

# Echocardiographic Assessment of Left Ventricular Diastolic Dysfunction: Differentiating a Pulmonary Vascular From a Pulmonary Venous Origin of Pulmonary Hypertension



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Pulmonary hypertension (PH) is a heterogeneous condition that may be due to a primary pulmonary arteriolar vasculopathy (pulmonary arterial hypertension or PAH: Group I), or secondary to left heart disease and pulmonary venous hypertension (PVH: Group II), chronic respiratory conditions (Group III), chronic thromboembolic disease (CTEPH: Group IV) or miscellaneous/multifactorial causes (Group V).<sup>1,2</sup> The clinical diagnoses themselves are as diverse as the varied hemodynamic compositions of PH. Pulmonary hypertension ultimately results from varying interactions between pulmonary blood flow, pulmonary vascular resistance (PVR), conduit vessel compliance, and downstream left atrial (LA) pressure. Therefore, PH may also result from abnormalities in one or more of these factors. Patients with PAH, CTEPH, and most Group III patients have a “precapillary” hemodynamic profile with a normal LA pressure and an increased PVR as the primary mechanism of their PH. In contrast, patients with PVH (“postcapillary”) have increased LA pressure, most often with a normal or only mildly elevated PVR.

Both clinical and hemodynamic distinctions need be made in order to assign the appropriate PH diagnosis. This is particularly true when discerning PAH from PVH, as PH-specific therapy (prostacyclins and endothelin receptor blockers, in particular) is intended for patients with PAH and will have either no effect, or will potentially exacerbate the condition of a patient with left heart disease.<sup>3-5</sup>

Patients with pulmonary vascular disease (ie, PAH or CTEPH) and those with PVH will present with dyspnea on exertion as their most common complaint. On initial Doppler-echocardiography (DE) examination, both groups will often have normal left ventricular (LV) systolic function (normal LV ejection fraction) and elevated pulmonary pressure estimations. Moreover, these patients will often have evidence of “diastolic dysfunction” on Doppler assessment,<sup>6-8</sup> albeit for different physiologic reasons. Thus, patients with PAH and PVH might appear to share some features on a cursory initial DE assessment, particularly if one merely relies on the echocardiogram report. However, this can be very misleading, as a more thorough DE assessment will often reveal marked phenotypic differences between the PAH and PVH patient. Clearly it is neither practical nor cost effective to refer

all patients with elevated pulmonary pressures for cardiac catheterization as an initial diagnostic strategy. However, 2-dimensional (2-D) and DE can provide a useful means of evaluating left-sided structural heart disease, LV diastolic dysfunction, and LA pressure, as well as providing key clues to the presence of pulmonary vascular disease that greatly assist in differentiating the etiology of PH.

## WHAT IS LV DIASTOLIC DYSFUNCTION?

The definition of LV diastolic dysfunction (LVDD) may vary depending on one’s perspective. From a physiologic viewpoint, the term LVDD may be used to describe the presence of impaired LV relaxation and/or increased passive LV stiffness in the presence of normal or abnormal LV systolic function. In the presence of LV systolic dysfunction (LVSD), LVDD is nearly universally present, given the functional and structural abnormalities that lead to LVSD also lead to LVDD. A fundamental aspect of LVDD in either context is an impaired diastolic pressure-volume relationship, leading to exaggerated increases in left heart filling pressures within a relatively narrow range of LV preload.

From the clinician’s perspective,

LVDD is often invoked when a patient presents with a clinical diagnosis of heart failure despite a preserved ejection fraction (HFpEF). Indeed, studies have shown that impaired LV relaxation and abnormal diastolic pressure-volume relations exist in HFpEF. However, there are clearly other factors involved, including increased systemic arterial stiffness, abnormal dynamic ventriculo-arterial coupling reserve, chronotropic incompetence, and impaired systemic vasodilatory reserve that exceed the scope of the current review.<sup>9-12</sup>

Another situation that often arises for the clinician is when LVDD is present on an echocardiography report, often when the study is being performed for the indication of dyspnea. Typically, this information refers to alterations in the transmitral Doppler filling pattern. Often, the report will indicate the presence of a normal left ventricular ejection fraction (LVEF), LVDD, along with some degree of PH. In this context, it is contingent upon the clinician to determine whether the LVDD is the cause or effect of the PH and which of these factors is primarily responsible for the patient’s dyspnea.

This last scenario is where we will primarily focus our discussion, as this is a situation quite commonly encountered in clinical practice. To be most effective in this context, the clinician must appreciate that LVDD is not an all or none phenomenon, but rather exists on a continuum of severity, provides evidence of a range of

resting LA pressure, and may arise directly from left heart disease or indirectly from right heart disease and its related and interdependent effects on the left heart.

## THE 2-D EXAMINATION AND DIASTOLIC DYSFUNCTION

Though DE is generally considered the principal means of assessing LVDD, standard 2-D assessment of left and right heart structures often provides powerful initial insight into the stereotypical and often requisite morphologic changes that should be present if LVDD is the primary underlying process. The size, shape, and function of left- and right-sided structures will typically assume that of the primary disease process, and thus may be thought of as bearing witness to the predominant underlying disease problem. As such, the 2-D examination should always be integrated with the DE examination to aid in the overall interpretation of LVDD.

