The Anesthetic Management of Children with Pulmonary Hypertension in the Cardiac Catheterization Laboratory

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KEYWORDS

• Pulmonary hypertension • Cardiac catheterization laboratory • Anesthesia
• Children

KEY POINTS

- A new classification of pediatric pulmonary arterial hypertension (PAH) has been developed that incorporates abnormalities of lung growth and development as well as syndromes frequently contributing to PAH.
- Children with PAH will require cardiac catheterization to establish the diagnosis and monitor the response to therapy.
- Children receiving general anesthesia for cardiac catheterization are at significantly increased risk of perioperative complications such as a pulmonary hypertensive crisis.
- There is no one ideal anesthetic agent for children with PAH, and it is essential to understand the different hemodynamic effects of anesthetic agents and adopt a balanced anesthetic technique for children with PAH.

INTRODUCTION

Pulmonary hypertension has many different causes, which all share the final common pathway of elevated pulmonary arterial pressure (PAP). Pulmonary arterial hypertension (PAH) is due to abnormalities in the pulmonary arterial vasculature. Pulmonary venous hypertension is a result of left-sided heart disease, for example, pulmonary vein stenosis or left-side valvar heart disease. The treatments of PAH and pulmonary venous hypertension are different, so the distinction of one from the other is of obvious clinical importance.[1] This article focuses on PAH in children. PAH is a life-threatening disease which, if undiagnosed, will eventually culminate in irreversible elevation of

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pulmonary vascular resistance (PVR), leading to right ventricular failure and death.[2] Unfortunately, delays in diagnosis and treatment are not uncommon because of nonspecific presenting symptoms, especially in young children, and the low incidence of the disease.[3] The estimated prevalence in adults is 15 to 50 cases per 1 million, whereas in children it is less than 10 cases per 1 million.[4,5]

Children with suspected PAH require invasive hemodynamic assessment in the cardiac catheterization laboratory to confirm the diagnosis of PAH and determine future therapy. To tolerate the procedure, most of these children will need general anesthesia provided by an anesthesiologist. It is essential, therefore, that the providing anesthesiologist understands the pathophysiology of PAH, which measurements are made in the catheterization laboratory, how anesthetic medications may affect these measurements, and how to manage a pulmonary hypertensive crisis.[6–9] Children with PAH, especially those with a new diagnosis who are not yet on any treatment, are at increased risk of complications under anesthesia in the cardiac catheterization laboratory. The cardiologist performing the procedure, the pediatric anesthesiologist, and the catheterization laboratory support staff must effectively communicate to provide safe perioperative care.

DEFINITION AND CLASSIFICATION

In normal, healthy individuals the mean pulmonary artery pressure (mPAP) at rest is around 15 mm Hg, and is independent of age, ethnicity, and gender. During exercise, mPAP increases and is dependent on the level of exertion and age. During mild exercise, mPAP is 20 $\pm$ 5 mm Hg in subjects younger than 50 years compared with 30 $\pm$ 5 mm Hg in subjects older 50, which makes it difficult to define normal mPAP during exercise; hence, the definition of PAH uses mPAP at rest.[10] PAH is defined as mPAP greater than 25 mm Hg at rest, with a normal pulmonary capillary wedge pressure ($\leq$15 mm Hg) and increased pulmonary vascular resistance index (PVRI) greater than 3 Wood units per m^2.[11] The normal pulmonary capillary wedge pressure excludes patients with pulmonary venous hypertension from left-sided heart disease. In patients with suspected PAH, the initial investigation is usually a transthoracic echocardiogram that can estimate the mPAP and diagnose any congenital cardiac lesions that may be contributing to the PAH. Echocardiography may support the diagnosis of PAH with qualitative images of elevated right ventricular pressure, such as right ventricular hypertrophy and septal-wall flattening. Quantitative information may be obtained on echocardiography if there is tricuspid regurgitation during systole. In this case, the modified Bernoulli equation may be applied to estimate mPAP, with a tricuspid regurgitant velocity of greater than 2.8 m/s being highly indicative of PAH (**Box 1**).[10,12]

