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Research Article

Assessment of Newly Detected Pulmonary Hypertension Cases

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Abstract

Pulmonary hypertension (PH) is a heterogenous disease. Left heart disease and chronic lung disease are the most common etiologies. Comorbidities, aging population, different pulmonary arterial hypertension phenotypes, and occult groups that show PH with exercise challenge, new molecular mechanisms for pathogenesis, and use of hemodynamic indices had changed the definition and treatment modalities.

Diagnostic algorithm, clinical evaluation, considering exact phenotype, comorbidities, shared decision-making before therapy, patient–clinician discussion, indices measuring right ventricle (RV)-pulmonary artery (PA) system and factors that have roles in the RV and the PA circulation will help to detect hemodynamic status and treatment response. Reconsidering the hemodynamic parameters thresholds that define PH and cardiopulmonary interactions is warranted for early detection and management strategies.

Keywords: pulmonary hypertension; definition; hemodynamic indices

Introduction

Pulmonary hypertension is a syndrome characterized by marked remodeling of the pulmonary vasculature and a progressive rise in the pulmonary vascular load, leading to hypertrophy and remodeling of the right ventricle. Death results from right ventricular failure if pulmonary hypertension is left untreated (1). Pulmonary hypertension (PH) is a pathophysiological manifestation of a heterogeneous group of diseases characterized by abnormally elevated pulmonary arterial pressures diagnosed on right heart catheterization (2).

PH leads to progressively worsening exertional dyspnea and right heart failure in untreated patients. Each patient presenting with a suspicion for PH must be thoroughly investigated to characterize their phenotype and identify the correct underlying pathophysiological mechanisms related to their specific diagnosis. Only then can patients be appropriately managed. Recent changes in the understanding of PH have justified an update to the hemodynamic definition and classification of PH (2). In this manuscript, diagnostic definitions and hemodynamic parameters in newly detected PH cases is reviewed.

Methods

A review of literature was performed in 2024-2025 to summarize scientific reports on pulmonary hypertension. Articles indexed in the PubMed and Medline, and Web of Science by using medical subject headings (MeSH) were searched by using the following key words: new detected pulmonary hypertension, definition and types, right ventricle and hemodynamic indices. Full text of relevant title and also their relevant references were extracted.

Definition of pulmonary hypertension

Pulmonary hypertension (PH) is a hemodynamic condition that is characterized by the elevation of mean pulmonary arterial pressure (mPAP) above the upper limit of normal (3).

In the 2022 ESC/ERS guidelines, major updates were made to the hemodynamic definition reducing the thresholds of PH to an mPAP > 20 mmHg and the PVR threshold to >2 WU to define pre-capillary PH, while the PAWP cut-off of ≤15 mmHg was maintained to distinguish pre-capillary from post-capillary PH (4). Additionally, exercise induced PH was reintroduced into the hemodynamic classification. Exercise pulmonary hypertension has been reintroduced into the hemodynamic definitions and is defined by an mPAP/cardiac output slope of >3 mmHg/L/min between rest and exercise (4).

Consequently, the current ESC/ERS guidelines recommend a PAWP threshold ≤ 15 mmHg is recommended by for the differentiation between pre-capillary and post-capillary PH, while acknowledging the presence of a grey area between 13 and 15 mmHg (4,5). This highlights the crucial

role of accurately phenotyping patients during the diagnostic evaluation (5).

Based on a large number of invasive hemodynamic measurements in healthy subjects in the supine position, the upper limit of normal mPAP is 20 mmHg (5-7). Pre-capillary PH is defined by mPAP >20 mmHg and the elevation of pulmonary vascular resistance (PVR) above the upper limit of normal that is considered to be 2 Wood Units (WU) (5,6,8), and by a pulmonary arterial wedge pressure (PAWP) ⩽15 mmHg. This form of PH is characteristic of hemodynamic conditions and diseases with pulmonary arterial involvement and no significant left heart disease (3). Post-capillary PH is defined by mPAP >20 mmHg and PAWP >15 mmHg and is strongly suggestive of left heart disease. The value of the PVR further distinguishes between isolated post-capillary PH (ipcPH, PVR ⩽2 WU) and combined post- and pre-capillary PH (cpcPH, mPAP >20 mmHg, PAWP >15 mmHg, PVR >2 WU). Exercise PH is a hemodynamic condition describing a normal mPAP at rest with an abnormal increase of mPAP during exercise and is defined as a mPAP/cardiac output (CO) slope >3 mmHg/L/min between rest and exercise (3).

