ISSN: 2643-4512

Araujo JJ. Int Arch Public Health Community Med 2025, 9:102
DOI: 10.23937/2643-4512/1710102
Volume 9 | Issue 1
Open Access

International Archives of Public Health and Community Medicine

REVIEW ARTICLE

Pulmonary Hypertension in Pediatric and Adult Congenital Heart Disease: Deciding When and When Not To Repair. An Overall Perspective of Latin America and the Caribbean Countries

John J. Araujo, MD, MBBS, NBE, FSIAC, FSISIAC, FACC, FASE [1,2,3]*

[1]*Associated Professor, Adult Congenital Heart Disease, National Autonomous University of Mexico, National Institute of Cardiology "Ignacio Chávez", Mexico*

[2]*Leader Adult Congenital Heart Disease Unit from Somer Incare Cardiovascular Center & Somer Clinic, Colombia*

[3]*Cardiologist Echocardilogist in Pediatric and Adult Congenital Heart Disease, Rionegro, Colombia*

***Corresponding author:** *John J Araujo, MD, MBBS, NBE, FSIAC, FSISIAC, FACC, Associated Professor Adult Congenital Heart Disease, National Autonomous University of Mexico, National Institute of Cardiology "Ignacio Chávez", Mexico; Tel: +5745624020*

Abstract

Congenital heart defects are very prevalent in the world, affecting 1 out of 100 live births. In Latin America and the Caribbean, more than 57,000 children are born with a congenital heart defect each year, 45% of which are moderately and highly complex. Globally, 6-8% of congenital heart defects may develop pulmonary hypertension and, of these, 50% will develop the most extreme form, Eisenmenger syndrome. These consequences depend on the type of congenital heart defect and the timing of surgical and/or hemodynamic repair, and are more prevalent in less developed countries. Latin America and the Caribbean are estimated to have more than 200,000 cases of Eisenmenger syndrome. Pulmonary arterial hypertension is the common and final outcome of various congenital heart defects. Timely diagnosis, hemodynamic analysis and specialized treatment help in deciding on medical treatment and surgical repair. This article reviews the definition, classification pathophysiology and hemodynamic diagnostic approach to pulmonary hypertension related to congenital heart defects. It provides a narrative description of the situation in Latin America and the Caribbean. Finally, it provides a general overview of medical treatment concepts and a brief description of Eisenmenger syndrome.

Keywords

Congenital heart disease, Pulmonary arterial hypertension, Right heart catheterization, Repair congenital heart defect

Introduction

Congenital heart defects (CHDs) are the most frequent congenital defect at birth. They have a global prevalence of approximately 10 cases per 1,000 live births [1]. However, they are estimated to have a five times higher prevalence, as many fetuses with CHDs do not reach birth, and resultin lost pregnancies (spontaneous abortions). These congenital defects encompass a heterogenous group of structural heart and/or large vessel defects. They have a varied pathophysiology, which depends not only on the severity of the CHD but also on the associated lesions, age at clinical onset and comorbidities, among others.

In Latin American (LATAM) countries, more than 57,000 children with CHDs are born each year, 45% of whom have medium and high-complexity defects. Timely diagnosis, medical treatment and, when needed, surgical and or/hemodynamic repair are essential steps for the recovery and rehabilitation of children born with CHDs. In general, approximately 6-8% of CHDs may develop pulmonary hypertension (PH) and, of these, 50% develop the most extreme form of PH: Eisenmenger syndrome (ES) [2]. However, in the less

Citation: Araujo JJ (2025) Pulmonary Hypertension in Pediatric and Adult Congenital Heart Disease: Deciding When and When Not To Repair. An Overall Perspective of Latin America and the Caribbean Countries. Int Arch Public Health Community Med 9:102. doi.org/10.23937/2643-4512/1710102

Accepted: July 18, 2025: **Published:** July 22, 2025

developed countries in the region, late diagnosis and delayed access to CHD repair increase the prevalence of PH in the pediatric population.

Definition and Classification

Pulmonary hypertension: a general term used to describe high blood pressure affecting the arteries of the heart and lungs. Pulmonary hypertension is defined as a hemodynamic condition with amean pulmonary artery pressure (mPAP) > 20 mmHg at rest, in healthy people, measured by right heart catheterization (RHC) in the supine position. This cut-off point is based on a normal resting mPAP considered to be 14 ± 3 mmHg, with a maximum normal limit of approximately 20 mmHg [3].

Pulmonary arterial hypertension (PAH): high blood pressure affecting the arteries of the heart and lungs, associated with increased pulmonary vascular resistance (PVR) in the pulmonary arterioles, which causes progressive overload and subsequent right ventricular (RV) dysfunction.

Hemodynamic Criteria for Pulmonary Hypertension

These classic hemodynamic measurement criteria have changed over time. Beginning withthe Dana Point classification in 2008, followed by the Niza classification in 2013, and the 2015 and 2022 guidelines [2022 European Society of Cardiology (ESC)/European Respiratory Society (ERS) Guidelines for the diagnosis and treatment of pulmonary hypertension] [4-7], the cut-off points for mPAP and PVR have been progressively lowered, as more has been learned about the natural course of PH.

In line with the most recent update published in 2024, the cut-off point has been set as a maximum mPAP of 20 mmHg. And, in relation to the other hemodynamic variables measured by RHC, PH is classified as follows:

- Pre-capillary PH is defined as mPAP > 20 mmHg and PVR above the upper limit of normal, taken to be 2 Wood units (WU), as well as a pulmonary capillary wedge pressure (PCWP) ⩽ 15 mmHg. This form of PH is characteristic of hemodynamic conditions and diseases that affect the pulmonary artery, without significant left heart disease, and constitutes true PAH.
- Post-capillary PH is defined by an mPAP > 20 mmHg and a PCWP > 15 mmHg. This type of PH is very suggestive of left heart disease.

