REGULAR ARTICLE

Echocardiographic Evaluation of the Right Heart in Pulmonary Hypertension

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Pulmonary hypertension (PH) is characterized by increased right ventricular (RV) afterload, which is accommodated early by dramatic increases in RV contractility to maintain right ventriculoarterial coupling. Related to its tissue biology, characteristics of RV contractility differ from those of the left ventricle (LV). As the RV undergoes adaptation in PH, echocardiographic signs emerge which can help identify PH and can be reassessed to noninvasively prognosticate outcomes in PH. Many of these indices can be calculated from standard echocardiographic views without significant modification to scanning procedures. This review will discuss contemporary diagnosis of PH, highlighting the role of echocardiography in this process. We will describe the differences between the LV and RV, including adaptations of the RV in PH, and how these factors impact echocardiographic assessment. We will conclude with a discussion of specific echocardiographic parameters and describe their role in diagnosis and reassessment. Routine assessment of the right heart improves noninvasive risk stratification in PH, may reduce delays in diagnosis, and ultimately may impact the significant and potentially modifiable disease burden in this patient population.

INTRODUCTION

Pulmonary hypertension (PH) refers to a diverse set of conditions that may act locally, at the level of the heart and lungs, or systemically to increase mean pulmonary arterial pressure (mPAP). In this way, PH represents a shared pathophysiology, with heterogenous upstream causes that ultimately impact the load experienced by the right ventricle (RV). The RV is able to accommodate dramatic increases in afterload to maintain cardiac output. These adaptive mechanisms have echocardiographic correlations, making echocardiography critical in both the screening for PH and for routine monitoring of PH patients.

This review will discuss contemporary diagnosis of PH, highlighting the role of echocardiography in this process. We will describe the differences between the left ventricle (LV) and RV, including adaptations of the RV in PH, and how these factors impact echocardiographic assessment. We will conclude with a discussion of specific echocardiographic parameters and describe their role in diagnosis and reassessment.

DIAGNOSIS AND THE ROLE OF ECHOCARDIOGRAPHY

In 1973, the first World Health Organization Symposium on PH was convened in Geneva, Switzerland. With minor revisions since that time, expert consensus defined PH as mPAP ≥ 25 mmHg. Subsequent studies have demonstrated a significant increase in mortality and hospitalization at mPAP below that value prompting societal guidelines to adjust the diagnostic threshold to mPAP > 20 mmHg.[1-5] This change has increased the population prevalence of PH, though the implications for patient management remain uncertain and it remains critically important for clinicians to recognize when referral to specialist care is necessary. Presently, the diagnosis of PH is estimated to be delayed by nearly 2 years, contributing to a significant and potentially modifiable disease burden.[6] Improved understanding of the role of echocardiography for PH screening provides an opportunity to identify patients who may be candidates for earlier, more invasive diagnostics and therapeutic interventions.

Role of Echocardiography

Right heart catheterization remains the "gold standard" of PH diagnosis and classification.[7] In spite of this, echocardiography serves an important role in PH screening, differentiation of PH etiologies, and disease monitoring following formal diagnosis. The 2022 European Society of Cardiology (ESC) and the European Respiratory Society (ERS) Guidelines for the Diagnosis and Treatment of PH recommend using peak tricuspid regurgitation velocity (TRV) as the first step for assigning echocardiographic probability of PH

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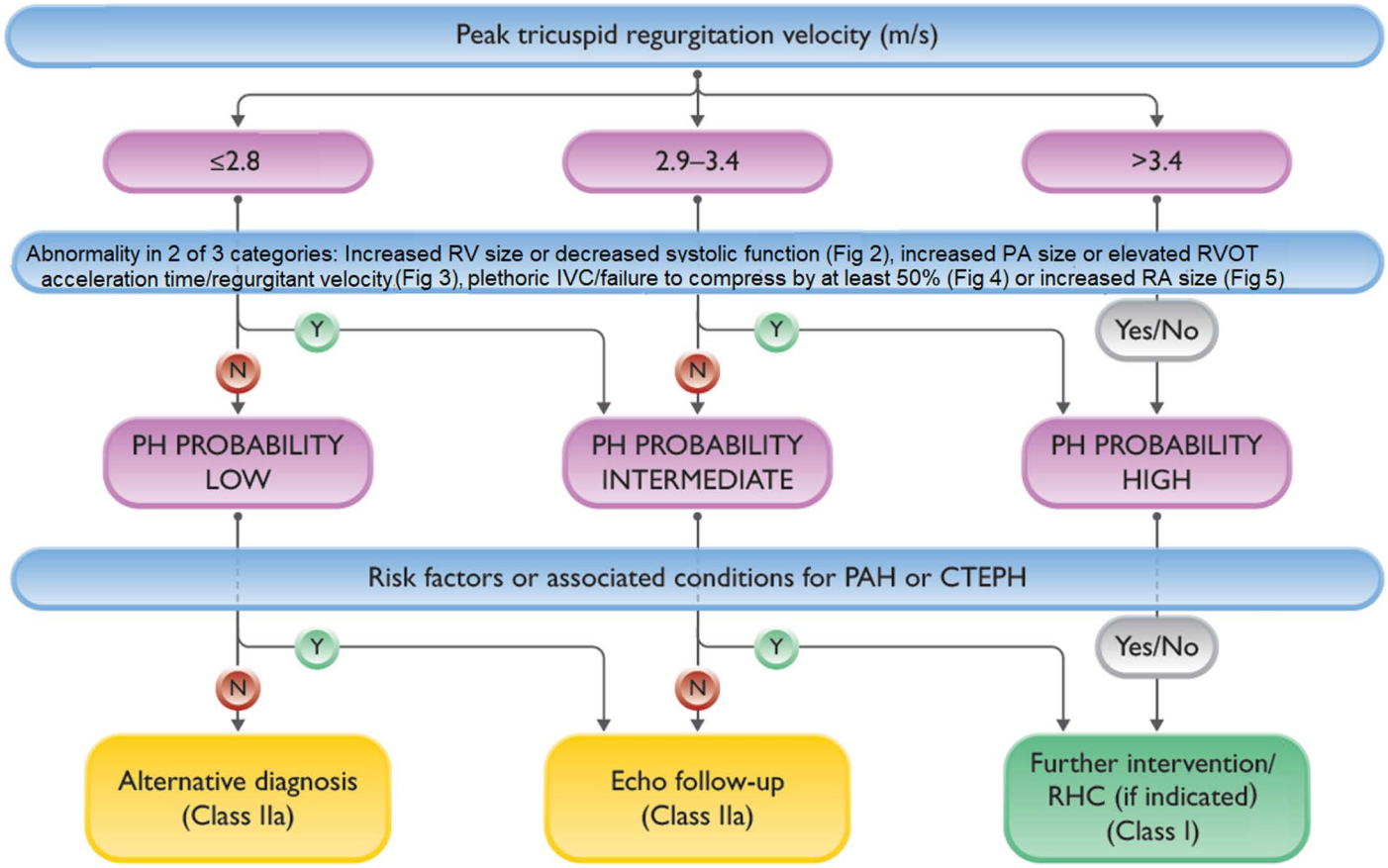