Transthoracic echocardiography is an attractive method to monitor children with PAH, and possibly enable the cardiologist to lengthen the interval between cardiac catheterizations that the child will require to monitor ongoing therapy. There are many echocardiographic techniques in the research and validation phase. One technique is to monitor the right ventricular systolic to diastolic duration ratio, whereby an increase has been shown to be associated with worse right ventricular function, exercise capability, and survival.[13] Another is to measure the degree of tricuspid annular plane systolic excursion (TAPSE), which has been shown to reflect right ventricular function and prognosis in PAH.[14,15]

In the absence of shunts, the pulmonary and systemic circulations receive the same amount of blood flow per minute. PVR beyond the newborn period is more than 10-fold lower than resistance in the systemic circulation, and the pressure in the venous bed draining the pulmonary arteries (pulmonary veins, left atrium) accounts

Box 1
Estimating mPAP from systolic tricuspid regurgitant jet velocity on echocardiography

Modified Bernouilli equation:

$sPAP = 4v^2 + RAP$

eg, $sPAP = 4\ (2.8^2) + 10 = 41$ mm Hg

Converting sPAP to mPAP

$mPAP = (0.61 \times sPAP) + 2$ mm Hg

eg, $mPAP = (0.61 \times 41) + 2 = 27$ mm Hg

Abbreviations: mPAP, mean pulmonary artery pressure; RAP, right atrial pressure; sPAP, systolic pulmonary artery pressure; *v*, tricuspid regurgitation velocity using Doppler on echocardiography.

for a much greater percentage of PAP (40%–60%) than the corresponding downstream venous pressure in the systemic circuit. Hence, pulmonary hypertension attributable to pulmonary venous hypertension from left-sided heart disease is the most common form of pulmonary hypertension in adults but not in children.[16]

Three factors can lead to an increase in mPAP: increases in left atrial pressure (LAP), cardiac output, or PVR. From these 3 parameters it is possible to consider 3 broad categories that cause elevated mPAP and pulmonary hypertension (**Box 2**).[2] The original classification of pulmonary hypertension was conceived at the 1998 World Health Organization (WHO) Symposium in Evian, and underwent subsequent revisions at symposia in Venice and Dana Point. However, using this WHO classification system for children has been problematic, as it often does not reflect the complex heterogeneity of factors that contribute to pediatric PAH. For example, children who are commonly evaluated for PAH may have been born prematurely and have chromosomal or genetic anomalies. In addition, such children may have congenital heart defects and acquired problems such as sleep-disordered breathing, chronic aspiration, and secondary lung disease. As a result, the Pulmonary Vascular Research Institute Pediatric Taskforce proposed a new classification of pediatric PAH at its meeting in Panama in 2011. The classification comprises 10 categories based on clinical pediatric practice (**Box 3**). The Panama classification includes an additional definition of pulmonary

Box 2
Deriving the potential causes of increased mPAP

Derived from Ohm's Law:

$PVR = \Delta P/Flow$

$\Delta P\ (TPG) = mPAP - LAP$

$PVR = (mPAP - LAP)/CO$

$mPAP = LAP + (CO \times PVR)$

eg, ↑ LAP: left-side heart dysfunction; ↑ CO: congenital heart disease with a large left-to-right shunt; ↑ PVR: pulmonary parenchymal disease or thromboembolic disease

Abbreviations: ΔP, difference in pressure; CO, cardiac output; LAP, left atrial pressure; mPAP, mean pulmonary artery pressure; PVR, pulmonary vascular resistance; TPG, transpulmonary gradient.

Box 3
The 10 categories of pediatric pulmonary hypertensive vascular disease

Category	Description
1	Prenatal or developmental pulmonary hypertensive vascular disease
2	Perinatal pulmonary vascular maladaptation
3	Pediatric cardiovascular disease
4	Bronchopulmonary dysplasia
5	Isolated pediatric pulmonary hypertensive vascular disease
6	Multifactorial pulmonary hypertensive vascular disease in congenital malformation syndromes
7	Pediatric lung disease
8	Pediatric thromboembolic disease
9	Pediatric hypobaric hypoxic exposure
10	Pediatric pulmonary vascular disease associated with other system disorders

Adapted from Cerro MJ, Abman S, Diaz G, et al. A consensus approach to the classification of pediatric pulmonary hypertensive vascular disease: report from the PVRI Pediatric Taskforce, Panama 2011. Pulm Circ 2011;1:288; with permission.