Left atrial enlargement (LAE) is very common in the presence of LVDD arising from left-sided structural heart disease and points to both the presence and chronicity of elevated left-sided filling pressures.<sup>8,13,14</sup> Left atrial size can be evaluated in both parasternal long axis and apical views, with a normal upper limit of 4.0 cm in anterior-posterior dimension, measured from the parasternal long axis. From the apical 4-chamber view, the left atrium is typically larger than the right atrium under normal circumstances, with this difference becoming more conspicuous in the presence of left-sided heart disease. When the reverse is true, a primary right-sided process should be a key consideration in the differential diagnosis.

The LV wall thickness is also measured from the parasternal long axis view using 2-D or M-mode echocardiography. The upper limit of LV septal and posterior wall thickness at end-diastole is 1.1 cm. The presence of even a mild degree of left ventricular hypertrophy (LVH) is strongly suggestive of decreased LV compliance with concomitant impaired diastolic relaxation.

Finally, the position of the interatrial septum can help to determine the relative difference between left and right atrial pressures. The interatrial septal position is

best appreciated from the apical 4-chamber view, and under normal circumstances will bow slightly from left to right in diastole due to the slightly higher pressure in the left atrium. In the context of LA hypertension, the left to right bowing becomes more conspicuous. However, if the interatrial septum bows from right to left into the left atrium, this is strongly suggestive of RA pressure elevation and consistent with PH due to elevated PVR.

## THE DOPPLER ASSESSMENT OF DIASTOLIC FUNCTION

Left ventricular diastolic function is most often expressed through a variety of Doppler parameters used to assess the pattern of LV filling. The most widely employed measure is pulsed wave (PW) Doppler of LV inflow through the mitral valve in diastole. This is typically obtained by placing the Doppler cursor at the tips of the mitral leaflets in the apical 4-chamber view. In the normal LV, the majority of filling occurs in early diastole producing an early or “E” wave. With atrial systole, an “A” wave is generated which is typically of lower velocity than the E wave, producing an E:A ratio  $>1$ , and typically between 1.0-1.5 m/s with an E wave deceleration time between 150-200 ms. In the presence of impaired LV relaxation and normal sinus rhythm, LV filling is redistributed from early to late diastole with a resulting fall in E wave velocity, rise in A wave velocity, and increase in E wave deceleration time to  $>200$  ms. This E/A reversal is termed grade I diastolic dysfunction, and is seen commonly in patients with hypertensive heart disease as well as in relatively healthy patients over 65 years of age.<sup>15,16</sup>

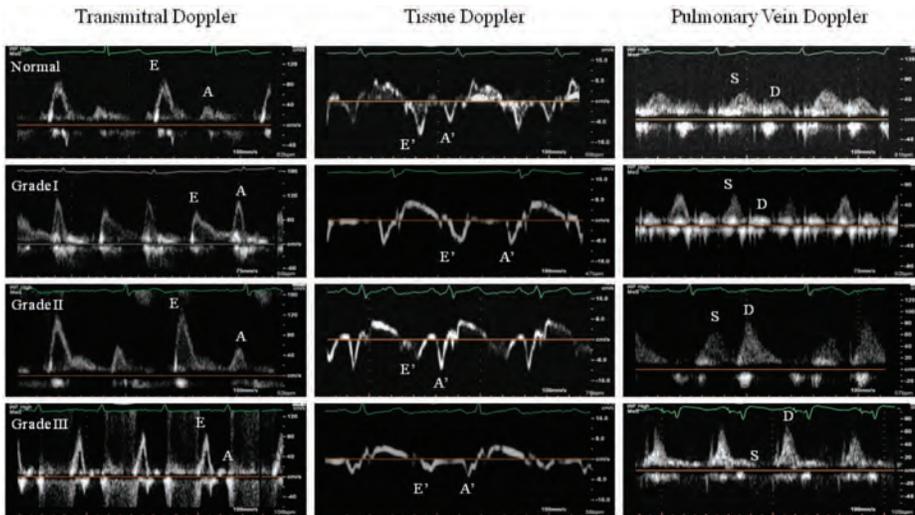
Generally, grade I diastolic dysfunction is associated with *normal* LA pressure, which belies the relatively low filling velocity across the mitral valve at the onset of diastole. A common misconception among clinicians is that the presence of *any* reported degree of LVDD is synonymous with LA hypertension. As a result, an increased Doppler pulmonary artery systolic pressure (PASP) in this context is often incorrectly assumed to be arising from an increased LA pressure. In fact, in PAH at least 70% of patients have grade I

diastolic dysfunction, owing to the interdependent effects of RV dysfunction on LV filling in the context of a normal LA pressure.<sup>6,17</sup> A crucial distinction here is that that the LVDD is the result, not the cause, of the PH. Moreover, PAH patients will often revert to a normal transmitral filling pattern following PH-specific therapy.<sup>18</sup>

As the LA pressure rises with worsening LVDD, the pressure gradient from left atrium to left ventricle in early diastole rises, increasing the E wave velocity and abbreviating the E wave deceleration time to 150-200 ms. As a result, the E:A ratio appears normal and thus, grade II diastolic dysfunction is also termed a “pseudonormal” transmitral flow pattern. The pseudonormal pattern can be differentiated from a normal pattern by use of imaging with a Valsalva maneuver, which briefly lowers LA pressures and unmasks the underlying grade I transmitral filling pattern. More simply, however, a “normal” transmitral filling pattern in the context of significant LVH and LAE is most often pseudonormal, and thus indicative of LA hypertension.

