Chapter

68

Pulmonary Hypertension in Children

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A three-year-old female, former 29-week preterm infant, presents for direct laryngoscopy and bronchoscopy due to stridor at rest. She has a history of chronic lung disease, bronchopulmonary dysplasia, small perimembranous ventricular septal defect, patent foramen ovale, moderate patent ductus arteriosus (PDA) (s/p coiling closure), pulmonary hypertension (on sildenafil), subglottic stenosis, and previously tracheostomy dependent.

Current vital signs include: BP 86/42 mmHg; heart rate 112/min; respiratory rate 25/min; SpO_2 98% on room air. Auscultation reveals a loud systolic murmur. ECG shows sinus tachycardia, ST abnormality and T-wave inversion in inferolateral leads. Transthoracic echocardiography reveals a residual PDA with continuous left-to-right shunting with a peak velocity of about 2 m per second; sometimes has evidence of minimal right-to-left shunting in systole. Patent foramen ovale with left-to-right shunting. Mild tricuspid regurgitation, peak velocity ~4.7 m per second, consistent with right ventricular systolic pressure of 88 mmHg + right atrial pressure. Blood pressure 93/48. Mild right ventricular hypertrophy with qualitatively normal right ventricular size and systolic function.

What Is the Incidence of Pulmonary Hypertension in Pediatric Patients?

Pulmonary hypertension (PH) is defined as a resting mean pulmonary artery pressure (mPAP) >25 mm Hg in children under three months of age in term infants at sea level.

In utero, pulmonary artery pressure is similar to systemic arterial pressure. After birth, pulmonary artery pressure decreases rapidly. By two to three months of postnatal age, the pressure generally achieves adult values. The annual incidence of idiopathic PH and congenital heart disease (CHD) associated PH is 0.7% and 2.2, respectively.

What Are the Causes of Pulmonary Hypertension in Pediatric Patients?

In the majority of pediatric patients, PH is idiopathic or associated with congenital heart disease. PH is classified into five major groups:

Group 1: PH associated with CHD. PH associated with CHD is most commonly seen among patients with large left-to-right shunts, such as a ventricular septal defect (VSD), patent ductus arteriosus (PDA), complete atrioventricular canal, truncus arteriosus, and transposition of the great arteries. The size of the shunt, the blood flow through the shunt and the location of the shunt are the most important risk factors for the development of pulmonary arterial hypertension.

Group 2: PH due to left-sided heart disease. Left-sided heart diseases that can lead to PH include left ventricle systolic and/or diastolic dysfunction, valvular disease, congenital/acquired left heart inflow/outflow tract obstruction, and cardiomyopathy.

Group 3: PH caused by chronic lung disease or hypoxemia. Chronic lung diseases that can cause PH include bronchopulmonary dysplasia (BPD), lung hypoplasia, congenital diaphragmatic hernia (CDH), or other lung lesions.

Group 4: PH caused by chronic thromboembolic disease.

Group 5: PH with unclear or multifactorial mechanisms. A combination of many rare diseases that infrequently causes PH is still seen in children.

What Is the Pathophysiology of Pulmonary Hypertension?

Increased pulmonary artery pressure (PAP) can be caused by decreased cross-sectional area of the

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pulmonary vascular bed. Although pulmonary veins may be the primary site of the problem, small pulmonary arteries are most affected in cases of PH. The diameter of small pulmonary arteries or veins may be narrowed by active vasoconstriction and/or pathological remodeling of small vessels through medial hypertrophy, proliferation of "neointimal cells" and deposition of connective tissues. Medial hypertrophy can resolve when the inciting stimulus is removed.

Increased PAP can also be caused by increased pulmonary blood flow (most commonly due to CHD) and/or increased pulmonary venous pressure (most commonly due to elevated left atrial pressure).

What Is a Pulmonary Hypertensive Crisis?

A PH crisis is characterized by a rapid increase in pulmonary vascular resistance (PVR) that results in pulmonary pressure exceeding systemic arterial pressure. Hypercarbia, hypoxemia, acidosis, and noxious stimuli from pain or airway manipulation can all cause a sudden increase in PVR, resulting in pulmonary hypertensive crisis and/or right heart failure. A sudden increased pulmonary pressure will compromise cardiac output from the right ventricle. Left ventricular stroke volume will also decrease, as there is limited volume available for left ventricular filling. Without rapid and effective treatment, a pulmonary hypertensive crisis can soon escalate to circulatory collapse and death.