The PVR value also distinguishes between two types of PH:

1. Isolated post-capillary PH: PH with PVR ≤ 2 WU, PCWP >15 mmHg and mPAP > 20 mmHg

2. Combined post-capillary and pre-capillary PH: PH with PVR > 2 WU, PCWP >15 mmHg and mPAP > 20 mmHg.

- Exercise PH is a hemodynamic condition with normal mPAP at rest and an abnormal rise in mPAP during exercise, and is defined as an mPAP/cardiac output (CO) slope > 3 mmHg/L/min between rest and exercise.
- Early PH: the latest update includes this concept due to European study results indicating that mPAP and PVR values above the upper limits of normal are associated with lower survival, regardless of pulmonary or heart disease and comorbidities. Furthermore, patients with liver cirrhosis and PVR of 2-3 WU often progress to PVR > 3 WU during follow-up, suggesting the presence of an early stage of progressive pulmonary vascular disease in these patients. Likewise, patients with systemic sclerosis with an mPAP of 21-24 mmHg and PVR between 2-3 WU often develop mPAP ≥ 25 mmHg during follow-up [8].

These findings suggest that patients with a risk condition for PH and an mPAP of 21-24 mmHg and/or PVR of 2-3 WU may be at risk of hemodynamic progression. Therefore, this condition could be termed “early PH.”

Clinical Classification of Pulmonary Hypertension

The overall objective of the clinical classification of PH is to categorize the clinical conditions associated with PH according to their pathophysiological mechanisms, clinical presentation, hemodynamic characteristics and similar treatment. The Sixth World Symposium on Pulmonary Hypertension (WSPH) [9] in 2018 and the 2022 ESC/ERS Guidelines offered a comprehensive and simplified version of the classification for both children and adults, which is divided into five groups with their respective subgroups.

Pulmonary Hypertension and Congenital Heart Defects In Latin America And The Caribbean: A General Overview

Overall, PH has a global prevalence of 1%. A recent systematic review of the global burden of disease found a mean reported prevalence of RHC-confirmed PH of 0.37- 15 cases per 100,000. Group 2 and 3 PH are the most prevalent forms and account for 90-95% of PH cases around the world. Within Groups 2 and 3, most patients have mild to moderate PH with limited pulmonary vascular involvement [10,11].

In LATAM, more than 57,000 children are born with CHD each year. Of these, 45% have moderate and high-complexity defects and, due to their severity, up to 25% will require urgent surgical or hemodynamic procedures during their first year of life to survive. It is currently estimated that only 8-12% of children with CHDreceive prompt and specialized treatment before one year of age, especially in the less-developed countries in the region. Of the rest, almost 50% will develop severe CHD sequelae like PAH, and 50% of these will develop the most severe form of PAH, which is ES [12].

Worldwide, 60% of CHDs are diagnosed and treated in childhood, 30% during adolescence, and up to 10% are diagnosed in adulthood. This is influenced by the availability of diagnosis and repair. In contrast, in LATAM and the Caribbean, up to 30% of CHDs may be undiagnosed in childhood or adolescence and only diagnosed for the first time in adulthood. The real problem is that many of these already adult patients have CHD sequelae, including PAH [13].

While there are more children than adults with CHD in the region today, the rapid increase of adults with CHD is not surprising, especially those with medium and high-complexity defects which,together, account for up to 60% of CHDs being followed in adults.

In 2020, there were approximately 2.3 million children with CHD in South America.In contrast, the projected number of adults with CHD (ACHDs) was 1.8 million and 677,000 in South and Central America and the Caribbean, respectively, with an annual growth of 5 to 6% [14,15].

Based on this information, it is estimated that there may be more than 200,000 ACHDs and patients with ES (135,000 and 101,500 in South America, Central America and the Caribbean, respectively) (Figure 1).

One feared complication in both unrepaired CHDs and those with delayed repair is the onset of PH. Even some complex CHDs, like transposition of the great arteries and left obstructive defects (Shone complex), develop PH for reasons that are not clear, even after successful surgical repair.

While the etiology of PAH is multifactorial in many cases, in CHDs, it can be summarized as depending on four factors:

- the size of the defect
- the location (pre-tricuspid, post-tricuspid)
- evolution time
- the timeliness of repair and follow-up

Keeping in mind the five PH classification groups, CHDs make up three of the five groups (1, 2 and 5). It is estimated that 80% of patients with PH live in developing countries and, in this population, CHDs are a significant cause of PH.

This is the case of CHDs with increased pulmonary flow (large ventricular septal defects, conotruncal defects without pulmonary stenosis, and single ventricle, among others) that were not repaired in childhood, had severe symptoms (heart failure, repetitive pneumonia, delayed growth and cyanosis, among others) and currently have severe sequelae of CHD combined with PAH. Thus, this now adult population has suffered symptoms inherent to their CHD with the addition of PAH symptoms that markedly affect their quality of life and functional class.