hypertension for children with univentricular circulations: following a cavopulmonary anastomosis PAH is defined as a PVRI greater than 3 Wood units/m^2 or a transpulmonary gradient (mPAP – LAP) greater than 6 mm Hg even if the mPAP is less than 25 mm Hg (**Box 4**).[17,18]

PATHOPHYSIOLOGY AND TREATMENT

The factors leading to an increase in mPAP may all eventually result in pulmonary vascular remodeling and increased PVR. As the pulmonary vasculature remodels in PAH, changes occur that may be reactive or fixed. Reactive changes will result in vasodilation of the pulmonary vasculature to an exogenously administered pulmonary vasodilator such as inhaled nitric oxide (iNO). Fixed changes are unreactive to such pulmonary vasodilators. As the disease processes leading to PAH progress, the cross-sectional area of the pulmonary vasculature exponentially decreases according to Poiseuille's Law, leading to increased PVR. Poiseuille's Law states that the

Box 4
The modern definition of pulmonary arterial hypertension in children with biventricular and palliated univentricular circulations

Biventricular Circulation

- mPAP >25 mm Hg and PVRI >3 Wood units/m^2
- Positive vasodilator response, defined as a decrease in mPAP and PVRI by 20% with no change in CO

Univentricular Circulation

- Following palliation with a cavopulmonary anastomosis
- PVRI >3 Wood units/m^2 or TPG >6 mm Hg even if mPAP <25 mm Hg

Abbreviations: CO, cardiac output; mPAP, mean pulmonary artery pressure; PVRI, pulmonary vascular resistance index; TPG, transpulmonary gradient.

resistance of a vessel is proportional to the fourth power of the radius. In other words, as the pulmonary arterioles develop thickening of their walls and a smaller intraluminal radius, the resistance will increase exponentially. A pulmonary hypertensive crisis is an acute on chronic increase in PVR during the perioperative period resulting from an acute increase in vascular tone of the reactive portion of the pulmonary vasculature. Early recognition and appropriate management of a pulmonary hypertensive crisis can be life-saving.

The current treatment strategies for PAH are aimed at the 3 pathologic processes. Vasodilators treat reactive vasoconstriction, antiproliferative drugs attenuate vascular remodeling, and anticoagulation may be used to treat and prevent thrombosis from forming in narrowed vessels. Based on the understanding of abnormalities of the vascular endothelium, 3 classes of drugs have been studied for the treatment of PAH.[19] The prostanoids epoprostenol (Flolan), treprostinil (Remodulin), and iloprost (Ventavis) act via cyclic adenosine monophosphate in the smooth muscle cell to produce vasodilation, and may also have some antiproliferative effects. The nitric oxide pathway acts via a cyclic guanosine monophosphate (cGMP) pathway in the smooth muscle cell to produce vasodilation. This pathway may be stimulated directly with iNO, or the breakdown of cGMP may be inhibited by phosphodiesterase type 5 inhibitors such as sildenafil (Revatio) and tadalafil (Adcirca). Recently the US Food and Drug Administration issued a warning against the use of sildenafil for pediatric PAH, because of an apparent increase in mortality during long-term therapy.[20] The endothelin pathway acts via endothelin receptors, which are present on both the endothelial and smooth muscle cells. The endothelin type 1 receptor has 2 further subtypes, A and B. Bosentan (Tracleer) is a nonselective antagonist of both subtypes, whereas ambrisentan (Letairis) is a selective type A antagonist. Both endothelin receptor antagonists require close monitoring of liver function tests. Whereas therapy for PAH in adults is evidence-based, most therapy for PAH in children is extrapolated from the adult data and is based on the experience of clinicians.[18]

CARDIAC CATHETERIZATION

Despite advances in noninvasive imaging techniques, cardiac catheterization with vasodilator testing is necessary for the diagnosis, treatment stratification, and prognosis of PAH in children.[21] There are 3 objectives during the catheterization procedure: to obtain hemodynamic data, to test vasoreactivity, and to rule out any associated disease states.