Review the Clinical Presentation and Investigation of a Patient with PH

Persistent and/or progressive PH are commonly associated with CHD, chronic lung disease, and idiopathic/heritable PH in children. Transient PH is also relatively common in newborns with persistent pulmonary hypertension or congenital diaphragmatic hernia. Children with PH often have chromosomal abnormalities and syndromes. Children with syndromes such as Down syndrome, DiGeorge syndrome, Pierre–Robin syndrome and Noonan syndrome are commonly found to have PH.

Symptoms of PH are often similar to other less severe childhood diseases. Common presentations include fatigue, difficulty breathing, or shortness of breath with activity, dizziness, fainting, swelling in the lower extremities, or chest pain. Because the symptoms are so common, the diagnosis for childhood PH is often delayed by several months.

PH should be suspected in any child with respiratory distress, labile oxygenation, and/or cyanosis. The physical examination may be unremarkable. The primary findings on physical examination include tachypnea, retractions, grunting, desaturation unresponsive to supplemental O_2, and cyanosis. Cardiac examination may have altered heart sounds, such as a loud P2, split S2, a systolic murmur secondary to tricuspid regurgitation, or a diastolic murmur of pulmonary valve regurgitation and the signs of right heart failure, such as hepatomegaly. The initial assessments include chest X-ray, electrocardiography (ECG), and echocardiography.

Describe the Appearance of a Chest X-Ray and ECG in a Patient with PH

The chest X-ray may be normal or may demonstrate changes of underlying disease. Radiographic signs of PH include right ventricle enlargement and enlarged main and hilar pulmonary arterial shadows with peripheral attenuation of peripheral pulmonary vascular markings. The ECG is abnormal in most cases, with right ventricular predominance. However, the findings from ECG are somewhat nonspecific.

What Echocardiographic Findings Are Suggestive of PH?

There are a host of echocardiographic signs suggestive of pulmonary hypertension. Enlargement of the right ventricle can be seen in the parasternal long axis view (Figure 68.1). Classically, a "D" shaped septum can be seen in the parasternal short axis view. Due to elevated right ventricle pressure, the interventricular septum bows toward the left ventricle (Figure 68.2). Cardiologists estimate the RV pressure by assessing the degree of regurgitation. RV pressure is always assessed in comparison to systemic blood pressure. RV pressure that is one-quarter to one-half of systemic is seen as mild to moderate. Pressures exceeding three-quarters of systemic blood pressure and certain RV pressure that is systemic or suprasystemic increases the risk for patients requiring anesthesia.

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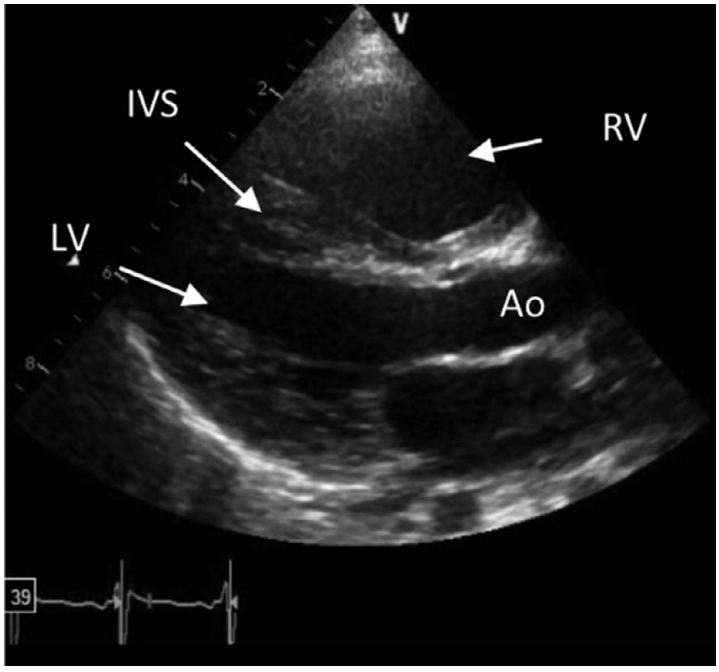