With further worsening of diastolic function and a further rise in LA pressure, an even higher proportion of LV filling will occur in early diastole, and the contribution of atrial systole diminishes such that the E:A ratio is greater than 2 and the E wave deceleration time shortens further to  $<150$  ms. This is termed grade III diastolic dysfunction or a restrictive filling pattern and is most often associated with severely elevated LA pressure. Representative examples of the various grades of diastolic dysfunction are illustrated in Figure 1.

Additional Doppler techniques can be employed to further clarify the pattern of diastolic function, including analysis of pulmonary vein inflow, color M-mode, and tissue Doppler imaging. Tissue Doppler imaging (TDI) is the most commonly utilized of these methods, and is performed by placing a PW Doppler cursor about 1 cm apical of the mitral annulus along the interventricular septum and/or lateral LV wall, directly measuring the velocity of myocardial relaxation. In the normal LV, TDI produces an E' wave and



**Figure 1: Transmitral Doppler, tissue Doppler imaging and pulmonary vein flow in the normal heart and with various grades of diastolic dysfunction. E, early wave; A, atrial wave; E', tissue Doppler early wave; A', Tissue Doppler atrial wave; S, pulmonary vein systolic wave; D, pulmonary vein diastolic wave.**

an A' wave similar to the normal pattern of PW Doppler of mitral valve inflow, but with much lower overall velocities. With worsening degrees of diastolic dysfunction and impaired LV relaxation, the velocity of early myocardial relaxation (E') decreases, and thus there is reversal of the E' and A' waves. An advantage of TDI is that the E' velocity has been shown to be relatively independent of loading conditions, and thus will remain low despite increased LV end diastolic pressure (LVEDP). As a result, the ratio of transmitral E wave velocity and TDI E' velocity (E/E' ratio) will increase in the context of a high LVEDP. An E/E' ratio >15 correlates well with a LVEDP >20 mm Hg, whereas an E/E' ratio <8 correlates well with a normal LVEDP.<sup>19,20</sup> An E/E' ratio between 8-15 is often indeterminate of LA pressure and, in this context, it is very important to integrate other features from the overall DE examination; for example, an E/E' of 14 is more likely to indicate left heart congestion in the context of LAE and LVH. Examples are shown in the center panel of Figure 1. One additional clue from TDI to the presence of PAH is a marked disparity in TDI velocities between the septal and lateral LV walls, possibly due to septal bowing from the RV slowing septal, but not lateral,

early LV relaxation velocities.<sup>21</sup> Tissue Doppler imaging is limited in patients with mitral annular calcification or prior mitral valve surgery, and also requires accurate placement of the TDI cursor on the septal and lateral walls under the mitral annulus.

As briefly mentioned above, the pattern of pulmonary vein inflow can also be used to evaluate diastolic function and, similar to TDI, provides important additional or corroborative evidence to the nature of LVDD. In the normal LV, the majority of flow from the pulmonary veins into the left atrium occurs during ventricular systole (S wave) with a lesser component in diastole (D wave); as a result, the S:D ratio is typically >1. With early impaired LV relaxation, the S wave velocity is accentuated such that the S:D ratio rises >1. However, with progressive LVDD and rising LA pressure, there is less systolic and greater diastolic pulmonary vein inflow. As a result, S wave velocity decreases, D wave velocity rises, the S:D ratio is <1, and the D wave deceleration time falls. Pulmonary vein Doppler is limited by the ability to accurately interrogate the pulmonary veins, and the Doppler profiles are also strongly impacted by the presence of significant mitral valve disease.

## DIFFERENTIATING A PULMONARY VEIN FROM PULMONARY ARTERIAL CAUSE OF PH

In the context of known or suspected PH, perhaps the single most common error in the DE interpretation is to overestimate the importance of the Doppler PASP estimate (PASP<sub>Doppler</sub>). The PASP<sub>Doppler</sub> is an *estimated* PASP and is not synonymous with an invasively derived PASP (PASP<sub>invasive</sub>). Prior studies have shown that approximately 50% of PASP<sub>Doppler</sub> estimates are >10 mm Hg different from PASP<sub>invasive</sub> measurements.<sup>22,23</sup> PASP<sub>Doppler</sub> overestimates and underestimates occurred with similar frequency, but for different reasons. Overestimates typically occur in the context of a well-visualized Doppler tricuspid regurgitation (TR) envelope, with an important percentage of the overestimates occurring due to right atrial pressure overestimation from the inferior vena cava method.<sup>23,24</sup> In contrast, PASP<sub>Doppler</sub> underestimates typically occur in the context of inadequate TR jet visualization, with underestimates generally being of greater magnitude, thus more often leading to clinical misclassification of the severity of PH. In addition, the mere presence of PH via Doppler, or for that matter, right heart catheterization, does not provide the additional information needed to determine why the individual patient has PH. In this same study, 4 of 6 subjects with no visible TR (thus precluding PASP<sub>Doppler</sub>) were found to have moderate or greater PH by right heart catheterization; thus a lack of TR should not be considered proof of a lack of PH.

