Congenital Heart Disease and Pulmonary Hypertension

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KEYWORDS

• Pulmonary hypertension • Adult congenital heart disease • Precapillary • Postcapillary
• Echocardiography • Cardiac catheterization • Eisenmenger syndrome

KEY POINTS

- Pulmonary hypertension is common in adults living with congenital heart disease.
- Thoughtful diagnosis and classification are required for appropriate management.
- Extensive expertise and a high index of suspicion allow timely and accurate diagnosis.

INTRODUCTION

Pulmonary hypertension (PH) affects 5% to 10% of patients with congenital heart disease (CHD) and is associated with significant exercise limitation and increased morbidity and mortality.[1–4] The presence of PH also carries significant implications with regard to pregnancy and surgical procedures, both cardiac and noncardiac, affecting perioperative risk. PH, thus, needs to be identified early in all adults with CHD (ACHD) and managed appropriately to avoid pitfalls and optimize outcome. However, the diagnosis and management can be intricate. This review provides a general guide on how to diagnose and manage the ACHD patient with suspected PH of various types.

APPROACH TO THE ADULT CONGENITAL HEART DISEASE PATIENT WITH SUSPECTED PULMONARY HYPERTENSION

Clinical History

The symptoms of PH are notoriously nonspecific, especially in the context of patients with CHD, who may experience symptoms caused by residual hemodynamic lesions, arrhythmias, heart failure, or extracardiac features of a coexistent syndrome. Exertional dyspnea is common and can be graded using the Borg dyspnea scale (eg, assessed before and after a 6-minute walk test). Fatigue is commonly an associated feature in PH. Effort-induced syncope in adults with PH and CHD may occur because of their inability to augment their cardiac output appropriately in

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response to the demand imposed by exercise or exertion and/or severe hypoxia, and is associated with increased mortality. Chest pain is not uncommon and can be ischemic in nature, the result of increased metabolic demands of the hypertrophied right ventricle, reduced right ventricular (RV) diastolic coronary perfusion, hypoxemia, or compression of the left main stem by a dilated main pulmonary artery (PA).[5] Noncardiac chest pain can arise from pulmonary embolism (eg, embolization of in situ PA thrombi in Eisenmenger patients), PA dissection, or rupture. Hemoptysis is also common and can be massive and life-threatening.

Components of the clinical history may raise suspicion for PH, especially the type of underlying CHD, timing and type of repair, and coexistent genetic syndromes, which may increase the risk of PH by various mechanisms. For example, patients with Down syndrome are prone to develop pulmonary vascular disease early in life in the presence of CHD but can also develop PH because of bronchopulmonary dysplasia, obstructive sleep apnea, and other reasons. History of associated thromboembolism, respiratory disease, HIV infection, or portal hypertension should also not be ignored.

Further evidence is gathered from the physical examination (**Table 1**) and routine tests, including electrocardiography, chest radiography, exercise testing, and echocardiography.

Echocardiography

Echocardiography is an essential tool in the assessment and follow-up of patients with CHD. Imaging should be performed in an accredited unit using a protocolized approach that includes screening for PH. Clinical and echocardiographic suspicion of PH should be confirmed by cardiac catheterization (**Fig. 1**). Standard echocardiographic criteria for PH, as recommended by international PH guidelines, do apply to many, but not all, CHD patients with biventricular circulation. For example, peak tricuspid regurgitation (TR) flow velocity and other supporting signs related to the ventricles, pulmonary artery, or inferior vena cava and the right atrium can help estimate

Table 1
Examination findings in pulmonary hypertension associated with congenital heart disease