The mPAP/CO slope defines exercise PH. For assessment, linear regression based on multipoint measurements is possible but cumbersome, and a more practical method is assessing the mPAP/CO relationship based on measurements at rest and peak exercise (9). Exercise PH is defined as mPAP/CO slope >3 mmHg/L/min (4,5,10). From the differential-diagnostic point of view, recognizing post-capillary causes of exercise PH is of significant relevance. The PAWP/CO slope >2 mmHg/L/min between rest and exercise (11), and an increase of the absolute value of PAWP>25 mmHg are considered markers of post-capillary exercise PH (12).

Among subjects with exercise intolerance and suspected early-stage pulmonary hypertension (PH), early identification of pulmonary vascular disease (PVD) with noninvasive methods is essential for prompt PH management (13). In a cohort of subjects with exercise intolerance and suspected early-stage PH, showed rest gas exchange parameters (minute ventilation to carbon dioxide production ratio (VE/VCO2) and end-tidal carbon dioxide (ETCO2) can identify patients who are likely to have PVD (13). Such patients may benefit from a prompt invasive hemodynamic evaluation and PH vasodilator therapy (13).

The main changes in the new classification of PAH1 include: (a) the identification of two subgroups of idiopathic PAH according to acute vasoreactivity test response, (b) the list of genes associated with heritable forms of PAH, (c) an update of the drugs and toxins that can induce PAH, and (d) the inclusion of pulmonary veno-occlusive disease (PVOD) within group (2).

Elevated PVR remains associated with a significant increase in the hazard for 30-day mortality after cardiac transplantation, even in the setting of lower pulmonary artery pressures (14).

PAH patients with comorbidities are increasingly seen in clinical practice and have been found in several studies to have a higher rate of adverse events with therapy (15,16) and possibly a less robust treatment response. Potential contributors include differences in PAH phenotype as well as the occurrence of occult group 2 PH, where patients meet typical hemodynamic criteria for pre-capillary PH at rest, but manifest group 2 hemodynamics with provocative maneuvers such as exercise or fluid challenge, resulting in misclassification (15).

Clinical manifestations

Clinical findings in patients with pulmonary hypertension are: Dyspnea (during stress or at rest), cyanosis, fatigue, dizziness, syncope, thoracic pain, palpitations, orthopnea, cough, croakiness, abdominal tension, peripheral edema, ascites, and hepatomegaly (17).

The most frequent symptoms in patients with PH are dyspnea on exertion, fatigue and rapid exhaustion. Bendopnea (dyspnea when bending forward), weight gain due to fluid retention or syncope during physical exertion may occur. Particular attention should be paid to risk factors in the patient's history that are associated with PH (e.g. connective tissue disease, portal hypertension, HIV, congenital cardiac disorders, thromboembolic disease, left heart diseases, lung diseases and illicit drug use) (3). A thorough physical examination of the patient may reveal an accentuated second heart sound and, in more advanced cases, a systolic murmur due to tricuspid regurgitation, or a diastolic murmur due to pulmonary valve insufficiency (Graham Steell murmur). Signs of right heart failure such as peripheral edema, distended and pulsating jugular veins, hepatic heave or ascites are suggestive of severe right heart failure (3).

Hemodynamic indices in pulmonary hypertension

Here some of the hemodynamic indices of pulmonary hypertension calculated by cardiac output monitoring devices and direct and indirect measurements during right heart catheterization is mentioned in (Table 1):

Name	Description
Cardiac index (CI)	is reflective of the global function of the RV (in patients with normal systolic and diastolic left ventricular function) and forms an integral component to assess the functionality of the cardiopulmonary unit. As PH worsens, the CI decreases, due to failure of the RV in the setting of a higher afterload. CI is a well-known predictor of outcomes in PH and the European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines assigned CI thresholds of ≥2.5 L/min/m², 2–2.4 L/min/m², and <2.0 L/min/m² for patients at low (<5%), intermediate (5–10%) and high risk (>10%) of dying at 1-year (18,19).
Cardiac output (CO)	(per Fick) formula is: [125 × body surface area (BSA)]/ [Hb × 1.36 × (SaO2-SvO2)], normal range: 4.0-8.0 L/min (20). Cardiac index (CI) formula is: CO/BSA, normal range: 2.5-4.0 L /min/m² (20).