The 2018 American Heart Association (AHA)/ American College of Cardiology (ACC) Guidelines for the management of adults with congenital heart disease introduced the anatomic-functional classification. This classification establishes four physiological stages (from lower to higher severity: A-D) [16]. The CHDs associated

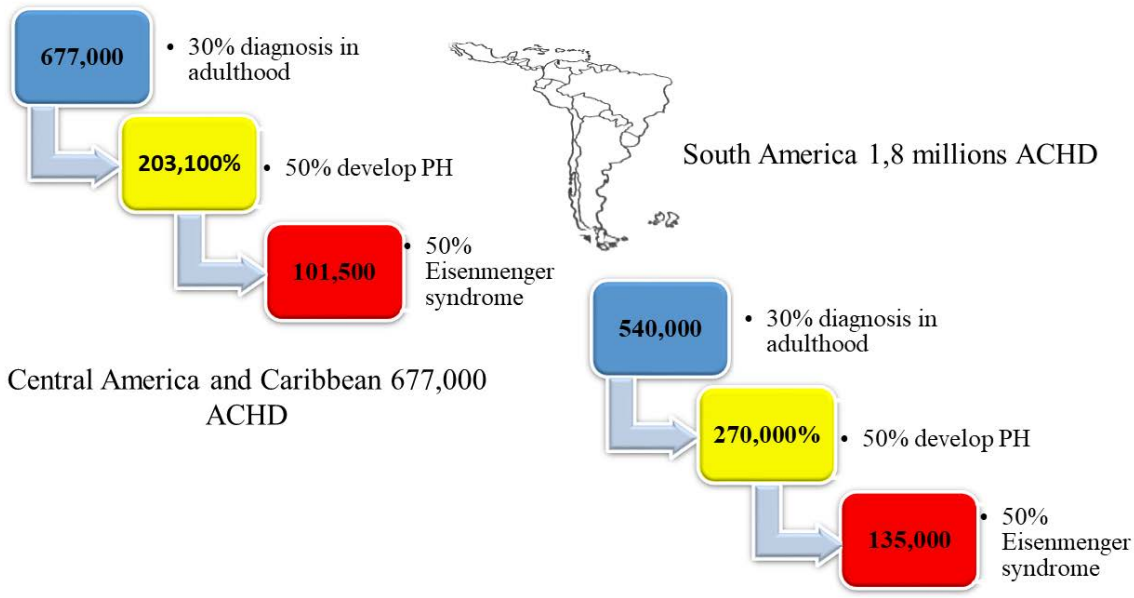

Figure 1: Estimate ACHD population with Eisenmenger syndrome living in South America, Central America and Caribbean countries.

with PH are considered to be the highest-risk group in the classification (Category D).

The association of PAH and CHD is a bad combination, as the population with CHD and PAH has never really been well. Patients with CHD and PH, compared to patients with CHD without PH, are more symptomatic and have at least twice the risk of death, except for some cases of Group 4 PH (chronic pulmonary thromboembolic disease) that can be cured with treatment. The remaining forms of PAH are not cured; they are stabilized with pulmonary vasodilators, most of which are high-cost medications (endothelin receptor antagonists and prostanoids, among others) for developing countries.

Clinical Classification of Pulmonary Arterial Hypertension Associated with Congenital Heart Disease

This classification is extremely important and allows an objective organization of patients with CHDs, according to their congenital defect and current clinical status (Table 1) [17].

Pathophysiology

In general, various CHDs share a similar pathophysiological mechanism, with some specific variations, depending on the defects associated with the main CHD.

The development of PAH is a complex pathophysiological mechanism influenced not only by the hemodynamic effects of the CHD, but also by a series of growth factor-mediated vascular changes associated with chronic inflammatory processes, which ultimately cause endothelial dysfunction in the pulmonary vascular bed.

Heart defects with a left-to-right (arteriovenous) shunt cause pressure and/or volume overload in the pulmonary circulation and pulmonary vascular bed remodeling due to constant vascular stress and arterial injury. These vascular changes lead to extracellular matrix degradation and growth factor release, inflammation, oxidative stress, and endothelial dysfunction [18].

Endothelial and tunica media hyperplasia develop first, which may be reversible if the heart defects are corrected, but if the shunts are not treated in time, remodeling will cause a progressive increase in PVR, which becomes irreversible in advanced stages of PAH. The irreversible damage is caused by vascular thromboses and the formation of plexiform lesions.

Elevated PVR translates into elevated right heart pressures, above the systemic vascular pressure. The heart defect flow changes to a two-way flow and then inverts to a right-to-left (venous-arterial) flow and causes hypoxemia and central cyanosis, as seen in ES (Figure 2 and Figure 3).

Ultimately, there are three main consequences [19] (Figure 4).

Based on the pathophysiology, there are four main PAH pathways:

- nitric oxide (NO)
- endothelin-1 (ET-1)
- prostacyclins
- activin

Each of these endothelial metabolic pathways produce specific molecules that play an essential role in vascular tone regulation and vascular remodeling. These metabolic pathways are being increasingly studied today, as this is where the modern pharmacological therapies for treating PAH are derived from.

1. Nitric oxide: NO is a potent vasodilator produced by the vascular endothelium. Under normal conditions, NO plays an essential role in maintaining normal vascular tone and preventing hypertension. However, in pulmonary hypertension, the synthesis and availability of NO tend to decrease, which causes vasoconstriction and vascular remodeling. Nitric oxide pathway dysfunction

Table 1: Clinical classification of pulmonary arterial hypertension associated with congenital heart disease.