Inspection	Clubbing of toes and/or fingers Abnormalities of facies, stature, or extremities (genetic syndrome) Skin discoloration (cyanosis, pallor, jaundice) Petechiae or purpura Tortuous retinal vessels (on fundoscopy) Raised jugular venous pulse Respiratory rate and use of accessory muscles Previous surgical scars Peripheral edema
Palpation/Percussion	Right ventricular heave Left parasternal tap Hepatomegaly Ascites Pitting edema
Auscultation	Eisenmenger • Loud pulmonary component of S2 • Single or narrowly split S2 • Ejection click at upper left parasternal border • Early diastolic decrescendo murmur of high-pressure pulmonary regurgitation (Graham Steell) • High-pitched tricuspid regurgitation murmur • 3rd and 4th heart sounds In PAH-CHD with systemic-to-pulmonary shunts • VSD: holosystolic murmur in 4th intercostal space at the left parasternal border • Post-tricuspid shunt with Qp:Qs >2: mid-diastolic flow murmur across the MV

Abbreviations: MV, mitral valve; PAH-CHD, pulmonary arterial hypertension associated with congenital heart disease; Qp:Qs, ratio of pulmonary to systemic flow; S2, second heart sound; VSD, ventricular septal defect.

Table 2
Assumptions of the recommended pulmonary artery systolic pressure calculation from peak tricuspid regurgitation velocity and examples of congenital heart defects in which these assumptions do not hold[8]

Assumption About "Normal" Physiology	Situation Where Assumption Violated
RV directly communicates with the PA	Unrepaired pulmonary atresia
RV does not directly communicate with the aorta/systemic circulation	Univentricular circulation Nonrestrictive VSD ccTGA and post-atrial switch for TGA
Absence of obstruction between the proximal RV and distal pulmonary arterioles	Double-chambered RV RV outflow tract obstruction/subpulmonary stenosis Valvular pulmonary stenosis Supravalvular pulmonary stenosis Branch PA stenosis
RA pressure can be estimated using IVC size and collapsibility with respiration	Torrential TR IVC not directly communicating with RA (eg, TCPC) Mechanical ventilation

Abbreviations: (cc)TGA, (congenitally corrected) transposition of the great arteries; IVC, inferior vena cava; PA, pulmonary artery; RA, right atrium; RV, right ventricle; TCPC, total cavopulmonary connection; TR, tricuspid regurgitation; VSD, ventricular septal defect.

the probability of PH.[6,7] However, a fundamental understanding of each patient's anatomy and physiology is critical because standard criteria do not apply and can mislead in subsets of patients with not only complex CHD but also simple forms of CHD. In pulmonary stenosis, the gradient across the right ventricular outflow tract or pulmonary valve contributes to the TR velocity, and must be accounted for in the estimation of PA systolic pressure. In more complex CHD, TR velocity may have no relation to PA pressure (Table 2) and alternative signs should be sought.[8]

Cardiac Catheterization

Right heart catheterization remains the only method for confirming a true diagnosis of PH, distinguishing between precapillary and postcapillary hemodynamics, assessing the severity of PH, and performing vasoreactivity challenge. Meticulous attention to detail and an in-depth knowledge of underlying cardiac anatomy are required to access the heart and pulmonary arteries and thus gather and interpret clinically useful information. Cardiac catheterization should, therefore, be undertaken at a specialist center combining ACHD and PH expertise.

Precapillary PH is characterized by the presence of a mean PA pressure (mPAP) $\geq$25 mm Hg, a pulmonary artery wedge pressure (PAWP) $\leq$15 mm Hg, and pulmonary vascular resistance (PVR) $\geq$3WU.[6] By contrast, postcapillary PH is defined by mPAP $\geq$25 mm Hg and PAWP greater than 15 mm Hg, and can be isolated or combined, based on a PVR of less than or $\geq$3 WU (Wood units) or a diastolic pressure gradient (diastolic PA pressure $-$ PAWP) of less than or $\geq$7 mm Hg, respectively. Recent data from normal subjects, showing that an mPAP greater than 20 mm Hg represents two standard deviations above the mean normal mPAP, have led to the adoption of this cutoff in the new hemodynamic definition of PH in the 6th World Symposium proceedings (Fig. 2).[9] Although this new definition is based on scientific data rather than an arbitrary limit, one must acknowledge that no specific evidence about this exists for CHD, and the 25-mm Hg cutoff has appeared ubiquitously in PH research. When PAWP cannot be accurately measured, the left ventricular (LV) end-diastolic pressure should be used to estimate left atrial pressure. In cases where the PAWP is <15 mm Hg but there is a history and echocardiogram suggestive of "left" heart disease and/or diuretic treatment, the use of an acute fluid challenge may unmask LV diastolic dysfunction and discriminate between pulmonary arterial hypertension (PAH) and left heart disease.[10,11] Although this approach is intuitively appealing (ie, seems to make sense), evidence on optimal fluid volume and timing, as well as the clinical relevance of a particular response, is still sparse.

