



MINI-REVIEW

Elevated Pulmonary Pressure Noted on Echocardiogram: A Simplified Approach to Next Steps

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ABSTRACT: An elevated right ventricular/pulmonary artery systolic pressure suggestive of pulmonary hypertension (PH) is a common finding noted on echocardiography and is considered a marker for poor clinical outcomes, regardless of the cause. Even mild elevation of pulmonary pressure can be considered a modifiable risk factor, informing the trajectory of patients' clinical outcome. Although guidelines have been published detailing diagnostic and management algorithms, this echocardiographic finding is often underappreciated or not acted upon. Hence, patients with PH are often diagnosed in clinical practice when hemodynamic abnormalities are already moderate or severe. This results in delayed initiation of potentially effective therapies, referral to PH centers, and greater patient morbidity and mortality. This mini-review presents a succinct, simplified case-based approach to the "next steps" in the work-up of PH, once elevated pulmonary pressures have been noted on an echocardiogram. Our goal is for clinicians to develop a good overview of diagnostic approach to PH and recognition of high-risk features that may require early referral.

Key Words: echocardiogram ■ PA pressures ■ pulmonary hypertension

Transthoracic echocardiogram (TTE) is a common noninvasive screening tool used to assess patients with shortness of breath.¹ Pulmonary hypertension (PH), often noted on TTE as elevated pulmonary artery systolic pressure (PASP), is caused by a heterogeneous group of disorders and is well recognized to be associated with higher morbidity and mortality, regardless of cause.² It is particularly important to identify patients who may have World Health Organization (WHO) group 1 pulmonary arterial hypertension (PAH) or WHO Group 4 chronic thromboembolic PH, since it has significant implications for their prognosis and management strategies. Unfortunately, in spite of published guidelines, there has been no meaningful decrease in the time from symptom onset to diagnosis of PAH in the past 20 years.¹ On the other hand, there is a rising tendency to the misuse of PAH-specific therapies in patients with left heart disease (LHD) or lung disease associated PH.³ This results in misdiagnosis/ incorrect categorization

of PH subgroups, inappropriate prescription of pulmonary vasodilator medications, and delays in referral to PH centers in clinical practice. Hence, there is an unmet need for increased awareness to more appropriately diagnose, manage, and/or refer patients with PH.

Although the finding of high PASP is not enough to diagnose PH, it warrants further diagnostic considerations in appropriate patients (Figure 1). Using a case-based narrative, we will review the fundamental principles in the diagnostic approach to patients found to have elevated PASP on TTE in common practice. All supporting data are available within the article. Our goal is to provide a simplified guide for clinicians in non-PH centers to navigate the "next steps" in assessing these patients and differentiate those who need referral to an expert PH center for further work-up (Figure 2).

Case 1: A 65-year-old obese man with a history of essential hypertension, atrial fibrillation, and obstructive sleep apnea presents to the clinic with progressively

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Nonstandard Abbreviations and Acronyms

HFrEF or HFpEF	heart failure with reduced or preserved ejection fraction (respectively)
LHD	left heart disease
PAH	pulmonary arterial hypertension
PASP	pulmonary artery systolic pressure
PAWP	pulmonary arterial wedge pressure
PH	pulmonary hypertension
RHC	right heart catheterization
TAPSE	tricuspid annular plane systolic excursion
TTE	transthoracic echocardiogram

worsening shortness of breath over the last several months. Blood pressure is elevated at 154/82 mm Hg and ECG shows left ventricular hypertrophy with rate-controlled atrial fibrillation. Echocardiogram shows normal left ventricular size and function, mild left ventricular hypertrophy, and an estimated PASP of 60 mm Hg. Right ventricular free wall is “not well seen,” but there appears to be mild-to-moderate dysfunction.

This scenario is commonly encountered in clinical practice and has a relatively broad

differential diagnosis. Although there are limitations to the echocardiographic estimations of PH severity,⁴ the estimated PASP of 60 mm Hg (any peak tricuspid regurgitation velocity >3.4 m/s) is consistent with a high probability of PH, even in the absence of other associated echocardiographic findings.^{1,5} PH may present with a variety of symptoms, including shortness of breath (as in this case), but also fatigue, weakness, chest pain, or near-syncope/syncope. Symptoms and physical examination findings of both left-sided heart failure (orthopnea, paroxysmal nocturnal dyspnea, S3 gallop, pulmonary rales, and pleural effusions) and right-sided heart failure (elevated jugular venous pressure, hepatjugular reflux, lower extremity edema, right upper quadrant pain, abdominal distension, and ascites) may be present depending on both the cause and severity of PH.