Figure 1: Echocardiography is an important screening tool for the diagnosis of pulmonary hypertension. This figure has been adapted from the 2022 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension. The first step is the assessment of peak tricuspid regurgitation velocity, followed by a careful review of right ventricular size and function, pulmonary arterial size and flow velocity tracings and inferior vena cava/right atrial sizes. If 2 or more of these categories are abnormal, the probability of pulmonary hypertension increases. High probability necessitates invasive assessment, while intermediate/low probability is further differentiated by associated risk factors and clinical conditions. Patients ultimately defined as intermediate probability should receive follow-up echocardiography, as they remain at risk for developing pulmonary hypertension. CTEPH indicates chronic thromboembolic pulmonary hypertension; IVC, inferior vena cava; PA, pulmonary artery; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; RA, right atrial; RHC, right heart catheterization; RV, right ventricle; RVOT, right ventricular outflow tract.

(Figure 1).[7] A peak TRV > 2.8 m/s should prompt further consideration of PH. The presence of additional echocardiographic findings help to further refine this assessment and justify subsequent invasive hemodynamic assessment via right heart catheterization.[7] These include assessments of RV size and systolic function (Figure 2), pulmonary size and outflow/regurgitant velocities (Figure 3), and inferior vena cava (IVC; Figure 4) and right atrial (RA) size (Figure 5). Echocardiography is therefore a critically important screening tool in the evaluation of patients with suspected PH.

Echocardiography may also help to distinguish between PH etiologies. It is particularly well suited to evaluate whether PH is related to LV dysfunction (group 2 disease); for this reason every echocardiographic assessment for PH should also include metrics of LV diastolic function, left atrial size, and measurement of LV wall thickness.[7] Echocardiography can also identify comorbid congenital heart disease, although additional studies including transesophageal echocardiography, computed tomography (CT), or cardiac magnetic resonance imaging (MRI) may be required to provide anatomic clarity. A bubble study should be performed during the initial echocardiographic study to evaluate for the presence of intracardiac or intrapulmonary right to left shunting. The former could be due to patent foramen ovale, a lesion present in over a quarter of the population. Whether patent foramen ovale was present from birth in the pulmonary arterial hypertension (PAH) patient or stretched open due to pressure and volume loading of the right atrium cannot be determined unless prior echo bubble injection was performed. A positive bubble study can also suggest the presence of an atrial septal defect, which can occasionally be the cause of PH. Often a secundum defect (in the middle of the atrial septum) can be identified by color Doppler. It's important to note that sinus venosus defect (present in the roof or the floor of the right atrium) also results in a positive bubble study, but can require a transesophageal echocardiograph, a cardiac CT scan, or a cardiac MRI for its detection. Finally, if the bubbles appear in the left atrium after more than 3 heartbeats of reaching the