Stroke volume (SV)	Stroke volume (SV) may be more accurate than CI in estimating RV function as it removes the compensatory heart rate (HR) response when CO is inappropriate to meet the body demands (SV = CO/HR) (18). Stroke volume (SV) formula is: CO/HR × 1000, normal range: 60-100 ml/beat (20).
Stroke volume index (SVI)	Stroke volume index (SVI) could allow for a more precise evaluation of the RV function in patients with PAH (18). Some investigators have proposed using SVI rather than CI as a treatment target in PAH since a decrease in SVI was independently associated with death or lung transplantation (a drop of 10 mL/m2 in SVI led to a 28% increase) at the first follow-up right heart catheterization after initiation of PAH therapies (21). Stroke volume index (SVI) formula is: CI/HR × 1000, with normal range: 33-47 ml (m²*beat) (20).
Cardiac power output	Cardiac power output formula is: (MAP × CO)/451, normal range: > 0.6 (20).
Cardiac power output index (CPOi)	Cardiac power output index (CPOi) = cardiac index x (MAP-CVP)/451. Lower CPOi associated with worse outcomes (22). Performs better with the inclusion of CVP, especially if CVP > 8 mm Hg. In cardiogenic shock (CS) or Impella support, cutoffs > 0.28-0.30 W/m² (22).
Left ventricular stroke work (LVSW)	Left ventricular stroke work (LVSW) = (MAP-PAWP) x SV x 0.0136. Limited data in CS (22).
Left/right filling pressures (CVP/PAWP)	Left/right filling pressures = CVP/PAWP, Higher ratio associated with poorer outcomes CVP/PAWP > 0.63 post-LVAD (left ventricular assist device), > 0.86 acute myocardial infarction (22).
Right ventricular stroke work (RVSW)	Right ventricular stroke work (RVSW) Varies with PVR. The formula is (mean PA – CVP) x SV x 0.0136: lower levels associated with poorer outcomes, < 15 (post-LVAD), < 10 (acute MI) (22).
Right ventricular systolic work index (RVSWI)	RVSWI is used to quantify the amount of work required by the RV for ejecting blood in each cardiac cycle when adjusted for BSA. RVSWI is calculated as (mPAP − mRAP) × SVI × 0.0136 (18). Parameter measured for Right ventricular work and used in PH for Survival prognosis in PAH and CTEPH (18).
Diastolic pulmonary gradient (DPG)	Diastolic pulmonary gradient (DPG) formula is: PADP-PCWP, normal range: < 7 mmHg (20). Diastolic pulmonary gradient (DPG)= dPAP-PAWP. Parameter measured is pulmonary vascular constriction/remodeling (18). Used for differentiate CpcPH and IpcPH in patients with PH-LHD (18). Diastolic pressure gradient (DPG) formula is: PA diastolic pressure – PAWP: Abnormal if > 5-7 mm Hg, suggests pulmonary vascular disease, But usually > 7 mm Hg in pressure-overloaded right heart failure (22). Diastolic pulmonary gradient (DPG): DPG is calculated by subtracting PAWP from the diastolic pulmonary artery pressure (dPAP) (18). A DPG of ≥7 mmHg showed the best combination of sensitivity and specificity to be an independent predictor of survival in patients with PH-LHD (18,23).
Trans-pulmonary pressure gradient (TPG)	Trans-pulmonary pressure gradient (TPG) formula is: MPAP-PCWP, normal range: < 13 mmHg (20). Usually, > 15 mm Hg in pressure-overloaded right heart failure (22). The TPG is calculated by subtracting the PAWP from the mPAP and higher values reflect pulmonary vascular constriction and/or remodeling (18). A TPG cutoff of >12 or ≤12 mmHg was used to distinguish IpcPH from CpcPH (23,24). As with mPAP, TPG is influenced by the same hemodynamic factors, including flow, resistance, and left heart filling pressures (18,25). Due to these limitations, TPG was removed, in favor of PVR (TPG/CO), as a tool to establish the different hemodynamic types of PH-LHD (18,26,19). In patients with PH due to valvular heart disease, a higher TPG also predicted worse outcomes. Patients with high TPG (>12 mmHg) who underwent restrictive mitral annuloplasty for severe mitral regurgitation had worse outcomes (all-cause mortality and readmission for heart failure) (18,27). Similarly, patients with markers of precapillary PH (including an elevated TPG and PVR) had worse survival after transcatheter aortic valve replacement (18,28).
Pulmonary vascular resistance (PVR)	Pulmonary vascular resistance (PVR) = Transpulmonary gradient/ cardiac output: Abnormal ≥ 2WU, But usually > 5WU in pressure-overloaded right heart failure (22). Pulmonary vascular resistance (PVR) formula is: (mPAP-PCWP)/CO (20). PVR is a static hemodynamic index based on Poiseuille's law and is calculated as (mPAP − PAWP)/CO. A meta-regression analysis of 21 trials showed that changes in PVR were independently predictive of adverse clinical events, particularly total mortality (18,29). While a PVR of ≥3 WU is currently used to define precapillary PH, this threshold is not based on evidence regarding the upper limit of normal which is <2 WU (70). In fact, a PVR >2.2 WU was