1. Eisenmenger syndrome	2. Left-to-right shunts	3. Pulmonary arterial hypertension (PAH) with coincidental congenital heart disease	4. Post-operative PAH
Includes all large intra and extra cardiac defects which begin as systemic to Pulmonary shunts and progress with time to severe elevation of Pulmonary vascular resistance (PVR) and to reversal (pulmonary to systemic) or bidirectional shunting; cyanosis, secondary erythrocytosis and multiple organ involvement are usually present.	-Correctabley -Non correctable Include moderate to large defects; PVR is mildly to moderately increased systemic to pulmonary shunting is still prevalent, whereas cyanosis is not a feature.	Marked elevation in PVR in the presence of small cardiac defects, which themselves do not account for the development of elevated PVR; the Clinical picture is very similar to idiopathic PAH. To close the defects in contraindicated.	Congenital heart disease is repaired but PAH either persists immediately after surgery or recurs/develops months or years after surgery in the absence ofsignificant postoperative hemodynamic lesions. The clinical phenotype is often aggressive.
Adapted from Simonneau G, et al. [17]			

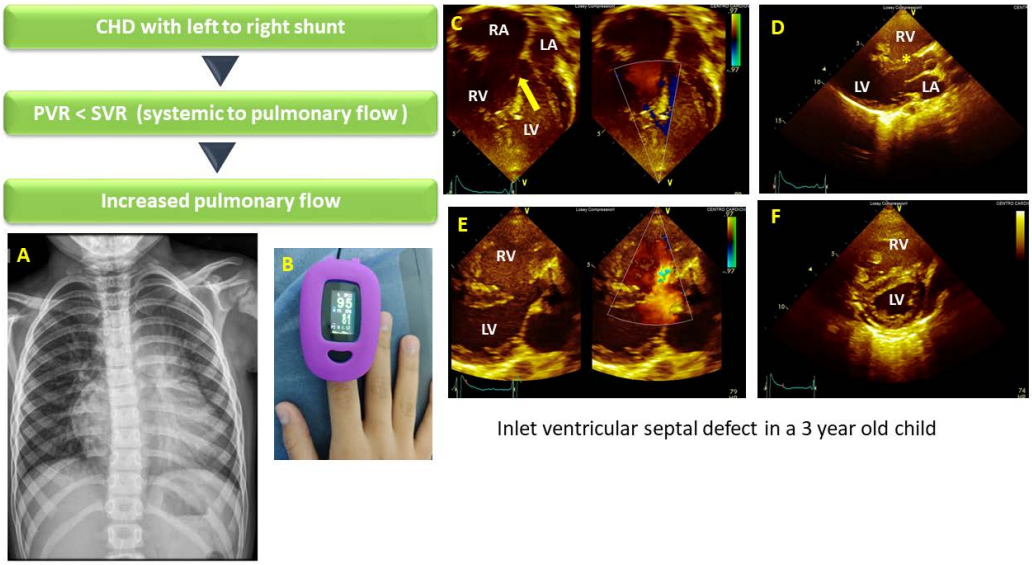

Figure 2: Inlet ventricular septal defect (VSD) in a 3 year old child with PH.

A) Chest X-ray shows cardiomegaly, increase pulmonary flow; **B)** Oximetry at room air 95%; **C-D** (echocardiographic evaluation :) **C)** apical 4-chamber view shows dilation of the cardiac cavities (yellow arrow shows VSD); **D)** long axis view (*) shows the VSD; **E)** long axis view color doppler, flow direction from left to right (arteriovenous direction), indicating that the PVR is less than the SVR, therefore PH, but not PAH; **F)** short axis view, RV dilation and D shape LV.

Due to the late diagnosis of this CHD, the evaluation was completed with right heart catheterization, the data were mPAP 35 mmHg, PVRI 1.4 WU (indexed against body surface area in m^2, see below in diagnostic approach section); SVR 6.7 WU, PVR/SVR ratio 0.2; QP/QS ratio 2.9. PCWP 5 mmHg.

The final diagnosis was pre-capillary PH. Surgical repair was performed successfully. Discharge after 7 days and currently on outpatient follow-up.

RA: Right Atrium; LA: Left Atrium; LV: Left Ventricle; RV: Right Ventricle

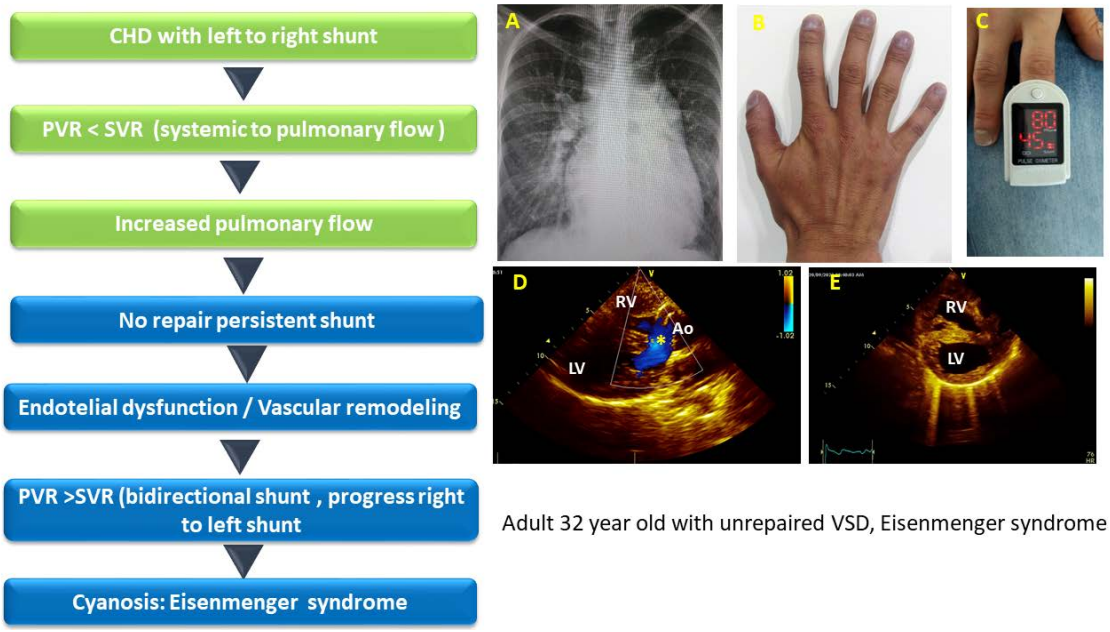

Figure 3: Subaortic VSD in a 32 year old adult with PAH.