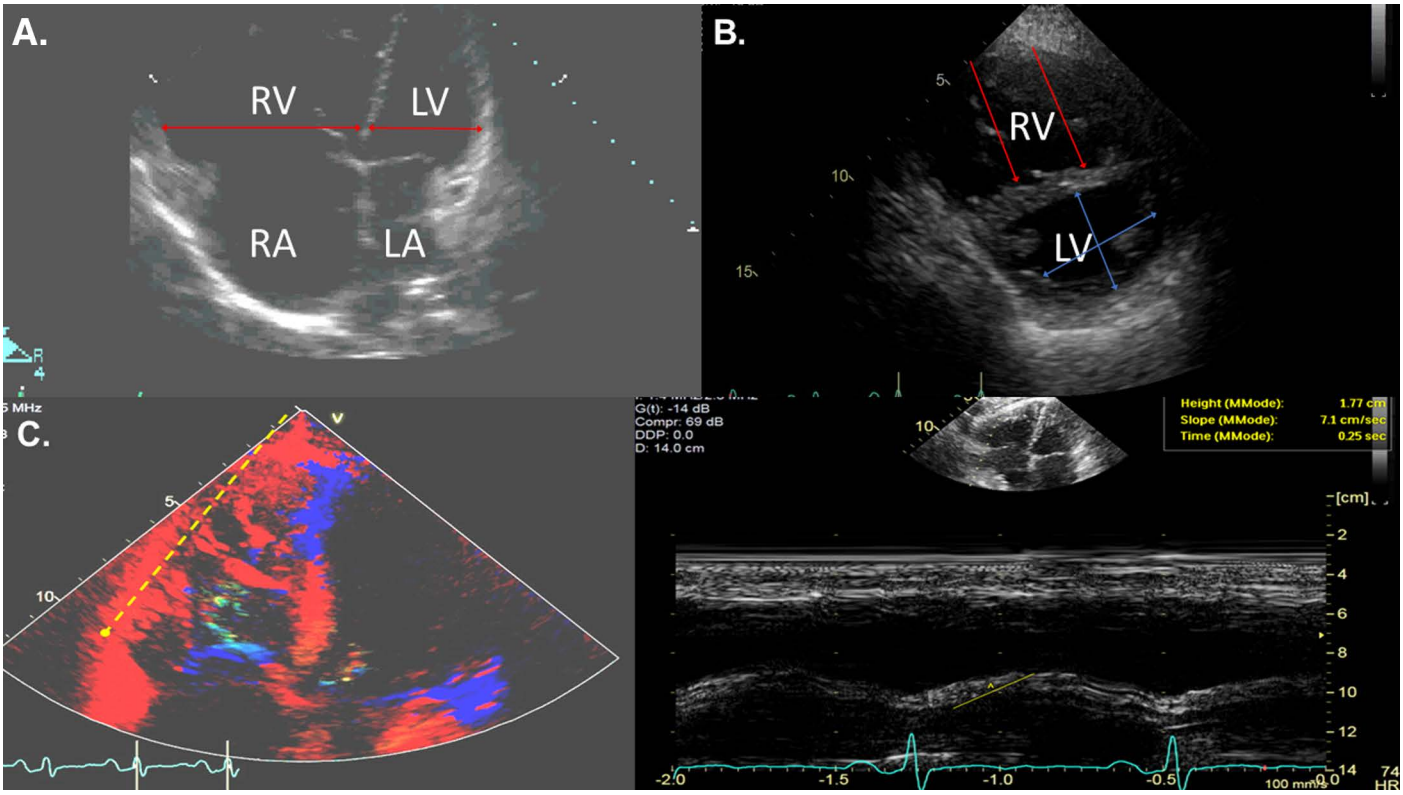

Figure 2: Assessment of the right ventricle for signs suggestive of pulmonary hypertension. The simplest assessment of right ventricular (RV) size is to compare it to the left ventricle (LV). Normally the RV should be smaller than the LV (ratio < 1). In (**A)** the RV:LV ratio is significantly > 1.0. Flattening of the interventricular septum (**B**) is also a common feature of pulmonary hypertension. The LV is essentially squashed by the RV, as assessed by the LV eccentricity index (the ratio of the LV axis parallel to the septum divided by the axis perpendicular to the septum > 1.1 as measured in the parasternal short-axis view at the level of the LV papillary muscles). (**C**) Because of the contractile pattern of the RV, tissue annular plane systolic excursion can be used to measure systolic function, with further refinement by comparing it to the systolic pulmonary artery pressure to assess RV-pulmonary arterial coupling. LA indicates left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

right atrium, it suggests the presence of pulmonary arteriovenous malformations. These are generally rare, but can develop in patients with advanced liver disease and result in profound hypoxia (hepatopulmonary syndrome).

Following diagnosis of PH and characterization of likely etiology, echocardiography is an important element for routine follow-up. For those with PAH (group 1 disease), noninvasive assessment with echocardiography is recommended every 3 to 6 months, following any change in therapy, and immediately upon suggestion of clinical worsening.[7] For PH related to LV dysfunction (group 2 disease), there is no current recommendation for echo cadence beyond what is recommended for reassessment of LV dysfunction. In PH related to underlying pulmonary disease (group 3 disease), the sensitivity of many echocardiographic indices of PH, including TRV, are reduced leading to lower utility of echocardiography for disease monitoring.[8] Given this, PH diagnosis in group 3 disease is often best aided by stepwise, composite echocardiographic assessment or pairing with contrast-enhanced CT imaging.[9,10] Echocardiography plays a clear role in the monitoring of chronic thromboembolic PH (group 4 disease) for which yearly posttreatment echocardiography is recommended in light of known recurrent or persistent PH in some patients.[7,11] For those with PH related to unknown or multifactorial mechanisms (group 5 disease), evidence to support routine echocardiographic monitoring has not yet been established.

RV ADAPTATIONS IN PH

Echocardiographic assessment of the right heart in PH necessarily seeks to identify, trend, and quantitate RV adaptive mechanisms that seek to preserve RV function in PH. During disease progression, echocardiography is also critical for identifying the point at which these mechanisms fail and RV dysfunction manifests. Recognizing anatomic and functional differences between the LV and RV, as well as the RV's response to stress, provides a foundation for understanding the specifics that echocardiographic assessment of the right heart intends to capture.

The functional and anatomic differences between the LV and RV draw both from their separate embryologic and hemodynamic environments. The LV originates from the primary heart field, which develops into 3 muscular layers that together form a truncated ellipsoid structure.[12] The fiber orientation of these 3 layers confers specific mechanical properties that impact ventricular contractility and function; specifically, the LV derives the majority of its contractility from circumferentially oriented fibers that serve to nearly ablate the ventricular cavity in systole

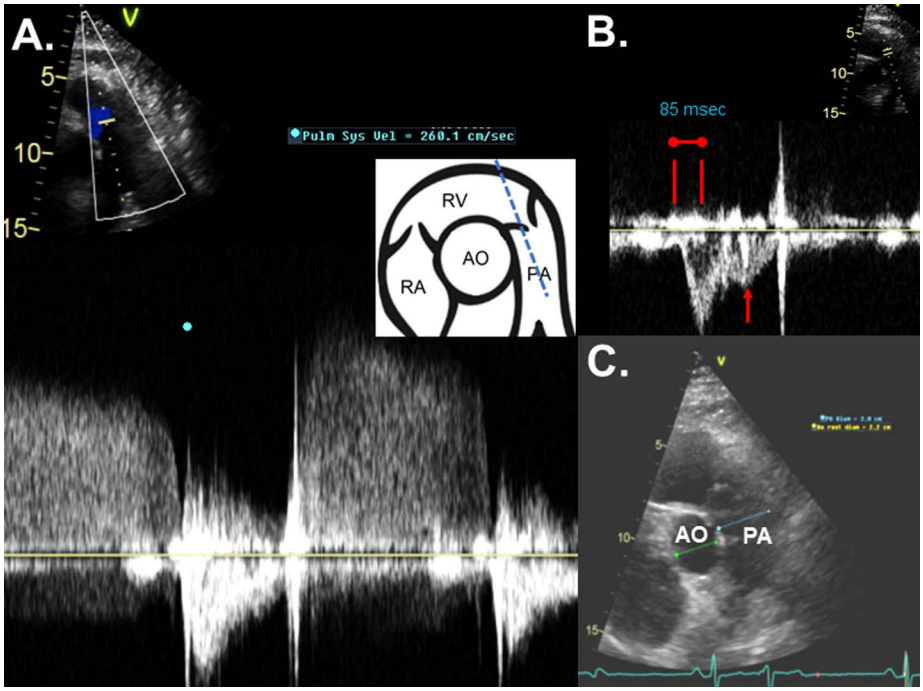

Figure 3: Assessment of the right ventricular outflow tract and pulmonary artery for signs suggestive of pulmonary hypertension. The peak regurgitant velocity in the patient in (**A**) is higher than the established threshold of 2.2 m/sec. In (**B**), the forward velocity is assessed. The acceleration time is measured from onset of flow to peak and in this patient was < 105 ms (the threshold for being abnormal). Also seen (arrow) is midsystolic notching (a very suggestive finding for significantly elevated pulmonary resistance). In (**C**), the pulmonary and aortic diameters are compared. A pulmonary artery diameter greater than the aortic diameter (as seen here) or > 2.5 cm is considered abnormal. AO indicates aorta; PA, pulmonary artery; RA, right atrium; RV, right ventricle.