Vasoreactivity testing has multiple uses in PH. In idiopathic PAH, a positive vasoreactivity response, defined as a reduction of the mPAP $\geq$10 mm Hg to

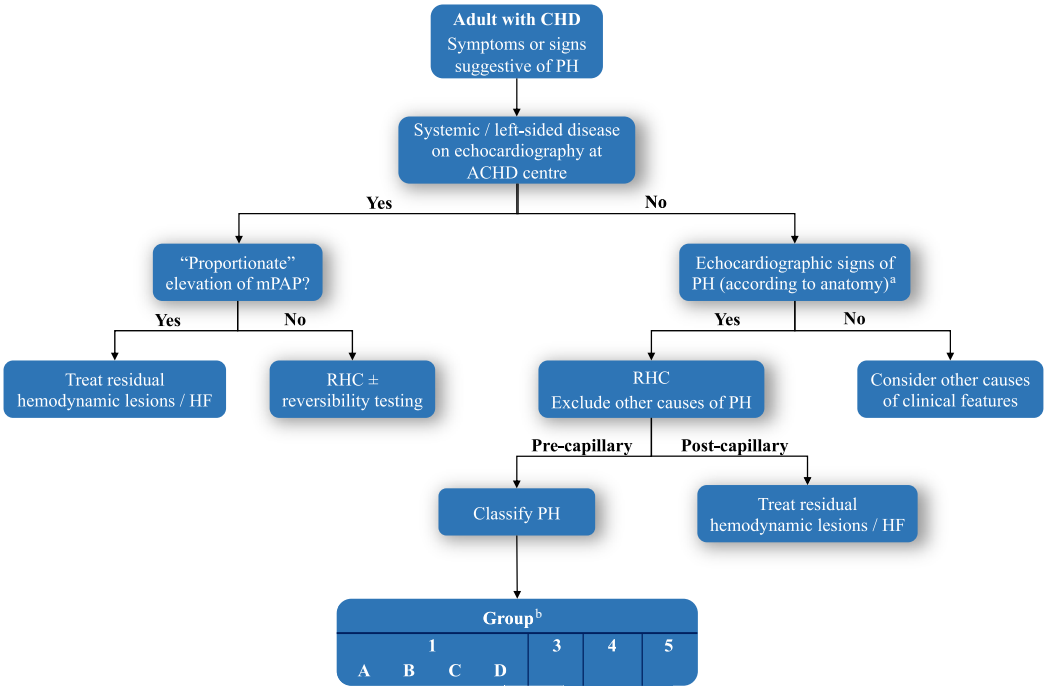


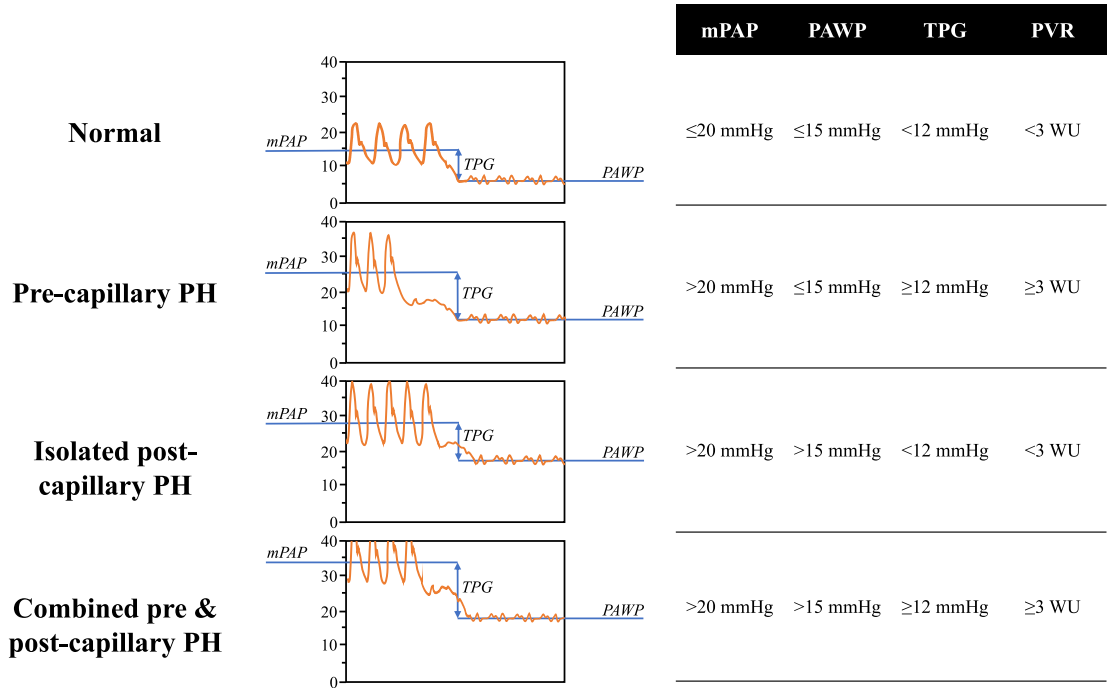
Fig. 1. Approach to the patient with congenital heart disease and features of pulmonary hypertension. In the presence of systemic/left-sided disease, clinical judgment is required to decide whether a small increase in pulmonary pressure is reflective of and proportionate to the degree of disease. [a] Refer to Dimopoulos and colleagues.[8] [b] See **Table 3** for pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD) classification. (A)CHD, (adult) congenital heart disease; HF, heart failure; mPAP, mean pulmonary artery pressure; PH, pulmonary hypertension; RHC, right heart catheterization.

reach an absolute mean value of $\leq$40 mm Hg with an increased or unchanged cardiac output, carries prognosis and management implications (treatment with calcium-channel blockers).[6] Vasoreactivity testing is also performed in patients with unrepaired CHD and borderline hemodynamics, that is, a PVR index between 4 and 8 WU $\cdot$ m^2, to assess "reversibility" of the pulmonary vascular disease and aid the decision to operate. The absence of evidence-based thresholds for deciding operability[12] and uncertainty about the prognostic relevance of preoperative vasoreactivity testing is, however, reflected in the latest American Heart association/American College of Cardiology ACHD guidelines, which do not advocate vasoreactivity testing in this context.[13] Of note, independent from any impact on clinical decision making, the degree of response to acute pulmonary vasodilator administration seems to carry some prognostic insight.

A different type of vasoreactivity testing is integral to heart transplant assessment. In patients with systemic ventricular dysfunction (or other left-sided disease) and combined precapillary and postcapillary PH, response to milrinone and/or sodium nitroprusside can help identify patients who may be eligible for heart versus heart-lung transplantation. In patients with low cardiac index, any medication that increases transpulmonary flow may decrease PVR via recruitment and distension of the pulmonary vasculature. This subset of patients does not have pulmonary vascular disease as a cause of elevated PVR, and the increase in flow unmasks preserved pulmonary vascular reserve. Patients with a fixed precapillary component may benefit from mechanical circulatory support, for example, LV assist device implantation, as a bridge to reassessment and heart transplantation.[14,15]