When evaluating a patient with PH, history and physical examination should detail the following: concomitant cardiac disease (prior coronary and valvular disease/interventions, arrhythmias including atrial fibrillation, congenital heart disease), history of pulmonary embolism or venous thrombosis (risk factors for chronic thromboembolic disease), manifestations of connective tissue disease (such as systemic sclerosis, lupus), history of drug use, family history of PH, presence of significant liver or lung disease, sleep apnea, and features of the metabolic syndrome (obesity,

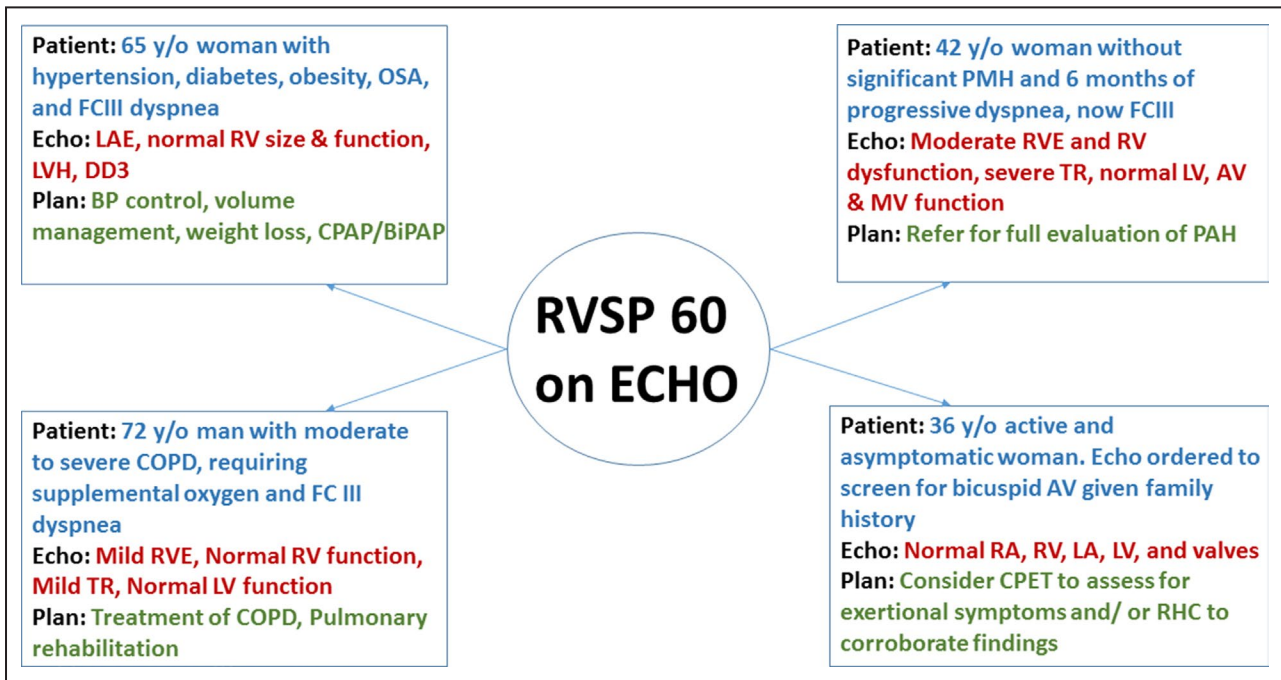


Figure 1. Approach to various clinical scenarios where elevated pulmonary pressures have been noted on echocardiogram. AV indicates aortic valve; BP, blood pressure; BiPAP, bilevel positive airway pressure; COPD, chronic obstructive lung disease; CPAP, central positive airway pressure; CPET, cardiopulmonary exercise test; DD, diastolic dysfunction; FC, functional class; LA, left atrium; LAE, left atrial enlargement; LV, left ventricle; LVH, left ventricular hypertrophy; MV, mitral valve; OSA, obstructive sleep apnea; PAH, pulmonary arterial hypertension; PMH, past medical history; RA, right atrium; RHC, right heart catheterization; RV, right ventricle; RVE, right ventricular enlargement; RVSP, right ventricular systolic pressure; TR, tricuspid regurgitation; and TSH, thyroid-stimulating hormone.