Accurate hemodynamic data are essential for the diagnosis and ongoing monitoring of patients with PAH. End-hole or flow-directed catheters are used to obtain hemodynamic data. Catheters with multiple side holes are used for angiography to prevent myocardial staining during injection. During catheterization, baseline measures include right atrial pressure, PAP, systemic arterial pressure, mixed venous and systemic arterial saturation, cardiac output, and pulmonary artery occlusion pressure. From these measures, important calculations can be made for pulmonary-to-systemic flow ratio (Qp:Qs) (**Box 5**) and PVR (**Box 6**).[22] It is important for the cardiologist performing the catheterization procedure to exclude intracardiac defects. It is essential that the anesthesiologist maintain stability during these periods of measurement and that the conditions under which they are made is clearly communicated. Most cardiac catheterization laboratories will obtain baseline measurements in room air followed by 70% to 100% oxygen, and then introduce an acute vasodilator such as iNO 20 to 40 ppm. In a recent review of cardiac catheterization laboratory protocols and hemodynamic data in pediatric patients with PAH, general anesthesia was found

Box 5
Calculating Qp and Qs

Based on the Fick principle:

$$Qp{:}Qs = (\text{Sat Ao} - \text{Sat MV})/(\text{Sat PV} - \text{Sat PA})$$

Abbreviations: Qp, pulmonary blood flow; Qs, systemic blood flow; Sat Ao, aortic saturation; Sat MV, mixed venous saturation; Sat PA, pulmonary artery saturation; Sat PV, pulmonary vein saturation.

to lower systemic arterial pressure, but there was no difference between general anesthesia and procedural sedation regarding mPAP or PVRI. It also demonstrated that pediatric patients with PAH demonstrate a higher incidence of PAH associated with congenital heart disease and neonatal specific disorders in comparison with adults. Pediatric PAH patients had baseline mPAP of less than 40 mm Hg but greater than 50% of their systemic blood pressure, illustrating the difficulty of applying adult criteria to children with PAH.[23]

The degree to which mPAP and PVR can be decreased acutely by the administration of fast-acting, short-duration vasodilators reflects the extent to which vascular smooth muscle constriction is contributing to the hypertensive state. The response to vasodilators has important therapeutic implications in PAH, and almost all patients will undergo a vasodilator trial during their initial cardiac catheterization. Intravenous epoprostenol, intravenous adenosine, and iNO are commonly used for acute vasodilator testing. The definition of a positive vasodilator response in adults is a reduction in mPAP by at least 10 mm Hg, and this number must be lower than 40 mm Hg. The pediatric definition of a positive response to vasodilators is a decrease in mPAP and PVRI by 20% with no significant change or increase in cardiac index. Such responders are likely to have a beneficial hemodynamic and clinical response to treatment with calcium-channel blocking drugs. It is estimated that 70% to 90% of children with severe PAH are nonresponders to acute vasodilator testing, and therefore require therapy other than calcium-channel antagonists.[18,24]

A pediatric anesthesiologist should be present during the cardiac catheterization, as anesthesia may pose a significant risk to the pediatric patient with PAH. Studies of children with PAH have demonstrated a high incidence of perioperative cardiac arrest and death. A benchmark estimate of the incidence of perioperative cardiac arrest in all pediatric patients is 0.014%.[25] By comparison, children with PAH experienced an

Box 6
Calculating PVR

Based on Ohm's Law:

$$\begin{aligned} PVR &= (P_{in} - P_{out})/Qp \\ &= (\text{mean PAP} - \text{mean LAP})/Qp \end{aligned}$$

PVR is measured in Wood units = mm Hg/L/min

or 80 $\times$ Woods units = dyne/s/cm^5 (metric units)

Abbreviations: LAP, left atrial pressure (equivalent to pulmonary artery occlusion pressure); P, pressure; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; Qp, pulmonary blood flow.

incidence of perioperative cardiac arrest of 1.6% associated with all types of procedures and 10% associated with major surgical procedures, including cardiac surgery.[26] Preoperative PAH has been shown to be significantly associated with perioperative death following pediatric open cardiac surgery.[27] The presence of PAH also adds significantly to perioperative risk in children undergoing cardiac catheterization (Fig. 1). The incidence of cardiac arrest during pediatric cardiac catheterization is reported to be 0.45%.[28] This incidence increases dramatically when only children with PAH undergoing cardiac catheterization are considered, with reports of 0.8%,[26] 1.2%,[29] and 5.7%.[30] Such morbidity is directly associated with the severity of PAH, with patients with suprasystemic PAH having a much greater incidence of major complications than those with systemic or subsystemic PAH (Fig. 2).[29]