A) Chest X-ray shows cardiomegaly, dilated pulmonary arteries and chronic changes in the pulmonary vasculature; **B)** central hypoxemia and hypertrophic osteoarthropathy; **C)** oximetry at room air 45%; **D-E** (echocardiographic evaluation :) **D)** Long axis view (*) shows the VSD with right to left shunt (systole view, open aortic valve and unsaturated flow to the systemic circulation); **E)** short axis view, RV hypetrofic and D shape of LV.

This case has developed the most extreme form of pulmonary arterial hypertension, surgical repair is not indicated. Medical management of PAH is necessary in an ACHD specialized center.

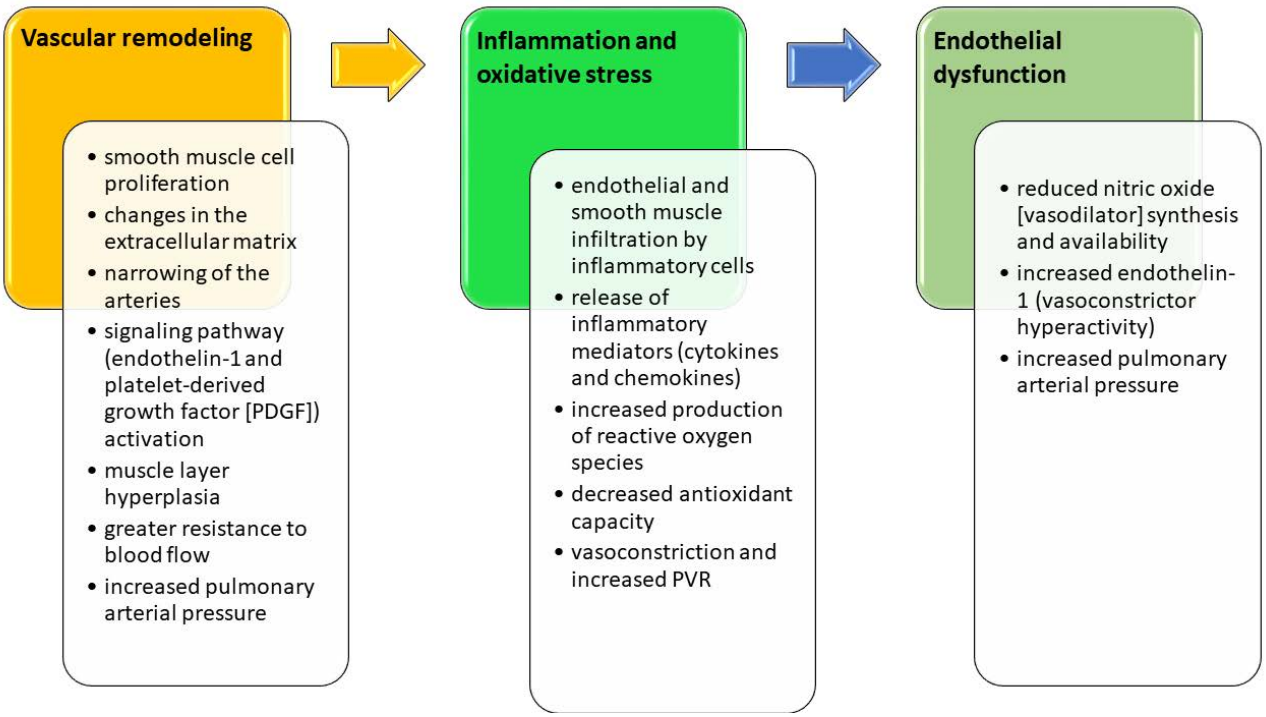

Figure 4: Summary of the pathophysiological consequences in the development of pulmonary arterial hypertension. The pathophysiological consequences include three mechanisms that include vascular remodeling, inflammation and oxidative stress, and endothelial dysfunction.

is related to more production of reactive oxygen species that worsen the endothelial dysfunction [20].

2. Endothelin-1: Is a potent vasoconstrictor, whose production is increased in PAH. Under normal conditions, it is synthesized in the endothelial cells and acts mainly on the ET-A and ET-B receptors that promote vasoconstriction and cell proliferation. Elevated ET-1 is one of the main factors contributing to vascular remodeling and right ventricular hypertrophy in patients with PAH.

3. Prostacyclins: are important mediators produced by the endothelium, that have vasodilating properties and inhibit platelet aggregation. The best-known prostacyclin is prostaglandin I2 (PGI2).

Prostacyclin synthesis is often reduced in PAH, which contributes to an imbalance between vasodilating/vasoconstricting mediators.

4. Activin: is a protein involved in regulating fibrosis and the inflammatory response. Recent studies suggest that activin may contribute to the pathogenesis of PAH by promoting vascular remodeling and interstitial fibrosis. Activin acts by stimulating the production of inflammatory cytokines and growth factors, which, in turn, exacerbate the inflammatory response and vascular remodeling. Activin signal blocking has been proposed as a new therapeutic approach for treating PAH [21].