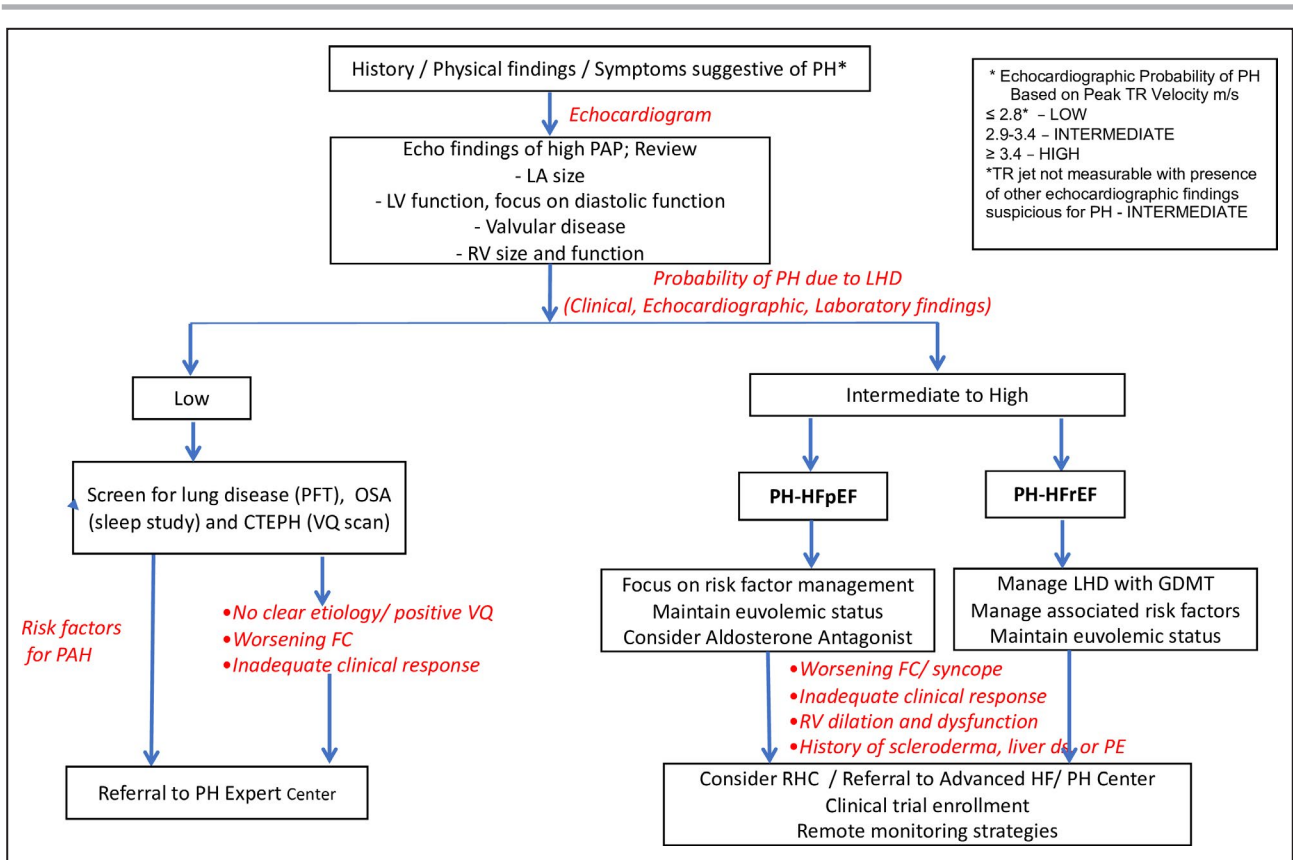


Figure 2. Diagnostic approach to PH.

CTEPH indicates chronic thromboembolic pulmonary hypertension; FC, functional class; GDMT, goal-directed medical therapy; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LA, left atrium; LHD, left heart disease; LV, left ventricle; OSA, obstructive sleep apnea; PAH, pulmonary arterial hypertension; PAP, pulmonary artery pressure; PE, pulmonary embolism; PFT, pulmonary function test; PH, pulmonary hypertension; RHC, right heart catheterization; RV, right ventricle; TR, tricuspid regurgitation; and VQ, ventilation perfusion scan.

hyperlipidemia, diabetes mellitus/glucose intolerance, systemic hypertension), etc.

TTE is the screening test of choice for patients suspected to have PH because it is noninvasive, readily available, inexpensive, and portable.⁵ However, a TTE can under- or overestimate PASP, especially in patients with coexisting lung disease.⁴ In addition to estimating PASP, TTE can assess right ventricular size and function. Right ventricular enlargement is categorized as normal, mild, moderate, or severe based on right ventricular basal diameter.⁶ Right ventricular systolic function is quantified by measuring tricuspid annular plane systolic excursion (TAPSE), S' velocity, or right ventricular fractional area change.⁶ Each measure has its own pros and cons (reviewed in⁶). TAPSE is measured using M-mode echocardiography in the apical 4-chamber view to generate an image that illustrates the systolic longitudinal displacement of the lateral tricuspid annulus toward the apex. This measure is easy to perform, widely available, and has strong associations with the outcome in PH.⁷ Elevated pulmonary artery pressure (PAP) increases the static and the pulsatile afterload of

the right ventricle, leading to right ventricular enlargement and dysfunction.⁸ An imbalance between the left and right ventricular contractility can result in the apex of the heart being pulled toward the LV during systole. As a result, the tricuspid annulus may be pulled along in unison—the so called “apical rocking” of the right ventricle (RV)—which may result in an overestimation of TAPSE. Hence, strain measures of the RV are often preferable in patients with PH. Additionally, the pressure and volume overload of the RV causes flattening or D-shaped interventricular septum. Pathological wave reflection because of elevated pulmonary vascular impedance can cause systolic deceleration or “notching” of the right ventricular outflow tract Doppler flow velocity envelope in patients with PH. The notching can be midsystolic or late systolic in nature. Both mid and late systolic notching have been associated with elevated pulmonary vascular resistance, poor right ventricular function, and worse outcomes.^{9,10} Thus, notching of the right ventricular outflow tract Doppler flow velocity envelope is an imaging biomarker for elevated pulmonary vascular resistance.