A second pitfall in the DE interpretation in the context of PH is to underestimate or not account for the importance of RV size, shape, and function. The RV is a thin-walled, distensible chamber that will take on stereotypical morphologic changes relatively early in the presence of pulmonary vascular disease. In contrast, these changes are most often less striking or conspicuously absent in the presence of PVH. Generally speaking, abnormal right-sided heart findings are underappreciated and underreported, which in part reflects clinical practice and also a hesitation to comment on such findings due to

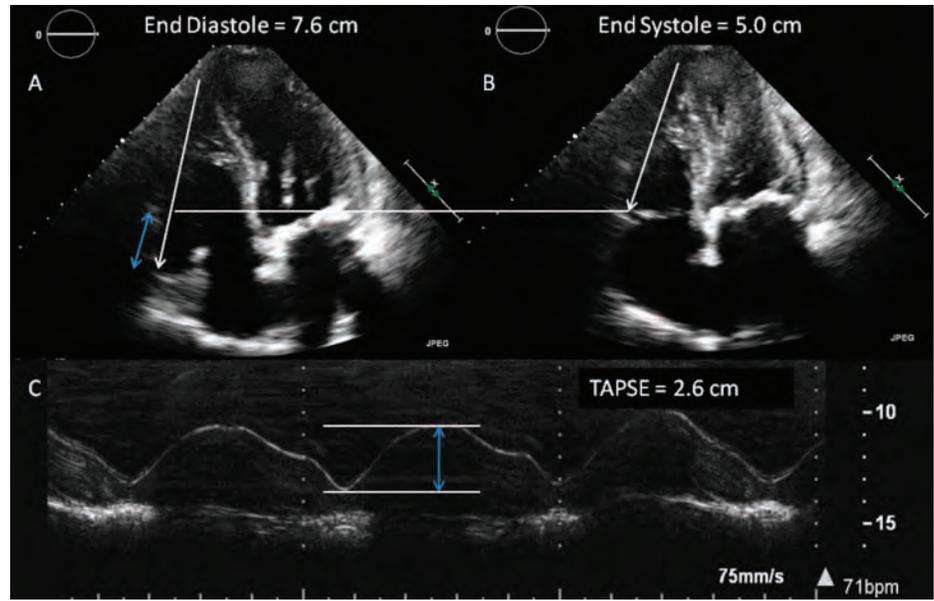
lack of confidence in the ability to quantify these parameters. Despite inherent limitations in RV image assessment related to complex RV geometry and endocardial definition, relatively simple and reproducible methods of RV size, shape, and function assessment do exist and can be easily applied to the routine DE examination (*vide infra*).

## PULMONARY VENOUS HYPERTENSION

### 2-D and Doppler Examination

The standard DE examination will typically reveal obvious left-sided structural heart disease in patients with PVH. The 2 most obvious examples are reduced LV systolic function and significant left-sided valvular heart disease. At minimum, the presence of a dilated, dysfunctional left ventricle strongly suggests the presence of PVH as the predominant mechanism of PH. Similarly, severe mitral stenosis or regurgitation will predictably lead to marked pulmonary venous congestion.<sup>25-28</sup> In either case, management of the PH must begin with treatment of the underlying LV systolic dysfunction and/or valvular disease. Of note, the severity of mitral regurgitation (MR) may be underappreciated by transthoracic echocardiogram, particularly if the MR jet is highly eccentric and adherent to the wall of the left atrium. In such cases, transesophageal echocardiography may better delineate the degree of MR. Moreover, the clinician should be cautioned on dismissing “moderate” MR as the cause of PH. Moderate MR may cause severe PH, especially if there is concomitant LV diastolic dysfunction that amplifies the degree of associated LA hypertension and/or if this degree of MR is chronic, thus exposing the pulmonary venous system to years of moderate left heart congestion.

In the presence of a normal LVEF, the etiology of the PH may not be as obvious, or may be perceived as less obvious. However, factors that directly reflect or predispose to pulmonary venous congestion may be equally prominent in the presence of normal LV systolic function. For example, the presence of LAE, expressed as either increased LA dimension or vol-



**Figure 2: Measurement of tricuspid annular plane systolic excursion (TAPSE) in a patient with PVH secondary to mitral valve disease and normal RV function. Panels A and B illustrate end-diastolic and end-systolic frames from the apical 4-chamber view. Normal TAPSE of 2.6 cm measured from the 2-D images is denoted by blue arrows. Panel C illustrates measurement of TAPSE using M-mode of the tricuspid annulus (blue arrows).**

ume, is one of the most powerful discriminants of HFpEF versus hypertensive heart disease without heart failure.<sup>8</sup> Given that PH is nearly universally present in HFpEF, LAE often provides an early and important clue that PH is arising from a left heart cause. In addition, a greater degree of LVH, and thus increasing LV mass, is another powerful predictor of HFpEF and PVH.