Figure 68.1 Parasternal long axis view of patient with severe pulmonary hypertension demonstrating a large right ventricle (RV), and bowing of the interventricular septum (IVS) into the left ventricle (LV) during systole. Ao, aorta. Courtesy of Adam C. Adler, MD

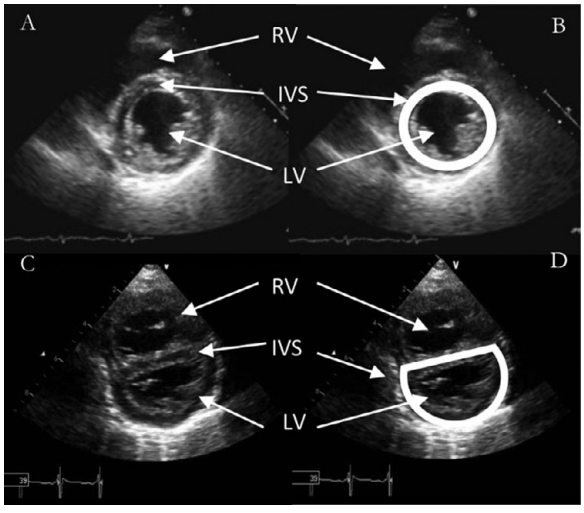

Figure 68.2 Parasternal short axis view demonstrating: (A) the normal position of the interventricular septum (IVS) and crescent shaped right ventricle (RV). (B) Schematic showing the normal relationship between the RV, IVS, and left ventricle (LV) in short axis. (C) Short axis view in the setting of severe pulmonary hypertension with large RV with downward displacement of the IVS. (D) Schematic showing the characteristic "D" shaped septum present with elevated RV pressures. Courtesy of Adam C. Adler, MD

How Is PH Diagnosed?

When PH is suspected, transthoracic echocardiography should be used to confirm the presence of pulmonary hypertension and provide additional information about the cause of PH. By measuring the systolic regurgitation of tricuspid flow velocity, Doppler echocardiography is able to estimate pulmonary artery systolic pressure. Pulmonary pressure obtained by Doppler echocardiography correlates with the values directly measured during right heart catheterization. Echocardiography is also useful to rule out congenital heart disease and to directly assess ventricular systolic and diastolic function. Cardiac catheterization is the gold standard to provide a definitive diagnosis of PH, and to determine the severity of PH. An acute vasoreactivity test is a particularly important component of cardiac catheterization to obtain the information for prognosis and to guide future treatment.

Review the Most Common Treatment Strategies for PH

The treatment of PH depends on the etiology of the original disease, the severity of PH, the cardiac and

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Table 68.1 Target pathways and mechanism of action for the commonly used antipulmonary hypertensive agents

Agent	Pathway	Mechanism
Sildenafil	Phosphodiesterase inhibitor (PDE-5)	Promotes smooth muscle relaxation through increased cGMP
Milrinone	Phosphodiesterase inhibitor (PDE-3)	Promotes smooth muscle relaxation through increased cAMP
Nitric Oxide	Guanylate cyclase pathway	Promotes smooth muscle relaxation through increased cGMP production
Bosentan	Endothelin receptor blocker	Reduced vasoconstriction by blocking endothelin receptor
Treprostinil	Prostacyclin (PGI_2)–Adenylate cyclase pathway	Direct vasodilation of pulmonary and systemic arterial vasculature/ inhibition of platelet aggregation
Iloprost	Prostacyclin (PGI_2)–Adenylate cyclase pathway	Direct vasodilation of pulmonary and systemic arterial vasculature/ inhibition of platelet aggregation
Epoprostenol	Prostacyclin (PGI_2)–Adenylate cyclase pathway	Direct vasodilation of pulmonary and systemic arterial vasculature/ inhibition of platelet aggregation