and forcefully eject blood, making it particularly well suited as a high-pressure pump.[13,14] In contrast, the RV is formed from the secondary (anterior) heart field, a structure contiguous with the conotruncus, which will ultimately give rise to the RV outflow track and the great arteries.[12,15] This proximity to structures that ultimately give rise to blood vessels belies the separate character of the RV myocardium in comparison to the LV. This thin-walled structure exists as a crescent attached to the anterior surface of the LV and is composed of 2 muscular layers with fibers oriented primarily longitudinally, from apex to base.[13,16] Such fiber orientation confers greatest contractility in the longitudinal direction, allowing the RV to serve as a pump that is particularly well suited to accommodate changes in volume.[16]

Typically, blood flow through the pulmonary vascular beds is maintained by an efficient pairing between RV systolic function and pulmonary vascular resistance (PVR), a process known as right ventriculoarterial (VA) coupling. This pairing maintains stroke volume (SV) over a wide range of PVR, including increases imposed by exertion. In PH, as PVR increases, many humoral and cellular responses are initiated that seek to maintain right VA coupling and preserve RV SV.[17,18] Structurally, these responses manifest first as progressive RV hypertrophy, whereby increasing wall thickness attempts to maintain the needed increase in contractility.[19] In contrast to systemic vascular resistance, which may increase by ~50% in states of systemic hypertension, PVR in PH often undergoes an ~400% increase from baseline values.[20] Remarkably, through cellular changes, including hypertrophy, the RV is able to achieve 4- to 5-fold increases in contractility to maintain VA coupling, albeit at a higher metabolic demand.[19] If elevated ventricular load continues or increases, additional humoral responses halt the hypertrophic process and the SV begins to drop.[18] As the next phase in adaptation, the RV dilates in order to maintain absolute SV; ultimately, as this mechanism fails, the heart rate will increase in order to preserve right-sided cardiac output. These factors dramatically impact RV myocardial oxygen supply and demand, resulting in mismatch, which is closely followed by VA uncoupling and reduced cardiac output.[19,21-23] Echocardiographic assessment of the RV in PH intends to trend ventricular health, determine the state of VA coupling, and ultimately guide the escalation of therapies.

ECHOCARDIOGRAPHIC ASSESSMENT OF THE RIGHT HEART

Echocardiographic assessment of the right heart is challenging due to the anterior position of the RV in the chest directly behind the sternum, its thin walls, and its complex contractile pattern. Considering these challenges, a complete assessment of RV structure and function requires the composition of multiple echo windows and metrics.

As previously noted, the 2022 ESC/ERS Guidelines for the Diagnosis and Treatment of PH propose a stepwise approach starting with TRV and followed by assessment of the ventricles, the pulmonary artery (PA), and the IVC and RA in order to improve diagnostic yield of invasive diagnostics. Below we will discuss the constituent metrics for this algorithm alongside additional echocardiographic metrics of RV function in PH.

Peak TRV

Traditionally, measurement of the systolic pulmonary arterial pressure (sPAP) has been a central focus of echocardiography in screening for PH. This is achieved, in the absence of pulmonary stenosis, through application of the modified Bernoulli equation ($4V^2$) using TRV. This provides the pressure gradient across the tricuspid valve during systole, which when added to noninvasive estimates of RA pressure, provides an estimate of the sPAP. This is no longer recommended as the sole screening tool given documented inaccuracies including fallacious estimates of RA pressure and amplification of measurement error

with the modified Bernoulli. Instead, new guidelines recommend use of peak TRV directly.[7]

Peak TRV is measured by continuous-wave Doppler across the tricuspid valve. Multiple views may be needed in order to obtain the optimal window; the best windows for assessment include the RV inflow, parasternal short axis (PSAX), and the apical 4-chamber (A4C) views.[24] The highest velocity with the cleanest signal most parallel to the regurgitant jet should be recorded. Accurate quantification of peak TRV requires colinearity between the continuous-wave Doppler ray and the axis of the regurgitant jet. Eccentricity will necessarily underestimate peak TRV through dot product of these 2 vectors. Peak TRV can additionally be underestimated in severe or "free" tricuspid regurgitation given the dispersion of focal flow acceleration and a broad local peak velocity. A peak TRV ≤ 2.8 m/s is considered within normal range.[7]

Tricuspid Annular Plane Systolic Excursion

Given that the principal axis of contractility in the RV is oriented apex to base, related to the fiber orientation described above, tricuspid annular plane systolic excursion (TAPSE) has evolved as a metric of RV contractility. This describes the apical movement of the tricuspid annulus during systole and is obtained using motion mode, typically from the A4C view (Figure 2). Grounded in the tissue biology of the heart, TAPSE appears to have close correlation with RV systolic function.[25-27] In PH specifically, investigation has identified a cutoff value of < 1.8 cm to have an unadjusted hazard ratio of 5.7 for risk of death over a 2-year interval.[28] TAPSE has been further combined with sPAP to form the TAPSE:sPAP ratio, which demonstrates good correlation when trended with both invasive hemodynamics and functional class in PAH.[29] More generally, TAPSE < 1.6 cm has been shown to be highly predictive of RV systolic dysfunction.[26,27,30]

Fractional Area Change

Given the prognostic significance of RV systolic function in PH, several metrics have been developed to assess it.[31,32] One such method is fractional area change (FAC), a 2-dimensional metric calculated by comparing manual tracings of the RV endocardial border in end-diastole and end-systole. In comparison to other methods like TAPSE, FAC has demonstrated similar or better correlation with high-resolution 3-dimensional RV ejection fraction measurement by cardiac MRI, with the added advantage of faster assessment and lower cost.[33,34] FAC is generally obtained from the A4C view, with normal values of ≥ 30% in men and ≥ 35% in women.[35]

Eccentricity Index

The eccentricity index (EI) assesses for RV pressure or volume overload by evaluating LV dimensions. The EI is a quantitative metric of the classic "D" sign and is calculated from the parasternal short-axis view midway along the LV (Figure 2), at the level between the papillary muscle and tip of the mitral valve leaflets. Two internal cavity dimensions are obtained from this view, one parallel to the septum (D2) and one perpendicular to the septum (D1). EI = D2/D1 and is typically ≤ 1 in both systole and diastole. RV volume overload causes eccentricity in diastole; while RV pressure overload causes eccentricity in both systole and diastole. A systolic EI > 1.1 increases the likelihood of PH, while values > 1.7 have been associated with a very poor prognosis.[7,31]