Ultimately, PAH generates RV pressure overload. Over time, this overload can cause right ventricular hypertrophy and, eventually, heart failure.

The Seventh WSPH emphasized the pathophysiological changes in the RV and their implications for disease progression. The data on inflammation and fibrosis, metabolic dysregulation, and the impact of sex hormones on RV dysfunction has been studied. Anatomically, the role of right atrial adaptation in PH and dissociation between the right atrium and RV appear to play an important role in the cardiac adaptation of patients with PH. Maladaptive hypertrophy, which is present in some PH phenotypes, also appears to be a field of interest for future research [22].

More recent studies on the sotatercept drug suggest that the BMP/TGF-beta signaling pathway may fulfill different functions in RV adaptation, and its long-term use will be essential for understanding the impact of the drug on right heart failure.

Diagnostic Approach

When faced with CHD with PAH, we always ask ourselves the following questions:

- Is the CHD causing the PAH?
- How severe is the PAH?
- Can the CHD be repaired?

We are well aware that CHDs with increased pulmonary blood flow develop PAH if they are not repaired in time. Adults with unrepaired atrial septal defects of more than 20 mm have a prevalence of PAH and ES of up to 10-17% after the second decade of life. For ventricular septal defects of more than 10 mm,

the risk is 50-60%, and for aortopulmonary windows, complete atrioventricular canals and truncus arteriosus, it is 100%.

When there are complex, unrepaired post-tricuspid CHDs with significant flow toward the pulmonary circulation (QP: > 1.5) and no protective mechanisms against PH, the answer inalmost 100% of these cases is that PAH was caused by these CHDs.

The severity of PAH is not always correlated with the severity or complexity of the CHD. For example, simple CHDs like persistent ductus arteriosus that are unrepaired and have high QP over many years can cause PAH and even ES, with all their ensuing complications.

In general, the severity of PAH is marked by the onset of ES.

Once the CHD is diagnosed using basic and advanced imaging techniques, the goal of evaluating the PAH will focus on two decisions:

- Treating the PAH and repairing the CHD, thus avoiding the onset of ES
- Treating the PAH and not repairing the CHD, due to a high surgical risk

As previously mentioned, RHC is the essential test fordecision-making regarding CHD repair. With better understanding of the pathophysiology of PAH and CHDs, it is well understood that the PVR values indexed against body surface area in m^2 (PVRI) and the PVR/SVR ratio are the hemodynamic data that allow the decision to be made (Table 2).

The most difficult point is an intermediate PVRI and PVR/SVR ratio, or what has been called the "grey area," in which the decision is not easy, and the risks and benefits must be carefully analyzed. For this area, a vascular reactivity test is recommended (Figure 5).

Treatment

Pharmacological treatment for PAH associated with CHDs is based on a combination of medications that act at different levels, thus potentiating their effect in controlling PH (23-26) (Table 3).

Eisenmenger Syndrome

This is the most extreme form of PAH, representing the final common pathway of various unrepaired CHDs. Its global prevalence is unknown, but it is estimated that approximately 5% of patients with PH who are being followed in large centers have ES.

With advances in the early diagnosis and treatment of CHDs, the incidence of ES has decreased over the last decades, but unfortunately continues to be high in developing countries. Generally, the onset of PAH and ES