Complementary Imaging

Multimodality noninvasive imaging of the heart and lungs, including cardiovascular magnetic resonance (CMR), computed tomography, and ventilation-perfusion (V/Q) scanning, is helpful to diagnose incidental CHD and exclude other forms of PH, for example, connective tissue disease-related or chronic thromboembolic PH. CMR-augmented cardiac catheterization (in a hybrid



	mPAP	PAWP	TPG	PVR
Normal	≤20 mmHg	≤15 mmHg	<12 mmHg	<3 WU
Pre-capillary PH	>20 mmHg	≤15 mmHg	≥12 mmHg	≥3 WU
Isolated post-capillary PH	>20 mmHg	>15 mmHg	<12 mmHg	<3 WU
Combined pre & post-capillary PH	>20 mmHg	>15 mmHg	≥12 mmHg	≥3 WU

Fig. 2. Patients with precapillary pulmonary hypertension (PH) have a raised mean pulmonary artery pressure (mPAP) with a normal pulmonary artery wedge pressure (PAWP), hence a raised pulmonary vascular resistance (PVR). Postcapillary PH is characterized by an abnormally elevated PAWP. Isolated or combined pre- and postcapillary PH are differentiated on the basis of PVR and/or diastolic pressure gradient (DPG = diastolic pulmonary artery pressure − PAWP).[6,31,60] dPAP, diastolic pulmonary artery pressure.

laboratory) may be useful in accurately assessing hemodynamics in patients with complex CHD and/or multiple sources of pulmonary blood flow, combinations of shunts, or significant valvular regurgitation, in whom estimates of PVR by cardiac catheterization may be inaccurate.[16]

TYPES OF PULMONARY HYPERTENSION OBSERVED IN ADULTS WITH CONGENITAL HEART DISEASE

Precapillary Pulmonary Hypertension in Patients with Congenital Heart Disease

PH is not a single disease, and different forms are best approached with entirely distinct management strategies. Classifying the type of PH is essential in the management of all patients, including those with CHD, because it directs management. **Table 3** describes types of PH that can be encountered in ACHD patients. Group 1, namely, PAH-CHD, has attracted the most attention, especially since the introduction of PAH therapies. The histologic changes seen in the pulmonary circulation are indistinguishable from what is seen in other types of PAH, including idiopathic disease. The histologic classification of pulmonary vascular disease, which is still used in a modified form, was first proposed by Heath and Edwards in 1958[17] describing a cohort of patients predominantly with PAH-CHD. The initial, potentially reversible changes of arterial muscular hypertrophy and intimal thickening (grades I–III) progress to plexiform lesions and necrotizing arteritis (grade IV), which are deemed irreversible. Even though an increasing PVR is observed in progressive histologic grades, a clear correlation between the two is lacking. Moreover, neither histology nor cardiac catheterization can dependably foresee the outcome of reparative surgery. Nowadays, lung biopsies are rarely performed in clinical practice.[18,19]

A clinical classification has been developed for PAH-CHD (group 1), aimed mainly at simple defects (see **Table 3**). Groups A and B are patients with Eisenmenger syndrome (A) and those with systemic-to-pulmonary shunts (B). These 2 groups reside at different points along a continuum in terms of both hemodynamics and histologic changes, with Eisenmenger syndrome at the severe end of the spectrum. Eisenmenger syndrome is defined by patients born with a systemic-to-

Table 3
Types of pulmonary hypertension in congenital heart disease

Grouping according to International PH Classification and WS	Subgroup
Group 1	(A) Eisenmenger syndrome (B) PAH associated with systemic-to-pulmonary shunt (C) PAH and coincidental/small defect (D) PAH following corrective surgery/defect closure
Group 2	Left heart disease (eg, systemic ventricular dysfunction, valve disease) Pulmonary vein stenosis Isolated Associated (BPD, prematurity) Cor triatriatum Obstructed total anomalous pulmonary venous return Mitral/aortic stenosis (including supra-/subvalvular) Coarctation of the aorta
Group 3	BPD Lung disease (eg, restrictive lung defect) OSA/nocturnal hypoventilation
Group 4	PH due to pulmonary artery obstructions Congenital Related to previous surgery Related to other conditions (eg, sarcoidosis)
Group 5 (complex CHD)	Segmental PH Isolated pulmonary artery of ductal origin Absent pulmonary artery Pulmonary atresia with VSD and MAPCAs Hemitruncus Other Single ventricle Unoperated Operated Scimitar syndrome

