Noninvasive Assessment of Pulmonary Artery Pressures
Moving Beyond Tricuspid Regurgitation Velocities
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Pulmonary hypertension (PHTN) has been classified according to the world health organization as (1) pulmonary arterial hypertension (including idiopathic, familial, and associated with collagen vascular disease or HIV), (2) PHTN with left heart disease, (3) PHTN associated with lung diseases and/or hypoxemia, (4) PHTN caused by chronic thrombotic and/or embolic disease, and (5) miscellaneous.1 PHTN commonly causes symptoms of breathlessness, fatigue, and eventually right heart failure. In addition to the functional limitations, elevated pulmonary artery pressures are associated with reduced long-term survival that is related to the severity of PHTN, the patient’s functional class, and the underlying etiology of the PHTN.2 The prognosis is worse in patients with HIV or collagen vascular disease, intermediate in those with idiopathic pulmonary hypertension, and best in those with congenital heart disease.2 Some medical therapies have been shown to improve functional class and survival in patients with PHTN.3 Because of the morbidity and mortality associated with this condition, reliable methods for diagnosing PHTN are needed. Equally as important, given the substantial expense of current medical treatments, it is imperative that we have reproducible methods for serially assessing pulmonary artery pressure noninvasively.

Echocardiography with Doppler interrogation of the tricuspid and pulmonic valves has been recommended by the European Society of Cardiology as one of the first steps in evaluation of the patient with suspected PHTN.4 The velocity of the tricuspid regurgitation (TR) jet measured with continuous-wave Doppler echocardiography correlates with pulmonary artery systolic pressure and is the mainstay of assessing the severity of PHTN. However, to be useful there must be a large enough regurgitant volume to produce a Doppler signal that allows accurate measurement of the peak TR velocity. This is frequently not the case,5 even in settings where PHTN is likely.6 In addition, to accurately measure pulmonary artery systolic pressure from TR velocities, it is necessary to know or estimate the mean right atrial pressure. Noninvasive assessment of right atrial pressure is challenging and often inaccurate.7 Because of these and other problems, traditional echocardiographic Doppler assessment of pulmonary artery pressures may be unfeasible or may lead to overestimation or underestimation of pulmonary pressures in up to 40% of individual patients.4,5,7 In short, the traditional echocardiographic approach is not as consistent or as accurate as it needs to be for research studies or clinical decision making.4,8,9

Chronic PHTN is associated with loss of elasticity in the pulmonary vascular bed. Stiffening of the vasculature results in greater reflection of pressure waves from bifurcations in the pulmonary vessels during the pulsatile ejection of blood from the right ventricle. Summation of forward and reflected pressure waves will result in truncation of the forward flow.10 In 1983, Kitabatake et al11 reported that acceleration time (AT) or the ratio of AT to ejection time (ET) measured from the pulsed-wave Doppler signal in the right ventricular outflow tract decreased with increases in mean pulmonary artery pressure. They found a very strong inverse correlation between AT/ET and log mean pulmonary artery pressure ($r = -0.90$). Subsequently, several groups have successfully used similar concepts and parameters to assess pulmonary artery pressures or pulmonary vascular resistance.12 Although the studies are not directly comparable, correlations between the spectral Doppler measures of right ventricular outflow systolic time intervals and invasively measured pulmonary artery pressures appear to be at least as strong as those between TR velocities and invasively measured pulmonary pressures. Good-quality pulsed-wave Doppler signals of the right ventricular outflow tract can be obtained in the vast majority of patients—probably more frequently than we can obtain measurable TR velocities. Given the relative ease of recording and quantifying right ventricular outflow tract Doppler signals, it is surprising that these measures have not caught on as part of routine clinical practice.

In this issue of Circulation Cardiovascular Imaging, Thibault et al13 describe the utility of pulsed-wave Doppler measurements at the tips of the pulmonary leaflets in murine models of acute and chronic PHTN. In the field of PHTN research, as in many others, transgenic mouse models will have a significant role in helping to unravel the pathophysiology of the disorder. In addition to many different transgenic models of elevated pulmonary artery pressures, PHTN may be induced acutely or chronically in small animals by using pharmacological interventions.14 Animal models that are useful in predicting which new treatments may have beneficial effects in humans would be of great value. Although mice have many advantages when used as models to study the pathophysiology of PHTN, it is difficult to obtain apical

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imaging windows in this species. The lack of apical windows limits the ability to accurately measure TR velocities. Even more problematic, mice tend to have very small amounts of TR, even when they have PHTN. Given the limitations of measuring TR velocities, an alternative noninvasive technique that is capable of serially assessing pulmonary pressures in mice would be welcome. The results from the current study look very promising. Using a high-frequency ultrasound system, clearly defined spectral Doppler signals from the proximal pulmonary artery were obtained in the mice. The Doppler waveforms showed marked shortening of the pulmonary artery AT and AT/ET as right ventricular systolic pressures rose. This was true in both acute (due to infusion of the thromboxane agonist U-46619) and chronic (interleukin-6 overexpression) models of PHTN. The sensitivity and specificity of pulmonary artery AT and AT/ET for detecting right ventricular systolic pressure >2 SD above normal were high (100% and 86%). Interobserver variability in the measurements was quite good (<6%). Using the ratio of AT to ET mitigates the effects of different heart rates that are likely to be present in long-term therapeutic studies. Interestingly, AT/ET is similar in mice and humans despite heart rates that are almost 10-fold higher in mice.

The findings of the current study should stimulate new research using murine models of PHTN. It will be important to prove whether the pulmonary artery ejection time intervals can accurately detect small or moderate reductions in right ventricular or pulmonary artery systolic pressure during chronic treatment. Similarly, it appears that measurement of right ventricular outflow tract or pulmonary artery systolic time intervals as a method for assessing pulmonary artery pressures has been sufficiently validated to warrant incorporation into clinical trials. Pulmonary artery AT and AT/ET should be compared directly with TR velocity in larger clinical populations with PHTN of various etiologies. Perhaps more importantly, these indexes should be studied for their ability to track response to treatments. Echocardiography is remarkably useful in the assessment of patients with known or suspected PHTN. Even without a wholly reliable method to assess pulmonary artery pressures, the ability to assess right atrial size; atrial and ventricular septal contours; right ventricular size, thickness, and function; pulmonary artery size; pericardial effusion; and the detection of intracardiac shunts is extremely useful. Adding an additional and perhaps more reliable noninvasive method for assessment of pulmonary pressures would represent an important advance in the PHTN field and another step forward for the remarkably durable and still evolving technique of echocardiography.

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**References**


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