Getting More From Right Heart Catheterization: A Focus on the Right Ventricle

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The primary challenge in the care of the patient with advanced pulmonary hypertension (PH) is right ventricular dysfunction with concomitant right heart failure, which is the most important cause of mortality in the disease. It is increasingly evident that the interaction of the heart and pulmonary circulation is a very important aspect that is largely understudied and our previous assessment of right ventricular function has been relatively crude. Here, we highlight the future of integrative assessment of ventricular-pulmonary vascular coupling via hemodynamic measures.

Current Use of Right Heart Catheterization

Cardiac catheterization remains the gold standard for diagnosing pulmonary hypertension, assessing disease severity, and determining prognosis and response to therapy. By directly measuring pressures and indirectly measuring flow, right heart catheterization allows for determination of prognostic markers such as right atrial pressure, cardiac output, and mean pulmonary artery pressure.[1] This procedure has been shown to be safe, with no deaths reported in the NIH registry study.[1] In addition, a recent study reported a procedure-related mortality of 0.055%.[2]

Right heart catheterization determines the presence or absence of pulmonary hypertension, may define the underlying etiology, and allows for prognostication. The most critical aspect of right heart catheterization is that it is performed appropriately, and the data are interpreted accurately. Since end-expiratory intrathoracic pressure most closely correlates with atmospheric pressure, it is important that all right ventricular, pulmonary artery, pulmonary wedge, and left ventricular pressures be measured at end-expiration.[3-5] This is especially true in patients in whom there can be significant variation between inspiratory and end-expiratory vascular pressures (obese patients and patients with intrinsic lung disease).

After determination of the presence of PH, pulmonary venous pressures should be evaluated by the pulmonary capillary wedge pressure (PCWP). Pulmonary arterial hypertension (PAH) is defined by a PCWP of 15 mmHg or less.[5,6] This value is based on the normal PCWP or left ventricular end diastolic pressure (LVEDP) of less than 8 mmHg and the observation that ~14 mmHg is 2 standard deviations from a normal PCWP.[3]

With the exception of patients with severe tricuspid regurgitation, both thermodilution and Fick methods are reliable in patients with PAH for the measurement of cardiac output.[7] Vasodilator challenges with inhaled nitric oxide or intravenous epoprostenol or adenosine are encouraged in all patients at the time of diagnosis and in follow-up studies.[3]

Other Testing During Right Heart Catheterization

Exercise and fluid challenge

Some patients with pulmonary vascular disease are not symptomatic at rest, but have symptoms with exertion. This observation provides a potential for exercise or volume challenge during right heart catheterization to better diagnose *early* pulmonary vascular disease. In patients with risk factors for nonsystolic left ventricle (LV) dysfunction (sleep disordered breathing, systemic hypertension, obesity, diabetes/glucose intolerance) one should consider confrontational testing (to uncover potential increases in PCWP) by administering a fluid bolus challenge or exercise during right heart catheterization particularly if the patient has a resting PCWP between 8 and 15 mmHg.

With regard to the threshold of a mean pulmonary arterial pressure (PAP) of 30 mmHg with exercise, the data to support this as a disease state that is similar to resting PAH are much less robust. The number of pulmonary hemodynamic studies that include exercise are made up of a smaller number of patients.[8] Exercise pulmonary hemodynamics have been reported in 218 healthy subjects (125 in one study of subjects aged 14 to 69 years).[8-10]

The purpose of exercise is not only to examine pulmonary arterial pressure in response to exertion. Rather, the benefit of confrontational testing is the observation of the change/increase in PCWP in an effort to diagnose pulmonary venous hypertension or nonsystolic heart failure. Although protocols for exercise and work-

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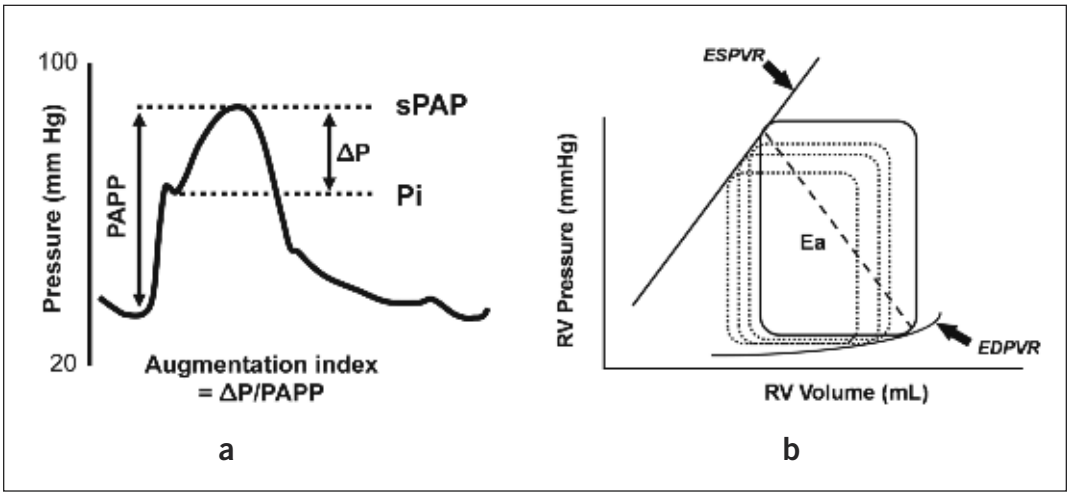