Although normal right ventricular size and function does not exclude PH, it is uncommon to have significantly elevated PASP with normal right ventricular size and function. Similarly, if right ventricular size and function are normal in a patient with significant dyspnea, PH is not likely to be responsible for their symptoms. In clinical practice, it is important to review the echocardiogram of a patient with dyspnea carefully to make sure that the PAP and right ventricular size and function have been appropriately interpreted and reported. This is especially relevant in patients whose PASP is not reported because of insufficient tricuspid regurgitation jet, before ruling out PH. In this case, the presence of right ventricular enlargement and dysfunction suggest significant PH. However, it is important to note that the presence of right ventricular enlargement and dysfunction alone does not help in differentiating precapillary PH from PH-LHD.

TTE can be very useful in establishing the cause of PH (Table). It can identify the presence of LHD including aortic valve disease, mitral valve disease, heart failure with reduced or preserved ejection fraction (HFrEF or HFpEF). While the presence of systolic dysfunction and valvular disease can be obvious, it can be challenging to differentiate PH associated with HFpEF (PH-HFpEF) from precapillary PH based on echocardiography alone. In both conditions, LV systolic function will be normal, medial mitral annular tissue Doppler velocity (E') can be reduced, and the right ventricle can be dilated and dysfunctional. While notching of the right ventricular outflow tract Doppler flow velocity envelope relates to elevated pulmonary vascular resistance, its presence, on its own, does not differentiate PAH from PH caused by left heart disease.

The presence of left ventricular hypertrophy with increased wall thickness is more suggestive of PH-HFpEF (Figure 3A). In PH-HFpEF, the interatrial septum bows towards the right because of elevated left atrial pressure (Figure 3A). Grade I diastolic dysfunction can occur in Group 1 PAH while usually advanced Grade II or III diastolic dysfunction indicates PH-HFpEF. Similarly, mitral flow Doppler E/A ratio >1, lateral mitral annulus tissue Doppler velocity (E') <8, and lateral mitral E/E' >10 are suggestive of PH-HFpEF (Figure 3B).

Left atrial enlargement is a strong indicator of PH-LHD. In fact, left atrial enlargement has been considered the hemoglobin A1C of left-sided filling pressures. Left atrial volume index >43 mL/m² by cardiac magnetic resonance imaging differentiates PH-LHD from precapillary PH with a 97% sensitivity and 100% specificity.¹¹ An echocardiographic model based on lateral mitral E/E' ratio, left atrial anteroposterior diameter, pulmonary artery acceleration time, and midsystolic notching of the right ventricular outflow tract pulse Doppler has been proposed to differentiate precapillary PH from PH-LHD.¹² A score of 0 in this model has 100% sensitivity, 62.6% specificity, and 69% positive predictive value for differentiating precapillary PH from PH-LHD.¹² This model, like several others, requires prospective, multicenter validation.

Pre-Test Probability of PH Caused by LHD/WHO Group 2

The clinical and imaging findings discussed above are required to help establish the pre-test probability of PH-LHD. In this case, elevated right ventricular systolic pressure along with moderately dilated and dysfunctional right ventricle suggest significant underlying

TABLE. Comparison of Echocardiographic Characteristics of Normal, Precapillary PH, and PH Caused by HFpEF

Characteristics	Normal	Precapillary PH	PH-HFpEF
Right ventricular size	Normal	Dilated	Normal or dilated
Right ventricular systolic function	Normal	Decreased	Normal or decreased
Left ventricular wall thickness	Normal	Normal	Increased
Left ventricular size	Normal	Normal or underfilled	Normal
Left ventricular systolic function	Normal	Normal	Normal
Mitral E/A ratio	>1	<1	>1
Medial mitral E'	Normal	Normal or decreased	Decreased
Lateral mitral E'	Normal	Normal	Decreased
Medial mitral E/E'	<8	<8	>10
Lateral mitral E/E'	<8	<8	>10
Interatrial septum	Midline	Bows from right to left	Bows from left to right
Left atrial volume	Normal	Normal or decreased	Increased
RVOT pulse Doppler	Normal	Midsystolic notching common	Midsystolic notching rare
PAAT	Normal	Decreased	Rarely decreased

Abbreviations: HFpEF indicates heart failure with preserved ejection fraction; PAAT, pulmonary artery acceleration time; PH, pulmonary hypertension; and RVOT, right ventricular outflow tract.

PH.¹³ The probability of PH in this case being caused by LHD is exceedingly high, further evidenced by older age, structural left heart disease (left ventricular hypertrophy, left atrial enlargement), metabolic syndrome features,¹⁴ and presence of atrial fibrillation.¹⁵ In fact, up to 60% of patients with HFrEF and up to 83% of patients with HFpEF have elevated PAP noted on echocardiograms.¹⁶

Although various clinical risk scores have been developed to aid in the differential process, most are single-center studies or lack prospective validation.^{12,17-22} A recent algorithm from the 6th World Symposium on Pulmonary Hypertension suggests proceeding to hemodynamic evaluation only in those with low pre-test probability of PH-LHD or intermediate pre-test probability in the setting of concomitant risk factors for precapillary PH (ie, right ventricular dysfunction, systemic sclerosis, history of pulmonary embolism, or dyspnea of unexplained origin).¹⁵