Based on the updated clinical classification of pulmonary hypertension from the Proceedings of the 6th World Symposium on Pulmonary Hypertension.[9,59]

Abbreviations: BPD, bronchopulmonary dysplasia; CHD, congenital heart disease; MAPCA, major aortopulmonary collateral artery; PAH, pulmonary arterial hypertension; PH, pulmonary hypertension; VSD, ventricular septal defect; WS, 6th World Symposium on Pulmonary Hypertension.

pulmonary shunt who eventually develop severe pulmonary vascular disease with consequent shunt reversal (now pulmonary-to-systemic or bidirectional shunting). PAH-CHD patients with left-to-right shunting have less severe pulmonary vascular disease, and some may be eligible for defect closure if the histologic changes can be deemed reversible. Defects that are more likely to lead to the development of pulmonary vascular disease include large central shunts (eg, truncus arteriosus, an aortopulmonary window, or large surgical shunts such as central, Potts, or Waterston shunts), large ventricular septal defects (VSDs) present in isolation or as part of complex cardiac anatomy (eg, univentricular hearts without pulmonary stenosis—an unprotected pulmonary circulation), or a large patent ductus arteriosus.[20–23] Improvements in diagnosis and surgical and interventional treatment have led to a decrease in the incidence and prevalence of Eisenmenger syndrome in developed countries, but it remains prevalent in developing countries.[24] Despite advances in treatment, Eisenmenger syndrome is associated with significant morbidity and mortality, related to PAH, chronic cyanosis, and the underlying cardiac defect (**Table 4**).

Group C PAH includes patients with only small or seemingly coincidental congenital defects. The presence of pulmonary vascular disease alongside a small cardiac defect, usually a VSD of less than 1 cm or an ASD of less than 2 cm in diameter, cannot be readily explained only by

Table 4
Multisystem complications of Eisenmenger syndrome

Cardiac	Hematologic	Other
Heart failure	Bleeding	Renal failure
Arrhythmias	Thrombosis	Hepatic dysfunction
Infective endocarditis	Hyperviscosity	Cerebral abscess
	Thrombocytopenia	Cholelithiasis
		Gout
		Paraganglioma

the small hemodynamic burden placed on the pulmonary vasculature by the defect itself, and likely reflects a separate process similar to idiopathic PAH.[6,9]

The fourth subgroup of PAH-CHD, namely postoperative PAH (which persists, recurs, or develops after CHD surgery), forms a growing proportion patients, currently about 20% of cases.[25] Following simple shunt repair, the prevalence of PH on echocardiographic screening is 3% to 5.7%.[2,26,27] In many patients, residual PAH after surgery or intervention is expected based on preoperative hemodynamics, whereas in others it may be unexpected and can develop years after the procedure. Certain genetic variants, such as the SOX17 and BMPR2 risk genes, have been documented in patients with PAH-CHD and may explain some of the phenotypic variation and the predisposition to PAH observed in these patients.[28,29] The presence of PAH significantly affects prognosis in these patients.

Other types of precapillary PH can be encountered in CHD, including PH resulting from pulmonary artery obstruction, coexisting bronchopulmonary dysplasia (often encountered in patients with Down syndrome), and "segmental" PH (currently classified under group 5, PH with unclear and/or multifactorial mechanisms, see **Table 3**). The latter group encompasses "any condition with abnormal underlying cardiac or vascular anatomy, usually including varied sources of pulmonary blood supply, which results in distal pulmonary vascular disease that affects various lung segments to differing degrees."[30] In this situation, the degree of V/Q mismatch determines the severity of symptoms and relates to differences in the perfusion of various lung segments and physiologic dead space (caused by collateral supply to the lung from the aorta, and coexisting intracardiac shunting). Segmental PH is typical of patients with tetralogy of Fallot with pulmonary atresia and major aortopulmonary collateral arteries. Cardiac catheterization to confirm segmental PH should only be performed in centers with expertise, because measurement of pressures and calculation of PVR in each lung segment can be difficult.