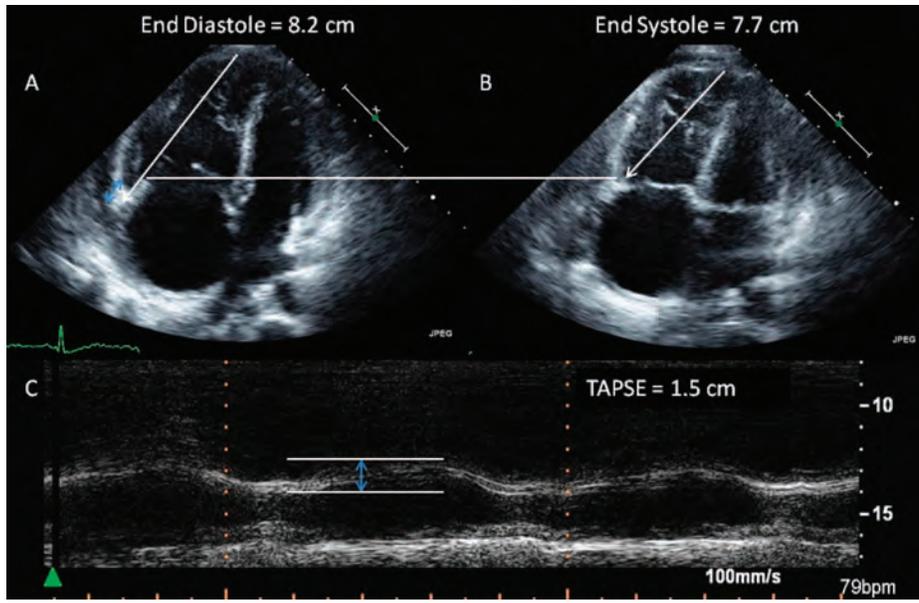
The reporting of any degree of LVDD should not be taken to indicate a patient's PH is arising from LA congestion. As mentioned above, LVDD exists on a continuum of severity, closely related to the degree of LA pressure elevation associated with each grade of LVDD.<sup>29</sup> The transmitral Doppler examination will typically reveal either grade II or grade III diastolic dysfunction in the presence of PVH.<sup>8</sup> In fact, a restrictive transmitral flow pattern is one of the most powerful predictors of PVH, and provides very strong evidence toward PVH and away from PAH well before invasive hemodynamics are obtained.

### RV Function

A quantitative measure of RV function should be a part of any routine DE exam-

ination. The most common and arguably least ideal method of RV function assessment by echocardiography is visual estimation, which is essentially a visual integration of the change in RV cavity area to estimate global RV function. This method is highly subjective and also requires a certain degree of endocardial definition, which often accounts for why one reader's “severe” may be another's “mild” RV dysfunction. A more quantitative approach to global RV function assessment is to measure total systolic area change of the RV, referred to as the RV fractional area change (RVFAC =  $\text{RV area end-diastole} - \text{RV area end-systole} / \text{RV area end-diastole}$ ) from the apical 4-chamber view. Although this method incorporates both longitudinal and transverse RV shortening into a single measurement, this method is also limited by incomplete endocardial definition, leading to relatively high inter- and intraobserver variability.<sup>30,31</sup>

Another approach to RV function assessment measures the longitudinal contribution to RV function, which accounts for the majority of total RV contraction in normal and PAH hearts.<sup>32-34</sup> The most commonly used method measures the total longitudinal systolic displacement of



**Figure 3: Measurement of tricuspid annular plane systolic excursion (TAPSE) in a patient with PAH and severely reduced RV function. Panels A and B illustrate end-diastolic and end-systolic frames from the apical 4-chamber view. TAPSE of 1.5 cm measured from the 2-D images is denoted by blue arrows. Panel C illustrates measurement of TAPSE using M-mode of the tricuspid annulus (blue arrows).**

the RV base toward the RV apex (referred to as tricuspid annular plane systolic excursion, or TAPSE). TAPSE can be derived from 2-D echocardiography or M-mode (Figures 2 and 3), is simple to perform, and has been shown to be highly reproducible, in part due to the lack of reliance on RV endocardial definition or geometric assumptions.<sup>31,33</sup> A normal TAPSE is 2.4-2.7 cm, with lesser values indicating mild (1.9-2.2 cm), moderate (1.5-1.8 cm), and severe (less than 1.5 cm) RV dysfunction.<sup>34-36</sup> Tissue Doppler imaging can also be used to measure the velocity of RV contraction in the longitudinal axis (denoted  $S'$ ), correlates with TAPSE ( $r=0.90$ ), and is also a simple and reproducible method of RV function assessment.<sup>37</sup>

Doppler echocardiography can also be used to provide a composite measure of RV systolic and diastolic function, through application of the myocardial performance index (MPI or Tei index) to the RV.<sup>38</sup> This utilizes pulsed wave, or more commonly, tissue Doppler signals to measure the following time intervals: isovolumic relaxation time (IVRT), isovolumic contraction time (IVCT), and RV ejection

time (RVET). The MPI is then calculated using the formula:  $(IVRT + IVCT)/RVET$  with increasing values representing worsening overall systolic and diastolic function. In children, the normal MPI is 0.24 and in adults, 0.28.<sup>39</sup> The Tei index has been used to quantify RV function in congenital heart disease with systemic right ventricles and in adults with PAH.<sup>39-41</sup> The major limitation of the RV MPI is that its derivation is somewhat cumbersome, and this has limited its widespread utilization in clinical practice. In addition, there is concern that significant RV hypertrophy can shorten the IVRT and lead to a paradoxically low MPI, despite an abnormal, hypertrophied RV with RV dysfunction.<sup>42</sup>

In subjects with LVSD, the degree of RV dysfunction varies widely, and depends on the relative amount of RV cardiomyopathy and degree of PVR (RV afterload). Importantly, an increased PASP only carries prognostic significance in the presence of RV dysfunction.<sup>43</sup> In the vast majority of patients with PVH, RV size, shape, and function will remain relatively normal, given that the PVR is within normal range.<sup>44</sup> As a result, in an

apical 4-chamber view, the RV dimension and area should remain smaller than the LV (RV:LV ratio  $<1.0$ ), the RV apical angle should remain relatively sharp and not form or share the apex of the heart, and the TAPSE should be relatively well preserved (ie,  $\geq 2.0$  cm). This triad of findings provides rapid insight into the relative lack of concomitant pulmonary vascular disease, and when combined with LAE, LVH, and grade II or III diastolic dysfunction, further strengthens the assessment in favor of PVH over PAH.<sup>45</sup>