Next Steps for This Patient

Given the high pre-test probability of PH-LHD in this patient, invasive hemodynamic evaluation at this point is not necessary. The initial management of PH-LHD is aimed at treatment of the underlying LHD, risk factor, and comorbidity modification (hypertension, arrhythmia management, coronary disease,

weight loss,²³ and obstructive sleep apnea), and optimization of right ventricular function (Figure 2). Guideline-directed heart failure therapy should be maximized for patients with HFrEF, but therapeutic options are more limited in our patient with HFpEF.²⁴ Most clinical trials on the efficacy of treatments for HFpEF to date have produced neutral results, but strong evidence supports the use of diuretics, mineralocorticoid receptor antagonists, and exercise training as effective therapies.²⁵ Aldosterone antagonists may be considered,²⁶⁻²⁹ assuming adequate kidney function and potassium monitoring. Caloric restriction and aerobic exercise training increased peak $\dot{V}O_2$ in older patients with clinically stable HFpEF.^{23,30} In the presence of volume overload, loop diuretics reduce left atrial pressure and improve symptoms. Importantly, reducing left atrial pressure also improves pulmonary vascular compliance, reducing afterload on the right ventricle.³¹⁻³³ In the setting of a dilated RV, preload reduction may reduce septal flattening and improve septal and global right ventricular function.^{34,35} Implantable PAP monitoring devices may also be helpful to titrate diuretic therapy, and have shown similar reductions in heart failure hospitalizations in HFpEF and HFrEF.^{36,37} Finally, observational studies suggest that rhythm control strategies of atrial arrhythmias may have some hemodynamic and functional benefits.³⁸⁻⁴⁰

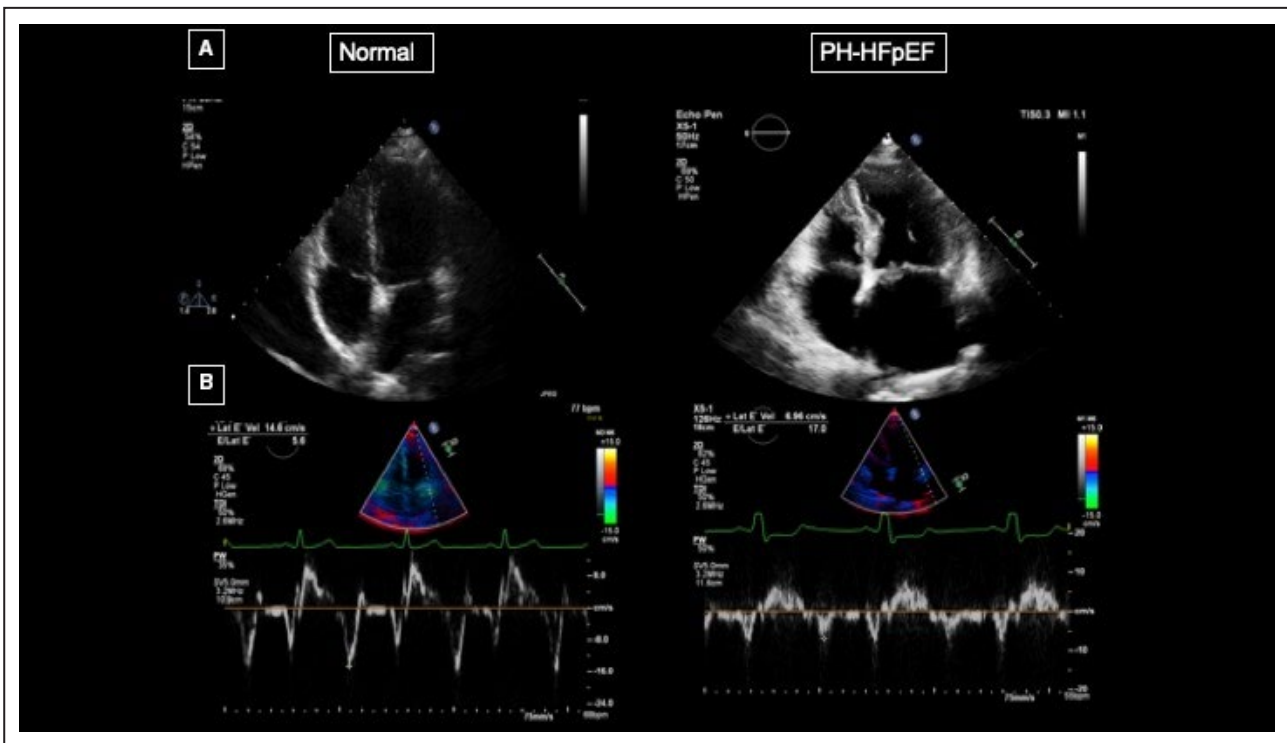


Figure 3. Echocardiogram comparison between a normal patient (left) and patients with PH-HFpEF (right). (A) Apical 4-chamber view. (B) Tissue Doppler across mitral valve annulus. HFpEF indicates heart failure with preserved ejection fraction; and PH, pulmonary hypertension.