RV Index of Myocardial Performance

The index of myocardial performance, also known as the Tei index, describes the ratio between the sum of isovolumetric contraction and isovolumetric relaxation times divided by ejection time. This is a metric that can be evaluated for both RV and LV and includes elements of both systole and diastole in an attempt to assess global ventricular function.[36,37] The RV index of myocardial performance (RIMP) has been studied in PH specifically to evaluate RV function, and has been shown to be an independent predictor of mortality and correlate with invasive hemodynamics.[38,39]

RIMP was developed using pulsed-wave (PW) Doppler; this method is technically challenging and requires comparison of PW signals at both the lateral tricuspid annulus and the RV outflow tract obtained during cardiac cycles with near-identical R-R intervals. Given this difficulty, a tissue Doppler RIMP methodology has been developed which requires a single tissue Doppler sample along the lateral tricuspid annulus. This tissue Doppler RIMP has demonstrated excellent correlation with RIMP and slightly improved correlation with RV ejection fraction and RV FAC as compared with RIMP.[40] RIMP > 0.43 by PW Doppler, or > 0.54 by tissue Doppler indicates RV dysfunction.[41] In PH specifically, RIMP > 0.64 is associated with lower overall survival at 4 years.[38]

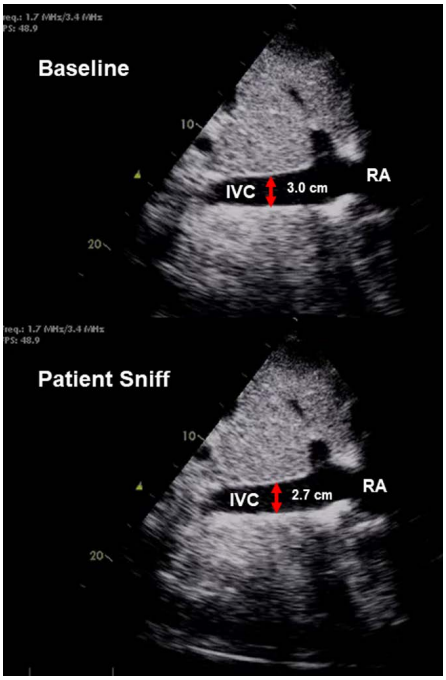

Figure 4: Assessment of the inferior vena cava (IVC) artery for signs suggestive of pulmonary hypertension. Normally the IVC diameter should be ≤ 2.1 cm in diameter on this subcostal view and should collapse > 50% with a sniff. This usually correlates to an estimated right atrial pressure of < 5 mmHg. If the IVC is either > 2.1 cm or collapses ≤ 50%, the RA pressure is ~5 to 10 mm Hg. If the IVC is both > 2.1 cm and collapses < 50% (as in this patient), the RA pressure is ~10 to 20 mm Hg. IVC indicates inferior vena cava; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

RV Strain

RV strain has been studied as a modality to assess RV contractility and prognosticate outcomes. Typically,

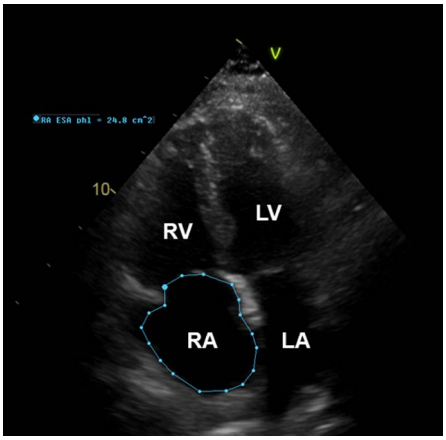

Figure 5: Assessment of the right atrium for signs suggestive of pulmonary hypertension. This patient has a right atrial area which is greater than the normal threshold of 18 cm^2. LA indicates left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

global RV strain is assessed in 6 segments obtained in the A4C view; this assessment can be technically challenging given that imaging must remain within 10° to 15° of the axis of contraction for full reliability. RV free wall longitudinal strain (RV-FWLS) analyzes the lateral 3 segments and excludes the 3 septal segments, which has the advantage of being far more angle-independent while still demonstrating good performance;[42-46] in PAH, RV-FWLS correlates with worsened function class, shorter 6-minute walk distances, higher N-terminal pro-B-type natriuretic peptide levels, and the presence of clinical RV failure.[44] RV-FWLS can identify subclinical RV dysfunction when other parameters like TAPSE are still within normal ranges.[42,43] Additionally, after adjustment for PVR, pulmonary pressures, and RA pressure, RV-FWLS has been shown to predict survival in PH.[44] Normal ranges for RV-FWLS are disputed, although meta-analysis has demonstrated patients with PH and RV-FWLS > –19% are at significantly greater risk of experiencing a combined endpoint of mortality and PH-related event. Furthermore, patients with RV-FWLS > –22% had significantly higher risk for all-cause mortality.[47]

PA Diameter

Mean PA diameter has been studied as a marker of elevated PA pressure and is measured in end diastole halfway between the pulmonary valve and bifurcation of the main PA (Figure 3). The PA dilates in the presence of either pressure or volume overload. CT measurements of PA diameter correlate with catheter-derived measurements of elevated pulmonary pressures, which have subsequently been correlated with echocardiographic measurements.[48,49] Guidelines support PA diameter > 2.5 cm as increasing the likelihood of PH.[7]

RA Area

Elevated mean RA pressure measured by right heart catheterization is an independent risk factor for mortality in PH.[50] Right atrial area (RAA) measured by echocardiography corrrelates to invasive assessments of mean right atrial pressure and has by itself been demonstrated to predict poorer survival.[51] RAA in PH is measured in the A4C view at end systole on the frame just prior to tricuspid valve opening (Figure 5). A RAA > 18 cm^2 is associated with a poor prognosis, with a relative risk of 2.6 for death or transplantation at 3 years compared to those with RAA ≤ 18 cm^2.[51]

RA Strain

As discussed earlier, emerging techniques are extending beyond structural metrics to assess functional parameters. In line with this trend, RA strain has emerged as a hopeful metric to prognosticate precapillary PH. Hasselberg et al.[52] performed 6-segment speckle tracking of the RA in 151 patients with precapillary PH. Over a follow-up interval of 5 years, 48% of patients died; those in the lowest quartile of RA strain experienced a significant risk of death ($P = .006$), while intact RA strain was independently associated with survival following multivariable analysis ($P = .039$).[52] When combined with RV strain, RA strain provided added prognostic value; individuals with preserved RA and RV strain demonstrated improved survival over those with intact RV strain and impaired RA strain, who in turn had improved survival over those with impaired RV and RA strain. Further development of these techniques may allow for quantification of strain value cutoffs that prognosticate disease progression or suggest a need for specific therapies.