## PULMONARY ARTERIAL HYPERTENSION

### 2-D and Doppler Examination

Among patients with PAH (WHO Group I), the 2-D echocardiogram generally reveals the absence of LV enlargement and LVH unless there is pre-existing concomitant left heart disease. At least 80% of subjects will have a normal LA size. Typically, LV cavity size is smaller than normal, owing to RV enlargement and LV compression with the confined pericardial space. Similarly, the LVEF is often in excess of 65% due to an underfilled and hyperdynamic function. Greater than mild mitral valve disease is found very infrequently in patients with PAH.<sup>6</sup>

Doppler evaluation of LV diastolic function reveals a pattern of E:A reversal in up to 70% of patients with PAH, along with reduced E' TDI velocities in the LV. This pattern occurs as a consequence of transmitted pressure from the RV through the shared interventricular septum in early diastole, causing impaired LV relaxation and diminished early LV filling. Though this transmitral pattern is labeled as grade I diastolic dysfunction, it is important to note that this pattern is not synonymous with LA hypertension. Indeed the combination of RV enlargement, RV dysfunction, and a pattern of E:A reversal strongly signifies a normal LA pressure and a high PVR.<sup>6</sup>

### RV Function

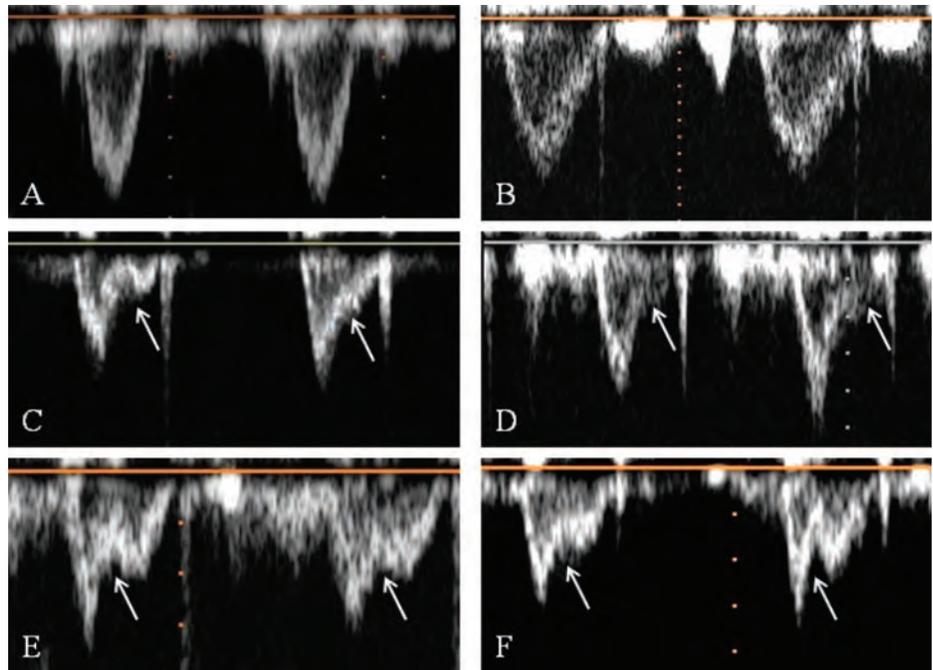
In patients with PAH, the RV almost universally bears morphologic evidence of the chronically elevated RV afterload,

with a characteristic *triad* of findings present: RV dilatation, systolic interventricular septal displacement or flattening (right to left), and RV systolic dysfunction.<sup>6</sup> In addition, patients with PAH will nearly always have an RV:LV area or dimension ratio >1.0, rounding of the RV apical angle, and the RV will either form or share the apex of the heart.<sup>31,46</sup> The degree of RVH varies, in part, related to the chronicity of the condition, and likely, the individual patient's hypertrophic response to afterload. The average TAPSE in patients with PAH prior to PH-specific therapy ranges from 1.6-1.9 cm, and is thus well below normal.<sup>31,34,47</sup> These same features are also seen in patients with CTEPH as well as in subjects with a chronic respiratory disorder and significant pulmonary vascular disease.

#### Additional Doppler Methods

Measurement of PVR is one of the primary reasons for referring many patients for invasive hemodynamic assessment. Several echocardiographic techniques have been employed to try to estimate PVR noninvasively. The most commonly employed method uses a quotient of a surrogate of pressure/flow ( $PVR_{Doppler} = TR \text{ jet velocity} / VTI_{RVOT}$ ). This method correlates with invasive PVR within a relatively normal PVR range, but performs less well when the PVR is markedly elevated.<sup>48,49</sup> In addition, this formula is inherently a measure of total pulmonary resistance (TPR) rather than PVR, and a recent study suggested a better correlation with invasive PVR when the formula was modified to include an estimate of LA pressure.<sup>50</sup>