The current European Society of Cardiology/² European Respiratory Society² PH guidelines and the recent 6th World PH Symposium expert consensus statement¹⁵ strongly recommend against the use of PAH-specific therapies in PH-LHD. Despite these recommendations, the off-label use of these therapies remains common in clinical practice.^{3,41} The use of phosphodiesterase-5A-inhibitors is particularly common, perhaps based on early, single-center studies that suggested improvement in hemodynamics and functional capacity.^{42,43} Larger, randomized studies did not find similar benefits, though may have limited ability to assess efficacy because the studies did not specifically enroll patients with PH-LHD.^{44,45} In the past year, however, a randomized study exposed important safety concerns with this approach. In the SIOVAC (Sildenafil for Improving Outcomes in Patients With Corrected Valvular Heart Disease) study,⁴⁶ treatment with sildenafil was associated with worsening functional status and an increased risk of major clinical events in patients with persistent echo-defined PH 1 year after left-sided valvular intervention. PAH-specific therapies, including phosphodiesterase-5A-inhibitors, should not be prescribed to the patient described above, outside of a clinical trial.⁵

Ongoing studies evaluating the utility of more rigorous pathophysiological characterization of HFpEF into distinct phenotypes may allow matching of individualized treatments to patients who are most likely to respond favorably.^{25,47} Specific interventions to target individual steps in the signaling cascade may be utilized to address the phenotypic diversity of HFpEF: metabolic risk by caloric restriction, systemic inflammation by statins, PH by phosphodiesterase 5 inhibitors, muscle weakness by exercise training, sodium retention by diuretics and monitoring devices, myocardial cGMP content by neprilysin, and myocardial fibrosis by spironolactone.⁴⁷

When to Consider Referring Patients to a PH Center

Once the phenotype for PH has been characterized and the patient successfully treated for underlying disease with appropriate volume management, it is reasonable to follow the patient clinically. However, if the patient continues to have poor functional class in spite of aggressive risk factor modification and volume management, it is reasonable to consider performing a detailed right heart catheterization (RHC) by expert operators (Figure 2). RHC should also be considered if the history and the rest of the work-up are suggestive of PAH or the patient has evidence of worsening end organ function (eg, renal failure).⁵ If the procedure is performed at a non-PH center, key focus should be placed on leveling the transducer to the right atrium,

zeroing to atmospheric pressure, and obtaining measurements at end-expiration. Focus on appropriate measurement of pulmonary arterial wedge pressure (PAWP) tracing cannot be overemphasized. If PAWP is noted to be elevated, and especially if higher than diastolic mean PAP, it should be confirmed by obtaining an oxygen saturation with the balloon inflated, which should be similar to the arterial oxygen saturation. Alternatively, left ventricular end diastolic pressure should be obtained.

In this patient with underlying atrial fibrillation and, hence, an absent a-wave, the PAWP will more closely approximate the left ventricular end diastolic pressure at 130 ms after the QRS. Cardiac output by thermodilution should be obtained in triplicate and if the values are not within 10% of each other, at least 3 measurements should be obtained and averaged. Although the Fick cardiac output (which directly measures the oxygen consumption) is the most accurate method to obtain this parameter, the indirect Fick cardiac output, which uses formulas to estimate the oxygen consumption, is unreliable and is not recommended,⁴⁸ even in the presence of severe tricuspid regurgitation and low cardiac output.⁴⁹ An elevated PAWP/left ventricular end diastolic pressure will confirm PH-LHD. However, there are some settings when the patient may be diuresed to a normal PAWP/left ventricular end diastolic pressure.⁵⁰ If suspicion of LHD is high, it is recommended that an infusion of 500 mL of normal saline be administered over 5 minutes and if the PAWP rises to >18 mm Hg, then PH-LHD is confirmed.⁵⁰⁻⁵³ Some centers alternatively perform exercise RHC, which requires specialized equipment and expertise. In these situations where the diagnosis is unclear, referral to an expert center is warranted.

Case 2: A 42-year-old woman with a 20 pack-year history of smoking presents to the clinic with an episode of syncope in the setting of progressively worsening shortness of breath over the last few months and symptoms consistent with Raynaud disease. Electrocardiogram and chest radiograph are unremarkable. Echocardiogram shows normal left ventricular size and function, severely dilated right ventricle, severe right ventricular dysfunction with a TAPSE of 11 mm, small pericardial effusion, and an estimated PASP of 60 mm Hg.

The similarities between this case and case 1 end with the significantly elevated PASP on echocardiography. The young age of this patient alone would make PH-LHD unlikely. However, she does have risk factors (smoking) that would prompt consideration for chronic obstructive lung disease (COPD). It is important to remember that the prevalence of PH in COPD is dependent on the severity of disease and requires quantification. Patients with a history of smoking (or oxygen dependency) often get labeled with COPD without

formal evaluation with pulmonary function testing. Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 1–3 do not usually cause significant PH. In fact, 90% of patients with GOLD stage 4 COPD have mean PAP >20 mm Hg, most ranging between 20 and 35 mm Hg, with only 1% to 5% of patients with COPD manifesting mean PAP >35 to 40 mm Hg at rest.⁵⁴