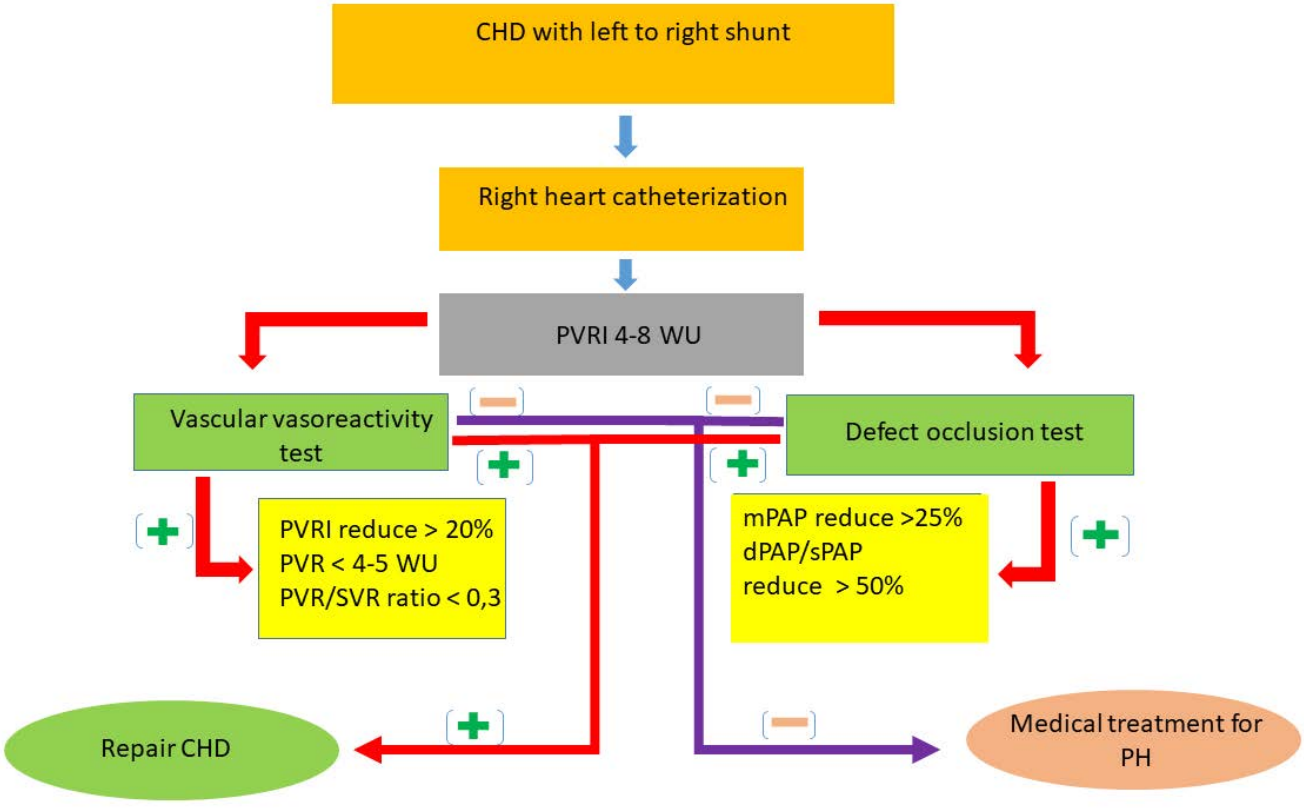

Figure 5: Hemodynamic approach using the pulmonary vasodilation test.
CHDs that are in the so-called "grey zone". The values obtained allow us to know the risk of surgical repair. **dPAP:** diastolic arterial pulmonary presure; **sPAP:** systolic pulmonary arterial presure

Table 2: Hemodynamic criteria for repair of cardiac defects with pulmonary arterial hypertension.

Conduct	Criteria	Absolute RVP
Repair	PVRI < 4 WU/m^2 PVR/SVR ratio < 0.5	PVR < 2.3 WU
No repair	PVRI > 8 WU/m^2 PVR/SVR ratio > 0.5	< 4.6 WU
Pulmonary vascular vasoreactivity test	PVRI 4-8 WU/m^2 PVR/SVR ratio > 0.5-0.3	2.3-4.6 WU

(Modified From Calderón J, et al. [18])

Table 3: Medications for the treatment of pulmonary arterial hypertension.

Pharmacological group	Medication	Dose
Phosphodiesterase 5 inhibitors	Sildenafil Tadalafilo	20 mg/8 h 20 mg/24 h
Endothelin receptor antagonists	Bosentan Ambrisentan Macitentan	125 mg/12 h 10 mg/12 h 10 mg/12 h
Prostacyclin analogues and IP receptor agonists	Selexipag Iloprosts inhaled Intravenous Epoprostenol	200-1.600 mcg/12 h Start 200 mcg 2/12 h, increase of 200 mcg 12/h, with intervals of 1 week between doses. Maximum dose 1,600 mcg/12 h 2.5 - 56 mcg/inhaled/6-9 times daily 20-40 ng/kg/min
Guanylate cyclase stimulators	Riociguat	1 mg 3/8 h for 2 weeks. Increase in increments of 0.5 mg/8 h every 2 weeks to a maximum of 2.5 mg/8 h

Table 4: Multisystemic disorder in adults with congenital heart disease and Chronic hypoxemic syndrome.

System and organ	Consequence
Hematopoietic system	Secondary erythrocytosis Iron deficiency hyperviscosity syndrome minor bleeds: bleeding gums, gastrointestinal bleeds, epistaxis or metrorrhagia) severity bleeds: massive hemoptysis, digestive or cerebral bleeding pulmonary arterial thrombosis thrombocytopenia deficiency of vitamin K dependent clotting factors: Factors II, VII, IX, X and Factor V are increased fibrinolytic activity and a deficit of the von Willebrand factor
Central nervous system	Neurological disordes due hyperviscosity síndrome : intense headaches, dizziness, syncope or pre-syncope, feeling of being far away, tinnitus, diplopía, vague visions, amaurosis fugax Parestesias on lips and fingers, mental fatigue, stroke, brain abscess
Gastrointestinal system	gallstones hyper bilirubinemia
Urinary system	hyperuricemia gout yarthritis renal dysfunction glomeurolopathy proteinuria hypocalcemia electrolyte disorders
Cardiovascular system	arrhythmias heart failure coronary ischemia
Immune system	Increased risk bacterial infections: brain abscess, endocarditis, pneumonia Dermatological disorders: hard-to-treat acne
Musculoskeletal system	myalgia, muscle weakness effort intolerance chest pain hypertrophic osteoarthropathy
Endocrine System	Neuroendocrine tumors: pheocromocytomas, paragangliomas, ganglioneuromas and neuroblastomas

(Modified From Araujo J [26])

is related to the promptness in diagnosing and repairing CHDs with high pulmonary blood flow.

Clinical Signs and Symptoms of Eisenmenger Syndrome

Central cyanosis is the common denominator and occurs due to right-to-left flow inversion through the unrepaired intra- or extra-cardiac defects, accompanied by the signs and symptoms of the constantly evolving CHD itself. Eisenmenger syndrome has many similarities with chronic hypoxemic syndrome, as a multisystemic disorder [26].

In summary, the multisystemic effects include effects in various organs and systems (Table 4).

Conclusions

One of the most feared complications of CHDs is the onset of PH. The goal of diagnosing PH associated with a CHD is to determine the possibility of repairing the defect. Applying the hemodynamic analysis and treatment guidelines, along with an understanding of the CHD pathophysiology, allows the best treatment option to be selected. Eisenmenger syndrome constitutes the most extreme form of PH, which is actually a multisystemic disorder whose complications must be addressed and monitored by centers specializing in CHDs.