An alternative means of evaluating PVR and pulmonary vascular disease takes advantage of visual evidence for pathologic wave reflection arriving at the RV during systole.<sup>44</sup> The normal PW Doppler profile in the RV outflow tract (RVOT) is smooth, parabolic, without notching of the Doppler envelope (Figure 4, panels A, B). This is strongly indicative of a normal pulmonary vasculature. In fact, the absence of Doppler notching in the presence of PH predicts an increased LA pressure and normal PVR with an odds ratio of approximately 30:1.<sup>44</sup> In

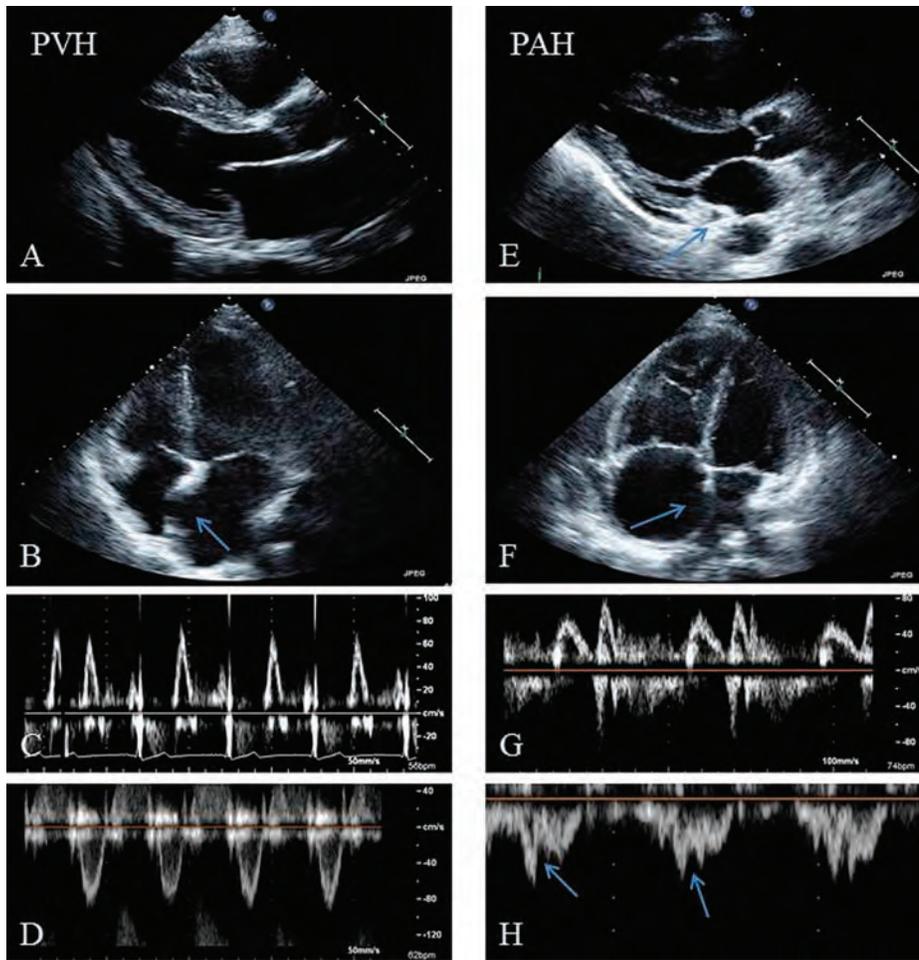


**Figure 4: Notching of the pulse wave Doppler profile in the right ventricular outflow tract in patients with pulmonary vascular disease. Panels A and B show normal, parabolic, or triangular RVOT Doppler profiles without notching. Panels C and D show examples of late-systolic notching. Panels E and F demonstrate mid-systolic notching (arrows).**

**Table 1: Typical 2-D and Doppler Echocardiographic Findings to Differentiate a Left- vs Right-Sided Etiology of Pulmonary Hypertension**

Left-Sided Origin of PH	Right-Sided Origin of PH
<i>2-D Echocardiographic Findings:</i>	
LVH, LAE	Normal LV size, normal LA size
Variable LV function	Normal LV function
Normal RV size	RV dilation (ratio of RV:LV size >1)
No interventricular septal bowing	Right to left interventricular septal bowing
Atrial septum neutral or bowed to right	Atrial septum bowed to left
Normal or mildly reduced RV function	Mild to severe RV dysfunction
No pericardial effusion	Mild to moderate pericardial effusion
<i>Doppler Findings:</i>	
≥2+ mitral valve disease (MR or MS)	Minimal or no MR or MS
Grade II or III diastolic dysfunction	Normal diastolic function or grade I diastolic dysfunction (E:A reversal)
Variable TR	Variable TR (TR severity > MR severity)
Absence of notched pattern in Doppler signal obtained from RVOT	Notched Doppler signal in RVOT
Variable PASP (typically <70 mm Hg)	Variable PASP (typically ≥70 mm Hg)

Abbreviations: LVH, left ventricular hypertrophy; LAE, left atrial enlargement; LV, left ventricle; LA, left atrium; RV, right ventricle; MR, mitral regurgitation; MS, mitral stenosis; TR, tricuspid regurgitation; RVOT, right ventricular outflow tract; PASP, pulmonary artery systolic pressure