	associated with all-cause mortality in patients undergoing right heart catheterization; and a PVR between 2.2 and 3 WU may represent early pulmonary vascular disease (18,30,8,31).
Pulmonary vascular resistance index (PVRI)	Pulmonary vascular resistance index (PVRI) formula is: 80 × (MPAP-PCWP)/CI, range: 255-285 dynes·sec/ cm^5/m^2 (20). Pulmonary vascular resistance index (PVRI): It is calculated as follows: PVRI = (mPAP − PAWP)/CI or PVRI = PVR × BSA (18).
Systemic vascular resistance (SVR)	Systemic vascular resistance (SVR) formula is: 80 × (MAP-RAP)/CO, normal range: 800-1200 dynes·sec/ cm^5 (20)
Systemic vascular resistance index (SVRI)	(SVRI) formula is: 80 × (MAP-RAP)/CI, normal range: 1970-2390 dynes·sec/ cm^5/m^2 (20).
Central venous pressure (CVP)	Represents right atrial pressure, and interprets right-sided filling pressures of the heart. CVP>15 mmHg indicates overloaded right-sided pressures (45).
Left/right filling pressures (CVP/PAWP)	Higher ratio associated with poorer outcomes CVP/PAWP > 0.63 (post-LVAD), > 0.86 (acute MI)
Pulmonary artery pulsatility index (PAPI)	(PAPI) formula is: (PASP-PADP)/RAP, normal range is: > 0.9 (20). (PAPI) formula is: PA pulse pressure/CVP. Lower PAPI associated with worse prognosis, but cutoff varies with PVR (22,32): < 1.85-3.3 (post-LVAD), and < 1.0 in primary RV dysfunction without pulmonary hypertension. PAPi is an indirect measure of RV function and is defined as the ratio of PAPP to RAP [PAPi = (sPAP − dPAP)/RAP] (18). PAPi reflects the adaptive response of the RV to increased afterload (RV to pulmonary artery coupling) with implications for prognosis and survival (18,33,34). Also, it is mentioned for vasopressors and inotropes wean in cardiogenic shock, if CPO is above >0.6 and PAPI >0.9 (56).
Proportional pulmonary pulse pressure (PPP)	Proportional pulmonary pulse pressure (PPP) = PA pulse pressure/mean PA pressure, Lower in right heart failure. If > 0.60 post-VA ECMO is associated with better hemodynamic response (22).
Pulmonary artery capacitance	Pulmonary artery capacitance formula is Stroke volume/ PA pulse pressure. Lower capacitance is associated with poorer outcomes. < 0.81 ml/mm Hg in pulmonary arterial hypertension, < 2 ml/mm Hg in heart failure (22).
Aortic pulsatility index (API)	Aortic pulsatility index (API) formula is: (SBP-DBP)/PAWP with variable cutoffs (≥1.45103 to ≥2.9104) (22). Lower API associated with worse prognosis, mostly in patients with heart failure (22).
Pulmonary arterial compliance (PAC)	Pulmonary arterial compliance (PAC): Unlike the static index PVR, PAC measures arterial distensibility and therefore provides information about the pulsatile load on the RV (18). A simplified approximation of PAC uses the ratio of SV and pulmonary artery pulse pressure (PAPP). The formula is PAC = SV/(sPAP − dPAP). Parameter measured is pulmonary artery distensibility, RV afterload (dynamic) (18).
Pulmonary effective arterial elastance (Ea)	Pulmonary effective arterial elastance (Ea): Ea and PAC were more strongly associated with RV dysfunction and were consistently better predictors of mortality than TPG and PVR in patients with PH-LHD (18).
RAP/PAWP	RAP/PAWP is another index that can serve to evaluate RV failure (18). As long as RV function is maintained, RAP remains lower than PAWP. When the RV starts failing, the RAP increases "out of proportion" to the PAWP, thus raising the RAP/PAWP ratio. Fluid overload and/or other organ dysfunction (left ventricular, kidney, and/or liver failure) would be expected to raise the RAP, but the RAP/PAWP ratio should remain <1 in the absence of RV failure (18). A RAP/PAWP value of ≥1 provided the best combination of sensitivity and specificity (36). RAP/PAWP ratio is higher in precapillary PH and CpcPH as compared to IpcPH. A ratio of ≥1 was associated with smaller left atrial volume, decreased tricuspid annular plane systolic excursion (TAPSE), and a higher RV/left ventricle size ratio (37). In addition, RAP/PAWP ratio may help to identify patients at high risk of developing right ventricular failure and mortality after the implantation of a left ventricular assist device (18,38). RAP/PAWP ratio increased immediately following left ventricular assist device (LVAD) implantation, then decreased for a short period followed by a gradual increase in the long-term that may represent the change in the RV function over time (18,39).
Pressure-volume loops (PV loops)	The gold standard assessment of RV function is done by determining pressure-volume loops that allow a meticulous evaluation of the RV-pulmonary artery coupling (18). This procedure assesses how efficient the RV function is transferred as energy to the pulmonary vascular load (40,41). It is