Additional Parameters

Several right heart echocardiographic indices have not been correlated to outcomes or disease progression in PH specifically but have been shown to indicate elevated right-sided pressures. These parameters remain important elements of a complete echocardiographic assessment of the right heart.

IVC Size and Collapsibility: From the subcostal view, with the IVC and cavo-atrial junction into the RA in view, the IVC diameter is measured across the width of the IVC, 1 to 2 cm from the cavo-atrial junction. This is most reliably obtained at end expiration, with normal values being ≤ 2.1 cm. The collapsibility should also be assessed. This is best done by assessing the IVC in motion mode and asking the patient to sniff; under normal circumstances the IVC should collapse by > 50% with a sniff (Figure 4). If the IVC is > 2.1 cm or collapses ≤ 50%, the RA pressure is ~5 to 10 mm Hg. If the IVC is both > 2.1 cm and collapses < 50%, the RA pressure is ~10 to 20 mm Hg.

RV to LV Diameter Ratio: Similar to EI, the basal diameters of the RV and LV may be compared. This measurement is obtained in the A4C view, mindful to exclude any foreshortening. Measured at end diastole, the basal cavity dimensions of the RV and LV are compared. A ratio of RV:LV > 1 suggests RV dilation.

Peak Regurgitant Velocity of the Pulmonary Valve: Imaging in the PSAX near the cardiac base with the RV outflow tract (RVOT) in view, the pulmonary regurgitant jet of the pulmonary valve can be registered on continuous-wave Doppler (Figure 3). This pulmonary regurgitant jet is measured in early diastole with values > 2.2 associated with elevated mPAP.[7]

PA Midsystolic Notching: Midsystolic notching is observed in the PSAX through placement of PW Doppler sample volume just below the pulmonic cusp in the RVOT. Increased PVR, and PA stiffness, change pulmonary vascular impedance in a manner that promotes earlier wave reflection and impedes RV ejection. Waves here refer to the transmission of energy, largely through compressive forces, separate from the flow

of blood that emanates from ventricular contraction and can be reflected back towards the ventricle. This early reflection is appreciated by a "notch" in the midportion of the RV systolic Doppler signal as the RV's ejection is momentarily reduced by early wave reflection seen with elevated PVR (Figure 3). Given this phenomenon's relationship to the material properties of the pulmonary arteries, it is more commonly observed in precapillary PH as compared to group 2 PH.[53]

RVOT Acceleration Time: In the same PSAX view and PW Doppler sample volume as above, the RVOT acceleration time can be assessed. Measured at end expiration, the Doppler profile of flow through the RVOT in systole is assessed. As PA pressures increase, the time from the onset of RV ejection until the profile's peak, referred to as the RVOT acceleration time, shortens (Figure 3). Heart rates between 60 and 100 beats/min provide the most reliable measurement.[54] In those with atrial fibrillation, values should be averaged over at least 5 beats. RVOT acceleration times ≤105 milliseconds have been correlated with elevated mPAP.[55]

CONCLUSION

PH is characterized by increased RV afterload, generally accommodated early by dramatic increases in RV contractility to maintain right VA coupling. As the RV undergoes early adaptation, characteristic echocardiographic signs emerge which can be followed in order to noninvasively prognosticate outcome in PH. As this process continues, the RV exceeds its ability to compensate for increased pulmonary pressures, which ultimately manifests as right VA uncoupling. The progression to this late finding can be observed on echocardiography through the evaluation of right heart structures. Many of these indices can be calculated from standard echocardiographic views without significant modification to scanning procedures. Routine assessment of the right heart for severity of PH holds promise to improve the noninvasive risk stratification for PH, reduce delays in diagnosis, and ultimately impact the significant and potentially modifiable disease burden.