Figure. (a) Schematic showing the measurement of augmentation index using the pulmonary arterial waveform. This augmentation index (ΔP/PAPP) relates the change in pressure (ΔP) to the pulmonary arterial pulse pressure (PAPP) and gives an estimation of pulmonary vascular stiffness. (b) Schematic showing a sample RV pressure volume loop relationship including effective arterial elastance (Ea), end-systolic pressure volume relation (ESPVR), and end diastolic pressure volume loop relationship (EDPVR).

load vary from study to study, and maximal workload exercise has been tested in few subjects, the main goal of exercise is to increase heart rate to 85% maximal age-predicted heart rate as is used in cardiology stress testing. Given increased thoracic pressure changes with exercise, particularly in overweight and/or deconditioned patients, it is critical that measurements be made at end-expiration to ensure uniformity in interpretation.

An increase in PCWP to greater than 15 mmHg in response to exercise or fluid challenge suggests the presence of pulmonary venous hypertension, a condition with dramatically different management than PAH. Because cardiac output can increase up to 5-fold above baseline, pulmonary vascular resistance (PVR) normally decreases with exercise.[8,9] Poor prognostic signs in exercise right heart catheterization are: (1) the inability of the right ventricle (RV) to augment in response to exercise, ie, lack of a significant increase in cardiac output; (2) angina; and (3) presyncopal symptoms or frank syncope.

Novel Hemodynamic Techniques

Assessment of the pulmonary arterial pressure waveform. Chronic pulmonary hypertension results from an increase in pulmonary vascular resistance, which is a simple measure of the opposition to the mean component of flow. However, given the low resistance/high compliance nature of the pulmonary circulation, the pulsatile component of hydraulic load is also critical to consider. The fact that the mean and the pulsatile components of flow are dependent on different portions of the pulmonary circulation suggests that they can be controlled separately, without much overlap.

The pulmonary circulation is pulsatile with multiple bifurcations; and wave reflection is an inevitable consequence. When the forward pressure wave from the heart collides with the backward pressure wave that was reflected from the bifurcations, pressure increases and flow decreases. Because the often used PVR only takes into account mean flow, it does not allow for changes in pulsatility of the pulmonary circuit.[11-14] One must consider the elastic properties of the pulmonary circulation and impedance on RV performance rather than the pure resistive properties since the heart could not function if it were not for the elastic properties of pulmonary vasculature. During systole, the pulmonic valve is open at a time when the mitral valve is closed. Thus, if it were not for the elastic properties of the pulmonary vasculature, the heart could not develop forward flow.[12-14]

Pulse pressure indicates the amplitude of pulsatile stress. Pulse pressure is mainly determined by both the characteristics of ventricular ejection and arterial compliance, so that the lower the compliance, the higher the pulse pressure. Moreover, pressure waveform analysis performed in the time-domain makes it possible to calculate the timing and extent of wave reflection in systemic and pulmonary circulation using measures such as augmentation index (as shown in the **Figure**) which roughly represents reflected wave summation (ΔP) in the pulmonary circuit and normalizes for pulmonary arterial pulse pressure.[15-23]

These values can be easily obtained at the time of right heart catheterization and the future studies will compare both analyses as potential prognostic indicators in patients with pulmonary hypertension.[24]

Right ventricular pressure volume loop relations. The use of pressure-volume (PV) loop analysis as a means of measuring load-independent contractility has largely been restricted to the study of LV hemodynamics and the interaction between the LV and the systemic vasculature.[21,25-36] This has primarily been due to geometric differences between the 2 ventricles and the optimal conductance properties required for proper volume measurements and the belief that it is difficult to obtain consistent data using conductance measurements in the crescent-shaped RV.

Under conditions of normal PAP and RV function, an analysis of the RV PV loop is somewhat complicated given the crescent shape of the normal RV (**Figure**) and the ellipsoid shape of the PV loop obtained under these conditions. However, under conditions of even only modestly increased load, the RV changes shape to one resembling the more spherical LV and allows for measurement of end-systolic elastance (Ees) and effective arterial elastance (Ea) as well as the more accurate measurements of indices of RV systolic and diastolic function as well as RV/PA coupling (**Figure**).

The performance of such studies is relatively easy and can be made in the same acquisition time as making measurements using FDA-approved equipment. Essentially, all of the currently used PAH therapies, particularly the phosphodiesterase inhibitors and endothelin receptor antagonists as well as many of the emerging experimental therapies (eg, imatinib) have primary—positive or negative—effects on the myocardium.[37-44] Thus, a study of the intrinsic contractility of the RV is perhaps the only reliable way to separate the effects of these therapies on pulmonary arterial systolic pressure versus the RV myocardium. In that sense, studies of the RV contractility are not only relevant to the clinical management of PAH patients but critical for the interpretation of data from clinical trials as well.

Summary

While traditional resting right heart catheterization techniques still remain the gold standard for diagnosing pulmonary hypertension and managing patients on therapy, there are novel techniques that do not add significant time or risk to the procedure that may add greatly to our understanding of the RV and the interaction of the RV with the pulmonary circulation.

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