An unremarkable chest radiograph for this patient makes group 3 PH (PH caused by lung disease) less likely but warrants formal pulmonary function testing. Regardless of her smoking history, her TTE should prompt the evaluating provider to consider connective tissue disease such as systemic sclerosis or scleroderma with the presence of Raynaud disease, which is commonly complicated by the development of PAH. The TTE findings in this patient are more consistent with precapillary PH. The findings of presyncope along with a dilated right ventricular and pericardial effusion are particularly concerning, and may be suggestive of low cardiac output and advanced disease.⁵⁵ Right ventricular enlargement, flattened interventricular septum, and reduced right ventricular function can occur in both precapillary and postcapillary PH, but severe right ventricular enlargement and dysfunction frequently occur in patients with precapillary PH (Figure 4A). The interatrial septum bows towards the left in patients with precapillary PH because of underfilled left atrium with lower left atrial pressure (Figure 4A). The medial mitral

tissue Doppler velocity (E') can be reduced and medial E/E' can be elevated in patients with precapillary PH because of the flattening of the interventricular septum, but the lateral mitral E' and E/E' ratio generally remains within normal limits. Importantly, in precapillary PH, the left ventricle and the left atrium will be either normal or small because of reduced left-sided preload from right ventricular failure (Figure 4A). Midsystolic notching of the right ventricular outflow tract pulse Doppler and reduced pulmonary artery acceleration time is more likely to occur in precapillary PH (Figure 4B).⁹

In addition to being the screening test of choice, an echocardiogram can also assist in risk assessment in patients with precapillary PH. Reduced right ventricular systolic function is associated with increased risk of death. In a single-center study of 63 patients with precapillary PH, TAPSE <18 mm was associated with a 5.7-fold increased risk of death when compared with TAPSE ≥18 mm.⁷ Every 1-mm decrease in TAPSE was associated with a 17% increased risk of death.⁷ Similarly, in another study of 59 patients with idiopathic PAH, TAPSE <15 mm was associated with a nearly 3-fold increased risk of death.⁵⁶ The presence of pericardial effusion is also associated increased mortality in patients with PAH.⁵⁷ Thus, severe right ventricular dysfunction and pericardial effusion are high-risk clinical characteristics in this patient, favoring the need for early referral

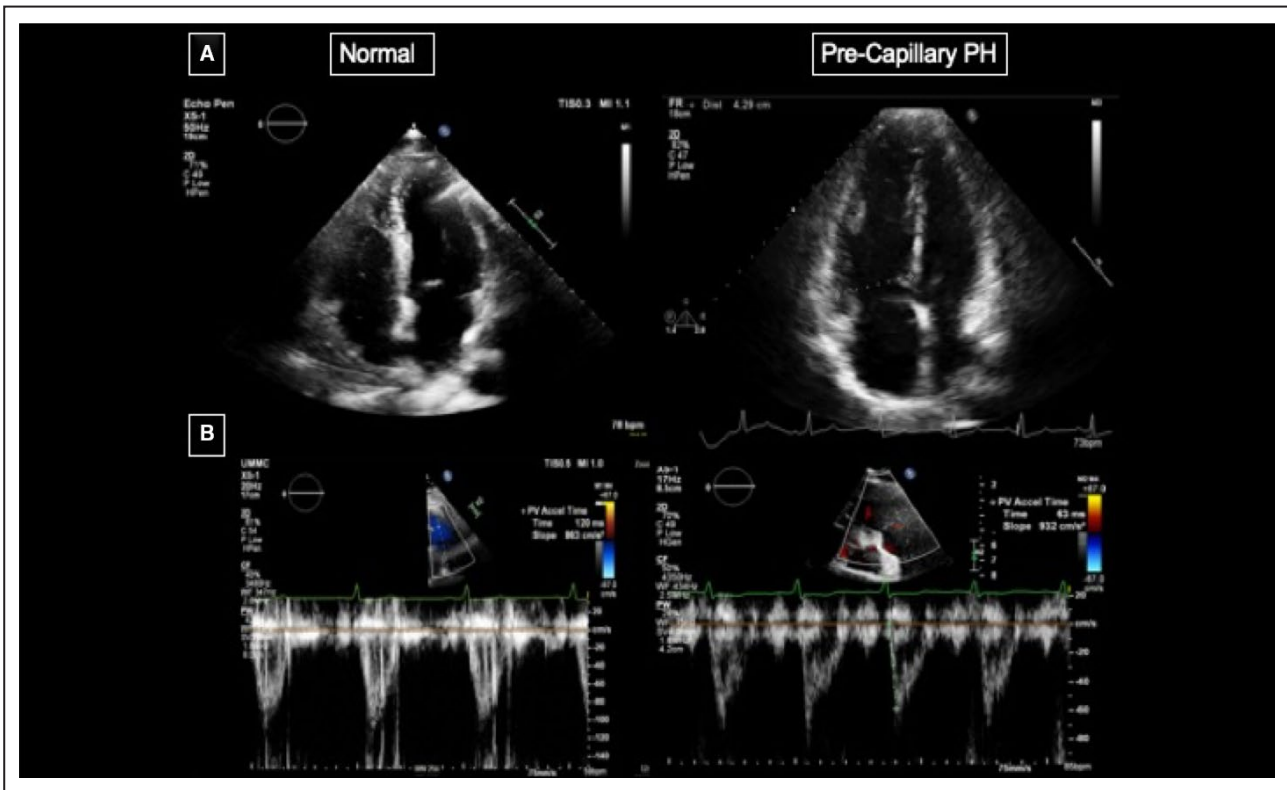


Figure 4. Echocardiogram comparison between a normal patient (left) and patients with precapillary PH (right). (A) Apical 4-chamber view. (B) Pulse wave Doppler across mitral valve annulus. PH indicates pulmonary hypertension.

