmonary hypertension

CO = cardiac output

DPG = diastolic pressure gradient

dPAP = diastolic pulmonary artery pressure

HCT = hematocrit

HF = heart failure

HR = heart rate

LAP = left atrial pressure

LVEDP = left ventricular end-diastolic pressure

LVOT = left ventricular outflow tract

mPAP = mean PAP

MRI = magnetic resonance imaging

PAH = pulmonary arterial hypertension

PAP = pulmonary artery pressure

PH = pulmonary hypertension

PP = pulse pressure

PVR = pulmonary vascular resistance

Q = pulmonary blood flow

RAP = right atrial pressure

RVOT = right ventricular outflow tract

sPAP = systolic pulmonary artery pressure

SV = stroke volume

TPG = transpulmonary pressure gradient

TR = tricuspid regurgitation

VTI = velocity time integral

Pulmonary blood flow (Q) is determined by mean PAP (mPAP) minus left atrial pressure (LAP). This is an extrapolation of the Hagen-Poiseuille's law which governs laminar flows within rigid straight and cylindric capillary tubes of Newtonian fluids. Thus the functional state of the pulmonary circulation can be approximated by a single number, pulmonary vascular resistance (PVR) which depends on the ratio between (mPAP-LAP) and Q:

$$\mathrm{PVR} = (\mathrm{mPAP\text{-}LAP})/\mathrm{Q}$$

In clinical practice, measurements of pulmonary vascular pressures and Q— assumed equal to cardiac output (CO) are usually performed during a catheterization of the right heart with a triple-lumen fluid-filled balloon- and thermistance-tipped catheter introduced by Swan, Ganz, Forrester and their colleagues in the early 1970s.[4,5] More than 40 years later, a right heart catheterization with a "Swan–Ganz" catheter is still recommended for the diagnosis of pre-capillary pulmonary hypertension.[6] The procedure allows for the measurement of the components of the PVR equation, with LAP estimated by a balloon occluded, or "wedged" AP (PAWP). Pulmonary hypertension (PH) is defined by a mPAP ≥25 mmHg.[7] Pulmonary arterial hypertension (PAH) is defined by a mPAP ≥25 mmHg, a PAWP <15 mmHg and a PVR ≥3 mmHg/L/min (Wood units).[7] Precapillary PH in heart failure (HF) is defined by a mPAP ≥25 mmHg, a transpulmonary pressure gradient (mPAP-PAWP, or TPG) ≥12 mmHg and a diastolic pressure gradient (diastolic PAP, dPAP, minus PAWP, or DPG) ≥7 mmHg.[8]

Are fluid-filled flow-directed thermodilution catheters reliable?

Because of the exclusive reliance on fluid-filled flow-directed thermodilution catheters for the diagnosis and differential diagnosis of PH and the widespread use of recommended cut-off numbers, it may be appropriate to re-examine how these measurements compare to gold standards. For this purpose, it is important to apply agreed statistics and undisputable gold standards, which are high-fidelity micromanometer-tipped catheters for pressures and the direct Fick method for pulmonary blood flow.[9]

Comparisons between methods of measurements often rely on correlation calculations. However, correlations largely reflect the variability of the subjects being measured. If one measurement is always twice as big as the other, they are highly correlated but do not agree. Bland and Altman addressed this problem by designing difference versus average plots.[10] This analysis has since become gold standard to compare methods of measurements.[11] Two crucial informations are provided: (1) the bias, or the difference between the means and whether it is constant over the range of measurements, and (2) the limits of agreement, or the range of possible errors. Bias informs about accuracy, and agreement informs about precision—or reproducibility.

The frequency response of fluid-filled catheters is generally assumed to be adequate for measurements of systolic and diastolic PAP (sPAP and dPAP), and derived calculation of mPAP. However, errors may be caused by overdamping or underdamping of signals related to the insufficient or excessive flushing or too long tubing systems.[12]

To answer the question about how accurate and precise optimally calibrated and flushed fluid-filled catheters are, Pagnamenta et al. measured PAP with fluid-filled catheters compared to gold standard high fidelity micromanometer-tipped catheters in 8 dogs with PH induced either by ensnarement of the pulmonary arteries or injection of micro-beads.[13] The comparison rested on pulse pressure (sPAP-dPAP, PP), because it is difficult to control the location of the catheter tip micomanometer with respect to the zero level of the external fluid-filled catheter. The results are shown in Fig 1. Measurements of PP were highly correlated, with an analysis according to Bland and Altman showing almost no bias, indicating excellent accuracy. However, the limits of agreement reached ±8 mmHg, which may be insufficiently precise in certain clinical circumstances.

Estimations of LAP by PAWP are generally believed to be accurate based on earlier reports of high levels of correlations.[14] This was recently revisited by Halpern and Taichman in a large quality-control study which included almost 4000 patients with PH who underwent measurements of PAWP during a right heart catheterization and LAP estimated by left ventricular end-diastolic pressure (LVEDP) during a left heart catheterization.[15] The results showed a high level of correlation, a bias of −3 mmHg, corresponding to an expected pressure gradient from small pulmonary veins to the left ventricle at end-diastole, thus indicating excellent accuracy, but limits of agreement ranged from −15 to