Another precapillary form of PH in CHD patients, classified under group 5 PH, is pulmonary vascular disease in Fontan patients. This rarely fulfills the classic definition of PH, because the low pulmonary blood flow and absence of a subpulmonary ventricle means that a relative and mild elevation in PVR can occur with low or normal PA pressures, but even this modest increase in resistance to flow has a large negative consequence in the absence of a subpulmonary pump.

Postcapillary Pulmonary Hypertension in Patients with Congenital Heart Disease

Postcapillary PH, which is PH with an increase in left-sided filling pressures (group 2 PH),[6] is common in ACHD patients and can occur as a result of left-sided lesions, including valve or outflow tract obstruction, valve regurgitation, and systolic or diastolic systemic ventricular dysfunction. Indeed, long-term sequelae involving the systemic ventricle and valves are common in ACHD patients with significant hemodynamic lesions and those who have undergone corrective surgery, especially when operated on in earlier surgical eras with higher rates of ventriculotomy and ischemic or reperfusion injury. Pulmonary venous obstruction, either congenital or as a complication of prior repair, can also contribute to PH in this group.

PH secondary to left heart disease reflects an increase in left atrial/pulmonary venous pressures, and can be isolated (with normal PVR) or combined with a precapillary component (and hence higher than normal PVR, see **Fig. 1**). The latter may be the result of chronic changes in the pulmonary vasculature, with endothelial dysfunction, infiltration of inflammatory cells, vasoconstriction, and vascular remodeling,[31] which leads to a further increase in mPAP and an increase in PVR.

Careful study of hemodynamics is required when assessing patients for heart transplantation, for example, individuals with impaired systemic right ventricles and/or systemic atrioventricular valve regurgitation with advanced heart failure refractory to treatment.

MANAGEMENT OF PULMONARY HYPERTENSION IN ADULT CONGENITAL HEART DISEASE

Management of Pulmonary Arterial Hypertension-Congenital Heart Disease

The management strategy and role of PAH therapies depends on the presence and type of PAH-CHD. The distinct features of Eisenmenger syndrome (group A), particularly the presence of long-standing cyanosis and the underlying cardiac defect, result in a range of systemic complications, which require regular contact with specialists in PAH-CHD working within a wider multidisciplinary team.[6,13] Expert-led supportive management and the avoidance of historical practices (such as routine venesection) are an essential part of the management of Eisenmenger syndrome.[32] Endocarditis prophylaxis around high-risk dental procedures, immunization against influenza and *Pneumococcus*, contraception (not containing estrogen), and screening for and treatment of iron deficiency are recommended. Pregnancy should be avoided and adequate contraception prescribed. General anesthesia and sedation carry significant risks and nonessential surgery should be avoided, and essential surgery should be performed in specialist centers with adequate expertise. Randomized controlled trials (RCTs) have shown a benefit of the endothelin receptor antagonist (ERA) bosentan and the phosphodiesterase inhibitors sildenafil and tadalafil on hemodynamics, exercise capacity, and quality of life.[33–36] The recent MAESTRO trial, which assessed the effect of macitentan (an ERA) versus placebo in patients with Eisenmenger syndrome (including those with Down syndrome and those in New York Heart Association functional class II) did not meet the prespecified primary end point of change in exercise capacity over a 16-week period, but was associated with a decrease in B-type natriuretic peptide and improved hemodynamics compared with placebo.[37] The prognostic implications of PAH therapy in this patient group have been in contemporary populations are supported by evidence from several retrospective studies.[4,38–40]