and use of more aggressive treatment options such as parenteral prostacyclins.⁵

Next Steps for This Patient

On first look, this patient has demographics consistent with WHO group 1 PAH and WHO functional class IV symptoms, given the history of syncope. The next steps will be to perform a careful history and physical examination, looking for stigmata associated with the subgroups of PAH. Evidence of right heart failure on physical examination or a history of syncope will require rapid evaluation and treatment. Of particular concern on physical examination are findings of low pulse pressure and cool extremity associated with low-output state and hypoperfusion, which would require admission for expedited evaluation and treatment. The practice to start monotherapy before obtaining a full hemodynamic assessment (even with phosphodiesterase inhibitors) should be avoided.

Referring Patients With Suspected PAH to a PH Center

Early referral to a PH expert center is warranted for this patient, given the poor prognostic indicators already evident on clinical evaluation: rapid progression of symptoms, syncope, dilated RV, and pericardial effusion. At the PH center, this patient would undergo rapid diagnostic evaluation to confirm WHO group 1 PAH and rule out significant contribution from other WHO PH group causes. Given the presence of Raynaud disease, she may also be at risk for connective tissue disease, although 5% of patients with idiopathic PAH may have Raynaud disease without underlying connective tissue disease. Additional testing at the PH center in such patients would typically include hepatitis and HIV serology, genetic screening, connective tissue disease serologies, TTE with agitated saline shunt study/cardiac magnetic resonance imaging to evaluate for possible intracardiac shunt, V/Q scan to screen for chronic thromboembolic PH, pulmonary function studies and computed tomography scan to screen for lung disease, sleep study, etc. Six-minute walk distance and B-type natriuretic peptide levels are determined at baseline to assess severity of disease and are monitored sequentially to assess response to therapy.

Accurate RHC with a vasodilator challenge using intravenous adenosine, inhaled nitric oxide, or intravenous prostacyclins is imperative to ascertain cause, determine severity, assess vasoreactivity, and guide therapy in patients with PAH. If the RHC were to show right atrial pressure of >15 mm Hg and a cardiac index of <2.0 L/min per m² without acute vasodilator response, her prognosis would be dire. Other parameters that would add to poor prognosis

would be high B-type natriuretic peptide levels and poor 6-minute walk distance. Given this patient's presentation, especially syncope, the most appropriate course of action would be instituting parenteral prostanoid therapy in combination with other oral agents. Once therapy is initiated, response to treatment should be closely monitored with assessment of WHO functional class, 6-minute walk distance, B-type natriuretic peptide levels, periodic imaging, and RHC. In situations of inadequate attainment of goals and ongoing evidence of right heart failure, medical therapy should be escalated and lung transplant evaluation initiated. Enrollment in clinical trials evaluating novel pharmacologic pathways and devices should be made available to the patient at expert PH centers.

What About Patients With “Borderline” PH?

The latest clinical PH guidelines recommend further follow-up of those patients in the “intermediate” probability range and any risk factors for PH.⁵ However, there is emerging data on the prognostic implications of a distinctly lower threshold of elevations in PASP noted on echocardiogram, regardless of cause of PH.^{58,59} In a large cohort of >150 000 patients with a median follow-up of 4.2 years, an estimated right ventricular systolic pressure of >30 mm Hg was associated with increased 1- and 5-year mortality.⁶⁰ This phenomenon was observed in all age groups, did not appear to be confounded by LHD or other comorbidities, and was consistent with increasing levels of RV dilatation and impaired function. Such data illustrate a continuum of risk according to mean PAP level, with even mild abnormalities being associated with increased mortality and hospitalization. Hence, any patient with abnormal PAP noted on TTE, even if the elevation is borderline, should be carefully evaluated for symptoms (eg, exertional dyspnea) consistent with PH and risk factors that would explain the presence of PH. Whether efforts to target subjects with borderline PH with more intense investigation and treatment to alter their outcomes requires further investigation.

CONCLUSIONS

PH is caused by a heterogeneous group of disorders, most commonly left heart disease, and is associated with poor prognosis, regardless of cause. However, in spite of being commonly noted on TTE, it is often underestimated in its implications. One of the reasons for this is the lack of clarity among treating physicians about which patients to work up further and how. As a result, further workup and appropriate categorization

of WHO groups is delayed and worse, mislabeled, leading to delays in therapy. Having a simplified approach may allow for a more appropriate adaptation of current guidelines in PH.

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