**Figure 5: Integrated 2-D and Doppler echocardiographic assessment of patients with PVH (left panels) and PAH (right panels). The PVH patient has left atrial enlargement (panels A and B), and the interatrial septum bows to the right (panel B, arrow). Note normal left atrial size with a dilated coronary sinus (panel E, arrow) in the PAH patient. The PVH patient has a grade II LVDD pattern (panel C), while the PAH patient has a grade I pattern (panel G). Pulsed wave Doppler of the RVOT reveals an absence of notching in the PVH patient (panel D) and midsystolic notching in the PAH patient (panel H, arrows).**

contrast, in the presence of increased pulmonary artery stiffness and a high PVR, reflected waves will return to the RV during systole, impede RV ejection, and cause notching of the Doppler profile (Figure 4, panels C-F). A midsystolic notch pattern is especially abnormal, and is associated with an average PVR >8 Wood Units (WU) and moderate to severe RV dysfunction. A notched Doppler pattern was present in 100% of incident cases of PAH, and predicted a PVR >3 WU with an odds ratio of 22:1.<sup>44</sup> Thus, visual inspection of the RVOT<sub>Doppler</sub> profile represents a simple, rapid method of glean-

insight into the relative presence (notched pattern) or absence (no notch pattern) of pulmonary vascular disease.

#### AN INTEGRATED APPROACH TO THE DE ASSESSMENT OF PH

It is customary that a transthoracic DE report will provide a list of normal and abnormal findings related to cardiac structure and function. Table 1 summarizes key 2-D and Doppler features of pulmonary venous versus pulmonary arterial hypertension. However, what is often lacking is the needed degree of integration of these findings in order to assist the clini-

cian in arriving at the correct overall diagnosis. For example, what information should prompt referral of a patient for invasive right heart catheterization? Below, we will provide 2 different patient examples and the integration of the DE information.

With a more integrated approach to DE interpretation in mind, we recently devised a Doppler-echo scoring system to help discern PH pathophysiology. The initial data included 76 consecutive patients with undifferentiated PH. Components of the score included left heart and right heart parameters, with features of each receiving a score.<sup>51</sup> The left heart parameters were LA enlargement, LVH, grade II or III diastolic dysfunction; yes=0 points, no=1 point. Right heart parameters included RV enlargement, TAPSE <2 cm, septal bowing (yes=1 point, no=0 points), and Doppler notching of the RVOT<sub>Doppler</sub> profile (yes=2 points, no=0 points). It is notable that a Doppler estimate of pulmonary arterial pressure was *not* part of the score. A high score (6-8) would thus be compatible with a pulmonary vascular disease, whereas a low score (0-2) would suggest PVH. Patients with a score of 0-2 were older, with an elevated pulmonary capillary wedge pressure (PCWP) of 18 mm Hg, only mild to moderate PH (mean pulmonary arterial pressure 33 mm Hg), and a mean PVR of only 2.8 WU. By way of contrast, patients with a score of 6-8 had a normal PCWP (12 mm Hg), severe PH (mean pulmonary arterial pressure 50 mm Hg) and mean PVR of 10 WU. Notably, all patients with a score >6 had a PVR >4.5 WU, whereas only 1 patient with a score <3 had PAH.<sup>51</sup>

Two examples of this integrated assessment are shown in Figure 5. All images on the left column correspond to patient 1 (PVH) and to the right, patient 2 (PAH). In the DE examination of patient 1, the parasternal long axis view (Figure 5, panel A) reveals LAE and LVH. The apical 4-chamber view (panel B) also reveals LAE and bowing of the interatrial septum to the right, suggesting higher LA than RA pressure. The LVEF is normal. The transmitral Doppler pattern reveals grade II diastolic dysfunction (panel C). The

RV:LV ratio is  $<1.0$  with a non-apex forming RV and a relatively normal TAPSE of 2.3 cm. The  $RVOT_{Doppler}$  pattern is not notched (panel D). The echo score is 1 of 8. This is highly suggestive of PVH without pulmonary vascular disease. We would not refer this patient for invasive right heart catheterization, as our suspicion for PAH or a high PVR is very low. Instead, we would manage the left heart condition and monitor the patient's symptoms and PH closely.

The parasternal long axis view in patient 2 (Figure 5, panel E) shows mild LVH and normal LA size. One can appreciate RV enlargement here, also. Note the dilated coronary sinus, often indicative of high RA pressure. On the apical 4-chamber view (panel F), the RV:LV ratio is  $>1.0$ , with a rounded RV apical angle and an apex forming RV. The LVEF is normal. The transmitral flow pattern reveals grade I diastolic dysfunction (panel G). The TAPSE is 1.6 cm, consistent with moderate RV dysfunction. The  $RVOT_{Doppler}$  pattern has a midsystolic notching pattern (panel H), which has been shown to be 96% specific for a  $PVR \geq 5$  WU.<sup>44</sup> The echo score here is 7 of 8, which is highly consistent with PH of pulmonary vascular origin. This patient should be referred for urgent right heart catheterization, and complete the needed imaging and functional studies in order to rule out underlying lung disease or CTEPH.

## CONCLUSION

Pulmonary hypertension is a descriptive term that merely refers to an elevation of pulmonary artery pressure, rather than to the underlying cause. On first glance, it may appear difficult to distinguish PH secondary to LA congestion/LVDD from PH of a pulmonary vascular cause based on routine DE information. However, a more complete and integrated approach highlights striking differences in the DE examination between patients with PH of left- and right-sided cause. When combined with the ability of the clinician to integrate the DE findings into the overall evaluation, the Doppler-echocardiogram becomes an extremely powerful diagnostic tool in determining the underlying etiology of PH.

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