For patients with PAH-CHD with systemic-to-pulmonary shunts (group B), the degree of elevation of PVR at cardiac catheterization, along with other metrics such as ratio of pulmonary to systemic resistance (R_p:R_s), is used to identify patients who could benefit from repair of the defect, with or without preceding PAH therapy. In patients with established pulmonary vascular disease (PVR index >8 WU · m^2 or R_p:R_s >2/3 and/or net right-to-left shunt), defect closure shortens survival and should be avoided.[41] Conversely, in patients with a sizable shunt and normal pulmonary vascular physiology (PVR index <4 WU · m^2, R_p:R_s <1/3), repair is strongly indicated and can be associated with an improved exercise tolerance, lower risk of atrial tachyarrhythmia, and better long-term outcome.[42,43] In patients with borderline hemodynamics (PVR index 4–8 WU · m^2, 2/3 > R_p:R_s > 1/3), who fall within the "gray zone" of guideline recommendations, a trial of PAH therapy with reassessment of hemodynamics and possible repair of the defect has been advocated (the so-called "treat-and-repair" strategy). This approach remains controversial and should only be considered in selected patients following review in expert centers.[21,44–46] The use of fenestrated devices or surgical patches, which allow decompression of the right heart,[47] have also been described.

Experts often use PAH therapies in patients with PAH and small or coincidental defects (group C), even though evidence is lacking. However, some of these patients (idiopathic PAH with small atrial communications) were included with other idiopathic PAH patients in major RCTs.[48,49] Patients who develop PAH following CHD repair were also included in small numbers in most RCTs of PAH therapies. Although underpowered for formal subgroup analysis, these trials have allowed the use of PAH therapies in this patient cohort.[41]

Management of Other Types of Pulmonary Hypertension in Adult Congenital Heart Disease

There is little evidence to guide management of segmental PH and abnormal pulmonary resistance in Fontan patients. Expert centers do occasionally trial PAH therapies in these patients, on a case-by-case basis, after careful synthesis of available information from the clinical history and underlying physiology. In patients with a "failing Fontan" circulation, PAH therapies have been used to optimize hemodynamics, especially when refractory to other treatments. In those with stable Fontan physiology, some short-term physiologic studies have suggested modest benefit, but findings are mixed and long-term effects remain unexplored.[50–56]

In contrast to precapillary PH, there is no role for PAH therapies in the management of postcapillary PH, which requires the identification and management of active hemodynamic lesions. There are few empiric data to guide the use of conventional heart failure medication, such as angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, and these medications are usually reserved for patients with systemic ventricular dysfunction, including those with systemic right ventricle. β-Blockers are used by some centers for patients with severe systemic ventricular dysfunction or in the presence of arrhythmias, but caution is required in the presence of RV dysfunction or conduction abnormalities. Mineralocorticoid receptor antagonists are used for right-sided congestive symptoms, and sometimes in higher doses for their renin-angiotensin-aldosterone system blocking effects. Loop diuretics are frequently used to control congestive heart failure. Despite a true absence of any evidence or experience in CHD, there is increasing interest for the use of newer heart failure therapies, such as sacubitril-valsartan,[57] GLP1 receptor agonists, and SGLT2 inhibitors, in this population.

FUTURE PERSPECTIVES

There has been significant progress in the understanding and management of PH related to ACHD over the past several decades, but numerous questions still remain. The epidemiology of PAH-CHD is changing and so should its management. As clinicians' understanding of the genetic basis of PH improves, personalized phenotyping and treatment is likely to improve outcomes. New tools to allow better assessment of operability in patients with borderline pulmonary vascular disease are sorely needed. It also remains unclear whether goal-oriented therapy (with specific targets aimed at optimizing outcome), as used in idiopathic disease, is effective for the management of PAH-CHD, and what the treatment targets should be. Indeed, risk-assessment tools specific to PAH-CHD are lacking, although multicenter efforts have allowed the identification of prognostic markers in Eisenmenger syndrome.[58] Finally, the role of PAH therapies in complex ACHD remains unclear.

SUMMARY

International collaboration and study designs that address the small sample size available at individual centers, heterogeneity of the population, and relatively low event rates are required to improve the understanding and treatment of CHD PH. In the absence of definitive evidence, expert multidisciplinary care[13] and education for patients and nonspecialist physicians is paramount in achieving wider engagement, preventing loss to follow-up, and supporting appropriate referrals to specialist services.

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