References

1. Valerio CJ, Schreiber BE, Handler CE, Denton CP, Coghlan JG. Borderline mean pulmonary artery pressure in patients with systemic sclerosis: transpulmonary gradient predicts risk of developing pulmonary hypertension. *Arthritis Rheum.* 2013;65(4):1074-1084. doi:10.1002/art.37838
2. Bae S, Saggar R, Bolster MB, et al. Baseline characteristics and follow-up in patients with normal haemodynamics versus borderline mean pulmonary arterial pressure in systemic sclerosis: results from the PHAROS registry. *Ann Rheum Dis.* 2012;71(8):1335-1342. doi:10.1136/annrheumdis-2011-200546
3. Douschan P, Kovacs G, Avian A, et al. Mild elevation of pulmonary arterial pressure as a predictor of mortality. *Am J Respir Crit Care Med.* 2018;197(4):509-516. doi:10.1164/rccm.201706-1215OC
4. Maron BA, Hess E, Maddox TM, et al. Association of borderline pulmonary hypertension with mortality and hospitalization in a large patient cohort: insights from the Veterans Affairs clinical assessment, reporting, and tracking program. *Circulation.* 2016;133(13):1240-1248. doi:10.1161/CIRCULATIONAHA.115.020207
5. Assad TR, Maron BA, Robbins IM, et al. Prognostic effect and longitudinal hemodynamic assessment of borderline pulmonary hypertension. *JAMA Cardiol.* 2017;2(12):1361-1368. doi:10.1001/jamacardio.2017.3882
6. Maron BA. Revised definition of pulmonary hypertension and approach to management: a clinical primer. *J Am Heart Assoc.* 2023;12(8):e029024. doi:10.1161/JAHA.122.029024
7. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension developed by the Task Force for the Diagnosis and Treatment of (ESC) and the European Respiratory Society (ERS). *Eur Heart J.* 2022;00:1-114.
8. Arcasoy SM, Christie JD, Ferrari VA, et al. Echocardiographic assessment of pulmonary hypertension in patients with advanced lung disease. *Am J Respir Crit Care Med.* 2003;167(5):735-740. doi:10.1164/rccm.200210-1130OC
9. Bax S, Bredy C, Kempny A, et al. A stepwise composite echocardiographic score predicts severe pulmonary hypertension in patients with interstitial lung disease. *ERJ Open Res.* 2018;4(2). doi:10.1183/23120541.00124-2017
10. Bax S, Jacob J, Ahmed R, et al. Right ventricular to left ventricular ratio at CT pulmonary angiogram predicts mortality in interstitial lung disease. *Chest.* 2020;157(1):89-98. doi:10.1016/j.chest.2019.06.033
11. Cannon JE, Su L, Kiely DG, et al. Dynamic risk stratification of patient long-term outcome after pulmonary endarterectomy: results from the United Kingdom national cohort. *Circulation.* 2016;133(18):1761-1771. doi:10.1161/CIRCULATIONAHA.115.019470
12. Kelly RG, Buckingham ME, Moorman AF. Heart fields and cardiac morphogenesis. *Cold Spring Harb Perspect Med.* 2014;4(10):1-10. doi:10.1101/cshperspect.a015750
13. Ho SY. Anatomy and myoarchitecture of the left ventricular wall in normal and in disease. *Eur J Echocardiogr.* 2009;10(8):3-7. doi:10.1093/ejechocard/jep159
14. MacIver DH. The relative impact of circumferential and longitudinal shortening on left ventricular ejection fraction and stroke volume. *Exp Clin Cardiol.* 2012;17(1):5-11.
15. Stefanovic S, Etchevers HC, Zaffran S. Outflow tract formation—embryonic origins of conotruncal congenital heart disease. *J Cardiovasc Dev Dis.* 2021;8(4). doi:10.3390/jcdd8040042
16. Walker LA, Buttrick PM. The right ventricle: biologic insights and response to disease: updated. *Curr Cardiol Rev.* 2013;9(1):73-81. doi:10.2174/1573403x11309010009
17. Piao L, Fang YH, Parikh KS, et al. GRK2-mediated inhibition of adrenergic and dopaminergic signaling in right ventricular hypertrophy: therapeutic implications in pulmonary hypertension. *Circulation.* 2012;126(24):2859-2869. doi:10.1161/CIRCULATIONAHA.112.109868
18. Sano M, Minamino T, Toko H, et al. p53-induced inhibition of Hif-1 causes cardiac dysfunction during pressure overload. *Nature.* 2007;446(7134):444-448. doi:10.1038/nature05602
19. Vonk Noordegraaf A, Westerhof BE, Westerhof N. The relationship between the right ventricle and its load in pulmonary hypertension. *J Am Coll Cardiol.* 2017;69(2):236-243. doi:10.1016/j.jacc.2016.10.047
20. Maron BA, Brittain EL, Hess E, et al. The association between pulmonary vascular resistance and clinical outcomes in patients with pulmonary hypertension: a retrospective cohort study. *Lancet Respir Med.* 2020;8(9):873-884. doi:10.1016/S2213-2600(20)30317-9.
21. Vogel-Claussen J, Skrok J, Shehata ML, et al. Right and left ventricular myocardial perfusion reserves correlate with right ventricular function and pulmonary hemodynamics in patients with pulmonary arterial hypertension. *Radiology.* 2011;258(1):119-127. doi:10.1148/radiol.10100725
22. Van Wolferen SA, Marcus JT, Westerhof N, et al. Right coronary artery flow impairment in patients with pulmonary hypertension. *Eur Heart J.* 2008;29(1):120-127. doi:10.1093/eurheartj/ehm567
23. Sarnoff SJ, Braunwald E, Welch GH, Case R., Stainsby WN, Macruz R. Hemodynamic determinants of oxygen consumption of the heart with special reference to the tension-time index. *Am J Physiol.* 1957;192(1):148-156. doi:10.14321/j.ctv1qmpd9d.20