	described by the ratio of end systolic elastance (Ees) over Ea (Ees/Ea). Ees is a measure of ventricular contractility that can be estimated by the ratio of end systolic pressure (ESP) to end systolic volume (ESV) (Ees = ESP/ESV). Pulmonary vascular load is estimated by the Ea derived from ESP divided by SV (Ea = ESP/SV) (18).
Cardiac output and oxygen delivery	There is general agreement that improving global oxygen delivery (DO2) is the main therapeutic objective; by extension, increasing cardiac output the therapeutic target in CS (22). Increasing DO2 to 3 times that of oxygen consumption (VO2) in CS has been proposed (43), as pathological supply dependence develops below a DO2:VO2 ratio of about 2(44), (this critical point of supply dependence may be higher in the presence of microcirculatory abnormalities). Therefore, the critical level of DO2 is ≥300 ml/min/m2 in the critically ill patient to achieve DO2:VO2 ratio of 2–3(22).
Mixed venous saturation (SvO2)	normal range is 60 – 80 %, Oximetry analysis of a blood sample taken from the pulmonary artery (distal lumen) (45). Central venous saturation < 60 % in myocardial infarction is indicative of low output state and cardiogenic shock. Mixed venous saturation < 60 % is an indicator of hypoperfusion, lactic acidosis and poor prognosis (45). It is described that mixed venous oxygen saturation is superior to thermodilution CI in predicting long-term mortality (18). A decrease in mixed venous oxygen saturation indicates that the CI (even if it is apparently adequate) is not sufficient to meet the tissue oxygen needs, hence there is an increase in oxygen extraction (18,42).
Intracardiac shunt (IS)	PA oxygen saturation greater than 75% may indicate the presence of a left-to-right IS, so it is recommended to measure the superior and inferior vena cava, RA (middle, high and low), RV and PA (45). Increased oxygen saturation ≥ 7% may be indicative of a left-to right atrial shunt, whereas ≥ 5% may indicate a shunt at the level of the RV or the PA. The direct Fick method is the preferred means of CO measurement when a left-to-right IS is suspected (45,46).
PA pressure-volume loops (PV loops)	The formula is End systolic elastance/Ea. Parameter measured is RV-arterial coupling (18). It is used for early diagnosis of PAH and CTEPH and evaluation of RV-PA coupling (18).

Table 1: Parameters in hemodynamic monitoring

Discussion

In a retrospective cohort study of 4343 patients undergoing routine RHC for clinical indication. Patients with mPAP values of 18 mm Hg or less, 19 to 24 mm Hg, and at least 25 mm Hg were classified as reference, borderline PH, and PH, respectively. Among whom the prevalence of PH and borderline PH was 62% and 18%, respectively (47). Borderline PH is common in patients undergoing RHC and is associated with significant comorbidities, progression to overt PH, and decreased survival. Small increases in mPAP, even at values currently considered normal, are independently associated with increased mortality (47). Prospective studies are warranted to determine whether early intervention or closer monitoring improves clinical outcomes in these patients. Future studies may consider evaluating the efficacy of closer interval monitoring or early therapeutic interventions, particularly in patients with left heart disease (47).