Acknowledgement

To my daughter D. Lynn Araujo, for her support.

Conflicts of Interests

No conflicts of interest to declare.

Funding

None.

References

1. Hoffman J (2013) The global burden of congenital heart disease. Cardiovasc J Afr 24: 141-145.
2. Araujo JJ (2020) Adults with pulmonary arterial hypertension and congenital heart disease: When it rains, it pours. Arch Cardiol Mex 90: 366-368.
3. Kovacs G, Bartolome S, Denton CP, Gatzoulis MA, Gu S, et al. (2024) Definition, classification and diagnosis of pulmonary hypertension. Eur Respir J 64: 2401324.
4. Humbert M, McLaughlin VV (2009) The 4th World Symposium on pulmonary hypertension. Introduction. J Am Coll Cardiol 54: S1-S2.
5. Balmor GR, Segal MJ (2013) [Insights from the 5th world symposium on pulmonary hypertension--NICE 2013]. Harefuah 152: 677-679.
6. Galiè N, Humbert M, Vachiery J, Gibbs S, Lang I, et al. (2016) 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J 37: 67-119.
7. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, et al. (2022) 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J 43: 3618-3731.
8. Puigrenier S, Giovannelli J, Lamblin N, De Groote P, Fertin M, et al. (2022) Mild pulmonary hemodynamic alterations in patients with systemic sclerosis: relevance of the new 2022 ESC/ERS definition of pulmonary hypertension and impact on mortality. Respir Res 23: 284.
9. Condon DF, Nickel NP, Anderson R, Mirza S, de Jesus Perez VA (2019) The 6th world symposium on pulmonary hypertension: what's old is new. F1000Res 8: F1000.
10. Emmons-Bell S, Johnson C, Boon-Dooley A, Corris PA, Leary PJ, et al. (2022) Prevalence, incidence, and survival of pulmonary arterialhypertension: A systematic review for the global burden of disease 2020 study. Pulm Circ 12: e12020.
11. Wang Y, Wang X, Wang C, Zhou J (2024) Global, regional, and national burden of cardiovascular disease, 1990-2021: Results from the 2021 global burden of disease study. Cureus 16: e74333.
12. Araujo JJ (2023) Building an adult congenital heart disease unit in colombia, a comprehensive model of specialized care for a growing population. Int Arch Public Health Community Med 7: 088.
13. Araujo JJ (2020) Adults with congenital heart disease in the Americas-where we are today and where we are heading: A general view of the inter-american adult congenital heart disease council. Journal of Integrative Cardiology Open Access 3: 2-5.
14. Araujo JJ, Rodríguez-Monserrate CP, Elizari A, Yáñez-Gutiérrez L, Mouratian M, et al. (2023) Position statement for the development of adult congenital heart disease units in Latin America and the Caribbean: recommendations by the adult congenital heart disease chapter and pediatric cardiology council of the interamerican society of cardiology. Int J Cardiol Congenit Heart Dis 13: 100461.
15. Araujo JJ (2024) Adults with congenital heart disease in South America: where are we today and what will the immediate future look like. Ann Public Health Reports 8: 328-331.
16. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, et al. (2019) 2018 AHA/ACC guideline for the management of adults with congenital heart disease: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. J Am Coll Cardiol 73: 1494-1563.
17. Simonneau G, Gatzoulis MA, Adatia I, Celermajer D, Denton C, et al. (2014) Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol 62: D34-D41.
18. Calderón-Colmenero J, Sandoval ZJ, Beltrán GM (2015) Hipertensión pulmonar asociada a cardiopatías congénitas y síndrome de Eisenmenger. Arch Cardiol Mex 85: 32-49.
19. Xu D, Hu YH, Gou X, Li FY, Yang XYC, et al. (2022) Oxidative stress and antioxidative therapy in pulmonary arterial hypertension. Molecules 27: 3724.
20. Kurakula K, Smolders VFED, Tura-Ceide O, Jukema JW, Quax PHA, et al. (2021) Endothelial dysfunction in pulmonary hypertension: cause or consequence?

Biomedicines 9: 57.

21. Hemnes AR, Celermajer DS, D'Alto M, Haddad F, Hassoun PM, et al. (2024) Pathophysiology of the right ventricle and its pulmonary vascular interaction. Eur Respir J 64: 2401321.

22. Liu C, Chen J, Gao Y, Deng B, Liu K (2013) Endothelin receptor antagonists for pulmonary arterial hypertension. Cochrane Database Syst Rev 3: CD004434.

23. Galie N, Beghetti M, Gatzoulis MA, Granton J, Berger RMF, et al. (2006) Bosentan therapy in patients with Eisenmenger syndrome: A multicenter, double-blind, randomized, placebo-controlled study. Circulation 114: 48-54.

24. Gatzoulis MA, Landzberg M, Beghetti M, Berger RM, Efficace M, et al. (2019) Evaluation of macitentan in patients with eisenmenger syndrome. Circulation 139: 51-63.

25. Iversen K, Jensen AS, Jensen TV, Vejlstrup NG, Søndergaard L (2010) Combination therapy with bosentan and sildenafil in Eisenmenger syndrome: a randomized, placebo-controlled, double-blinded trial. Eur Heart J 31: 1124-1131.

26. Araujo JJ (2018) Chronic hypoxemic syndrome and congenital heart disease in adults: A multisystemic disorder. J Cardiol & Cardiovasc Ther 10: 555793.