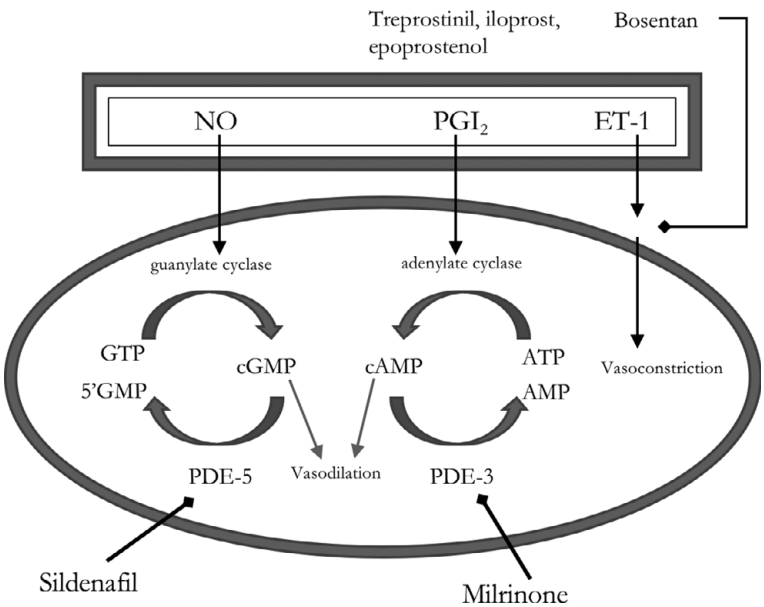

Figure 68.3 Depiction of the pathway and mechanism of action of the primary agents used to treat pulmonary hypertension. Courtesy of Adam C. Adler, MD

respiratory function, and the response to treatments. The treatment includes the management of the underlying disease, the maintenance of adequate systemic and pulmonary arterial blood pressure, the maintenance of adequate oxygenation, the mechanical ventilation to retain normocapnia, and the administration of medications to decrease pulmonary vascular resistance (Figure 68.3; Table 68.1).

Commonly used vasodilators include inhaled nitric oxide (iNO), sildenafil, milrinone, and calcium channel blockers and others. Extracorporeal membrane oxygenation (ECMO) may be considered in critically ill children with persistent PH who do not respond to the above therapies.

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What Are the Major Anesthetic Considerations for Patients with PH?

The anesthetic management of children with PH is a great challenge for anesthesiologists. Intubation, surgical stimulation, inadequate oxygenation, and ventilation can cause pulmonary artery vasoconstriction and induce a pulmonary hypertensive crisis. Children with PH undergoing anesthesia have a higher morbidity and mortality from cardiovascular complications. The goals of anesthetic management in patients with PH are (1) to provide an adequate depth of anesthesia and analgesia to minimize the autonomic response to surgical stimulation and airway manipulation; (2) to maintain adequate central venous pressure and right ventricle stroke volume; (3) to optimize myocardial function; (4) to choose a ventilation and oxygenation strategy that decreases pulmonary vascular resistance (PVR); and (5) to be prepared to treat a pulmonary hypertensive crisis and cardiac collapse.

What Are the Best Anesthetic Agents to Use for Patients with PH?

No single anesthetic agent or technique has been proven superior to others for patients with PH. A balanced anesthetic technique combining volatile agents, opioids, ketamine, and/or muscle relaxants is commonly used to provide adequate anesthesia and analgesia.

All medications to treat pulmonary hypertension and heart failure MUST be continued before, during, and after the procedure, and specific medications for the treatment of pulmonary hypertensive crisis such as iNO should be immediately available.

Propofol and inhalational agents can reduce both pulmonary and systemic vascular resistance and should be carefully titrated to facilitate induction and maintenance of anesthesia. Opioids have minimal pulmonary and systemic hemodynamic effects and are the mainstay of anesthetic medication for children with PH.

Maintaining adequate intravascular volume and preload to the right ventricle is also critically important. Hypotension caused by induction agents should be treated promptly with fluid administration and inotropic support of the circulation.

Review the Treatment Strategies for an Intraoperative Pulmonary Hypertensive Crisis

Treatment of PH crisis includes: (1) The administration of 100% oxygen to maintain adequate oxygenation; (2) Correction of metabolic and respiratory acidosis. PVR is directly related to H+ concentration and PCO_2 level. Metabolic acidosis should be promptly corrected with sodium bicarbonate. Hyperventilation to generate respiratory alkalosis may also help reduce PVR. (3) Administration of fentanyl will help suppress endogenous catecholamine release and subsequently reduce pulmonary artery pressures. (4) Administer pulmonary vasodilators. iNO provides selective pulmonary vasodilatation and is the first line of medication used intraoperatively because of its rapid onset and effectiveness. (5) Support cardiac output with adequate preload and inotropic support with dopamine, epinephrine, and/or milrinone.

Suggested Reading

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