24. Schneider M, Pistritto AM, Gerges C, et al. Multi-view approach for the diagnosis of pulmonary hypertension using transthoracic echocardiography. *Int J Cardiovasc Imaging*. 2018;34(5):695-700. doi:10.1007/s10554-017-1279-8
25. Ghio S, Recusani F, Klersy C, et al. Prognostic usefulness of the tricuspid annular plane systolic excursion in patients with congestive heart failure secondary to idiopathic or ischemic dilated cardiomyopathy. *Am J Cardiol.* 2000;85(7):837-842. doi:10.1016/S0002-9149(99)00877-2
26. Kaul S, Tei C, Hopkins J, Shah P. Assessment of right ventricular function using two-dimensional echocardiography. *Am Heart J.* 1984;107(3):526-531. doi:10.1177/108925329700100304
27. Miller D, Farah MG, Liner A, Fox K, Schluchter M, Hoit BD. The relation between quantitative right ventricular ejection fraction and indices of tricuspid annular motion and myocardial performance. *J Am Soc Echocardiogr.* 2004;17(5):443-447. doi:10.1016/j.echo.2004.01.010
28. Forfia PR, Fisher MR, Mathai SC, et al. Tricuspid annular displacement predicts survival in pulmonary hypertension. *Am J Respir Crit Care Med.* 2006;174(9):1034-1041. doi:10.1164/rccm.200604-547OC
29. Tello K, Axmann J, Ghofrani HA, et al. Relevance of the TAPSE/PASP ratio in pulmonary arterial hypertension. *Int J Cardiol.* 2018;266:229-235. doi:10.1016/j.ijcard.2018.01.053
30. López-Candales A, Dohi K, Rajagopalan N, Edelman K, Gulyasy B, Bazaz R. Defining normal variables of right ventricular size and function in pulmonary hypertension: an echocardiographic study. *Postgrad Med J.* 2008;84(987):40-45. doi:10.1136/pgmj.2007.059642
31. Ghio S, Klersy C, Magrini G, et al. Prognostic relevance of the echocardiographic assessment of right ventricular function in patients with idiopathic pulmonary arterial hypertension. *Int J Cardiol.* 2010;140(3):272-278. doi:10.1016/j.ijcard.2008.11.051
32. Vanderpool RR, Saul M, Nouraie M, Gladwin MT, Simon MA. Association between hemodynamic markers of pulmonary hypertension and outcomes in heart failure with preserved ejection fraction. *JAMA Cardiol.* 2018;3(4):298-306. doi:10.1001/jamacardio.2018.0128
33. Evaldsson AW, Lindholm A, Jumatate R, et al. Right ventricular function parameters in pulmonary hypertension: echocardiography vs. cardiac magnetic resonance. *BMC Cardiovasc Disord.* 2020;20(1):1-12. doi:10.1186/s12872-020-01548-4
34. Hoette S, Creuzé N, Günther S, et al. RV fractional area change and TAPSE as predictors of severe right ventricular dysfunction in pulmonary hypertension: a CMR study. *Lung.* 2018;196(2):157-164. doi:10.1007/s00408-018-0089-7
35. Kou S, Caballero L, Dulgheru R, et al. Echocardiographic reference ranges for normal cardiac chamber size: results from the NORRE study. *Eur Heart J Cardiovasc Imaging.* 2014;15(6):680-690. doi:10.1093/ehjci/jet284
36. Harjai KJ, Scott L, Vivekananthan K, Nunez E, Edupuganti R. The Tei index: a new prognostic index for patients with symptomatic heart failure. *J Am Soc Echocardiogr.* 2002;15(9):864-868. doi:10.1067/mje.2002.120892
37. Vonk MC, Sander MH, van den Hoogen FHJ, van Riel PLCM, Verheugt FWA, van Dijk APJ. Right ventricle Tei-index: a tool to increase the accuracy of non-invasive detection of pulmonary arterial hypertension in connective tissue diseases. *Eur J Echocardiogr.* 2007;8(5):317-321. doi:10.1016/j.euje.2006.06.002
38. Grapsa J, Pereira Nunes MC, Tan TC, et al. Echocardiographic and hemodynamic predictors of survival in precapillary pulmonary hypertension. *Circ Cardiovasc Imaging.* 2015;8(6):45-54. doi:10.1161/CIRCIMAGING.114.002107
39. Grignola JC, Ginés F, Guzzo D. Comparison of the Tei index with invasive measurements of right ventricular function. *Int J Cardiol.* 2006;113(1):25-33. doi:10.1016/j.ijcard.2005.10.012
40. Zimbarra Cabrita I, Ruisanchez C, Dawson D, et al. Right ventricular function in patients with pulmonary hypertension; rhe value of myocardial performance index measured by tissue Doppler imaging. *Eur J Echocardiogr.* 2010;11(8):719-724. doi:10.1093/ejechocard/jeq051
41. Lang RM, Badano LP, Victor MA, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr.* 2015;28(1):1-39.e14. doi:10.1016/j.echo.2014.10.003
42. Puwanant S, Park M, Popović ZB, et al. Ventricular geometry, strain, and rotational mechanics in pulmonary hypertension. *Circulation.* 2010;121(2):259-266. doi:10.1161/CIRCULATIONAHA.108.844340
43. van Kessel M, Seaton D, Chan J, et al. Prognostic value of right ventricular free wall strain in pulmonary hypertension patients with pseudo-normalized tricuspid annular plane systolic excursion values. *Int J Cardiovasc Imaging.* 2016;32(6):905-912. doi:10.1007/s10554-016-0862-8
44. Fine NM, Chen L, Bastiansen PM, et al. Outcome prediction by quantitative right ventricular function assessment in 575 subjects evaluated for pulmonary hypertension. *Circ Cardiovasc Imaging.* 2013;6(5):711-721. doi:10.1161/CIRCIMAGING.113.000640
45. Focardi M, Cameli M, Carbone SF, et al. Traditional and innovative echocardiographic parameters for the analysis of right ventricular performance in comparison with cardiac magnetic resonance. *Eur Heart J Cardiovasc Imaging.* 2015;16(1):47-52. doi:10.1093/ehjci/jeu156
46. Motoji Y, Tanaka H, Fukuda Y, et al. Efficacy of right ventricular free-wall longitudinal speckle-tracking strain for predicting long-term outcome in patients with pulmonary hypertension. *Circ J.* 2013;77(3):756-763. doi:10.1253/circj.CJ-12-1083
47. Hulshof HG, Eijsvogels TMH, Kleinnibbelink G, et al. Prognostic value of right ventricular longitudinal strain in patients with pulmonary hypertension: a systematic review and meta-analysis. *Eur Heart J Cardiovasc Imaging.* 2019;20(4):475-484. doi:10.1093/ehjci/jey120
48. Shen Y, Wan C, Tian P, et al. CT-base pulmonary artery measurementin the detection of pulmonary hypertension. *Med (Baltimore)*. 2014;93(27):1-9. doi:10.1097/MD.0000000000000256
49. Kuriyama K, Gamsu G, Stern R, Cann C, Herfkens R, Brundage B. CT determined pulmonary artery diameters in predicting pulmonary hypertension. *Invest Radiol.* 1984;19(1):16-22.
50. Benza RL, Gomberg-Maitland M, Miller DP, et al. The REVEAL registry risk score calculator in patients newly diagnosed with pulmonary arterial hypertension. *Chest.* 2012;141(2):354-362. doi:10.1378/chest.11-0676
51. Austin C, Alassas K, Burger C, et al. Echocardiographic assessment of estimated right atrial pressure and size predicts mortality in pulmonary arterial hypertension. *Chest.* 2015;147(1):198-208. doi:10.1378/chest.13-3035
52. Hasselberg NE, Kagiyama N, Soyama Y, et al. The prognostic value of right atrial strain imaging in patients with precapillary pulmonary hypertension. *J Am Soc Echocardiogr.* 2021;34(8):851-861.e1. doi:10.1016/j.echo.2021.03.007
53. Arkles JS, Opotowsky AR, Ojeda J, et al. Shape of the right ventricular Doppler envelope predicts hemodynamics and right heart function in pulmonary hypertension. *Am J Respir Crit Care Med.* 2011;183(2):268-276. doi:10.1164/rccm.201004-0601OC
54. Mallery JA, Gardin JM, King SW, Ey S, Henry WL. Effects of heart rate and pulmonary artery pressure on Doppler pulmonary artery acceleration time in experimental acute pulmonary hypertension. *Chest.* 1991;100(2):470-473. doi:10.1378/chest.100.2.470
55. Marra AM, Benjamin N, Ferrara F, et al. Reference ranges and determinants of right ventricle outflow tract acceleration time in healthy adults by two-dimensional echocardiography. *Int J Cardiovasc Imaging.* 2017;33(2):219-226. doi:10.1007/s10554-016-0991-0