In analysis of the VA-CART (Veterans Affairs- Clinical Assessment, Reporting, and Tracking (CART) program, which links cardiopulmonary hemodynamic and outcome data from all 76 VA catheterization centers), national hemodynamic database demonstrates that borderline PH, defined as mPAP of 19 to 24 mmHg, is a common and independent risk factor for adverse clinical outcomes in a large cohort of patients with underlying cardiopulmonary disease, particularly left heart dysfunction or parenchymal lung disease, who are referred for invasive hemodynamic testing(48). Overall, these data illustrate the continuum of PH risk on mortality and hospitalization and support future prospective studies that investigate the significance of borderline PH in other patient populations, as well as the consequences of treatment on clinical end points in this cohort of at-risk patients (48).

Although the new mPAP >20mmHg and PVR >2.0 WU criteria for PH are positioned to identify at-risk patients earlier in the disease arc, most patients with PH are diagnosed late and at a time point when hemodynamics are severely abnormal (49). It is possible, that abnormally high cardiac output states, such as liver failure or large arterio-venous fistula, may result in mPAP >20mmHg and PVR <2 WU. Lowered thresholds aim to identify patients early in the disease course, which is important because delay to diagnosis of PH is common and linked to elevated morbidity and shortened lifespan (49). This clinical primer highlights key changes in diagnosis and approach to PH management, focusing on concepts that are likely to be encountered frequently in general practice. Specifically, this includes hemodynamic assessment of at-risk patients, pharmacotherapeutic management of pulmonary arterial hypertension, approach to PH in patients with heart failure with preserved ejection fraction, and newly established indications for early referral to PH centers to prompt co-management of patients with pulmonary vascular disease experts (49). Pathologic data confirmed the findings of adverse vascular remodeling in patients with lower PVR beginning approximately at 1.8–2 WU (4,50).

Patients with exercise PH are characterized by a normal mPAP at rest, but an abnormal increase of mPAP during exercise. The clinical relevance of current hemodynamic criteria of PH has been supported by recent studies. They represent the cornerstone for diagnosis of different forms of PH, but they should always be interpreted within the individual patient's clinical context. For diagnosis of PH, we propose a stepwise approach, starting with simple, noninvasive tools, and with the main aim of discerning those patients who need to be referred to a PH center and should undergo invasive hemodynamic assessment (3).

The mPAP/CO slope was investigated for prognostic relevance similarly to the mPAP and PVR thresholds (4,51-54). The largest study was performed in a group of patients evaluated for unexplained dyspnea (4,53). The authors found that an mPAP/CO threshold of 3 mmHg/L/min for exercise PH was associated with a worse cardiovascular (CV) event-free survival regardless of whether there was resting PH. Further, both pre- and post-capillary contributions to the abnormal mPAP/CO slope were independently associated with increased hazard of CV hospitalization or death (4). In systemic sclerosis patients without manifest PH, exercise PH is a known predictor of disease progression and poor outcomes but further investigation found that an mPAP/CO slope > 3.5 mmHg/L/min identifies those with increased mortality at 10 years despite normal resting hemodynamics (4,54,55).

Most patients who undergo diagnostic evaluation for PH present with symptoms of dyspnea, exercise intolerance and/or clinical signs of right heart failure. The authors suggest a stepwise diagnostic approach for these patients, starting with simple, noninvasive tools and followed by more complex diagnostic methods, including the assessment for common cardiac and pulmonary conditions (3). Future advances in the management of PAH will focus on right ventricular function and involve deep phenotyping and the development of a personalized medicine approach (57).

Conclusion

Different pulmonary arterial hypertension phenotypes, occult groups that show PH with exercise challenge, and new pathogenesis molecular mechanisms had changed the definition and treatment modalities. Focused research on hemodynamic parameters would impact on better management of at-risk patients. Considering clinical evaluation, comorbidities, diagnostic algorithm, patient–clinician discussion, shared decision-making before therapy, indices measuring different aspects of the RV-PA system will help to early detection and better hemodynamic management strategies.

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