ANESTHETIC MANAGEMENT

Cardiac catheterization is rarely tolerated in the awake child. Pediatric anesthesiologists working in the cardiac catheterization laboratory needs to consider some of the unique issues of their surrounding environment. The cardiac catheterization laboratory may be in a remote location away from the main operating rooms, and as a result there may be a delay in help arriving when it is called for. It is therefore essential to work closely with the team in the laboratory, as they may offer the most immediate help during an acute crisis.[31] The position of the cameras in the catheterization laboratory may hinder access to the patient, especially the airway, during a procedure. Usually the anterior-posterior camera may be swung out of the way for a mask induction of the patient, but this may be more difficult to achieve rapidly during a case if there is an airway problem. It is essential to have all necessary equipment and monitoring available. Standard intraoperative American Society of Anesthesiologists (ASA) monitoring should be used, and consideration given for additional monitoring such as a radial arterial line if the cardiologist performing the procedure does not plan to place a femoral arterial line. There may also be frequent interruptions in the invasive pressure wave form as catheters are changed in and out of the femoral arterial sheath, which may again influence placement of a dedicated radial arterial line. Children should be placed on a forced air-warming blanket, as the catheterization laboratory is usually kept cool because everyone is wearing a lead apron to protect against the radiation being used for taking images. Patient monitors such as pulse oximetry and

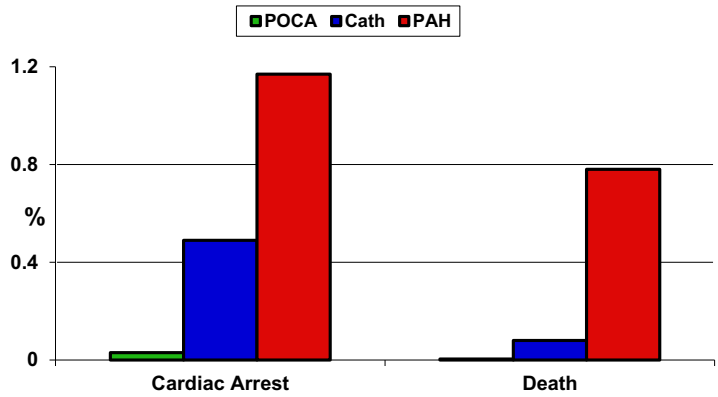

Fig. 1. Estimated incidence of perioperative cardiac arrest and death. Green bars, Perioperative Cardiac Arrest Registry (POCA), all children; blue bars, children undergoing cardiac catheterization (Cath); red bars, children with pulmonary arterial hypertension (PAH) undergoing cardiac catheterization. (*Data from* Refs.[25,28,29])

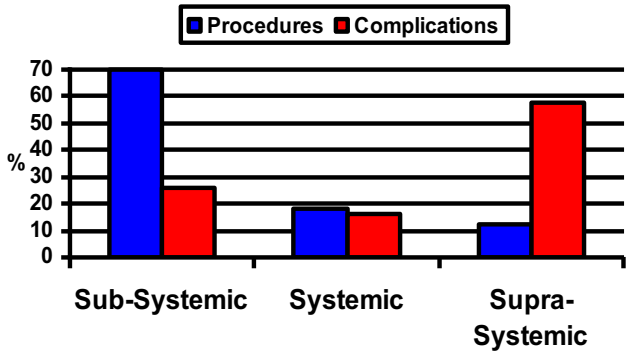

Fig. 2. Perioperative complications are directly related to severity of pulmonary hypertension. (*Adapted from* Carmosino MJ, Friesen RH, Doran A, et al. Perioperative complications in children with pulmonary hypertension undergoing noncardiac surgery or cardiac catheterization. Anesth Analg 2007;104:521–7; with permission.)

noninvasive blood-pressure cuff, in addition to peripheral vascular access, are generally best placed on an upper extremity, because the cardiologist will be accessing the femoral vessels. Appropriate drugs to manage a pulmonary hypertensive crisis should be readily available for each patient.[32,33]

The specific anesthetic technique and drugs chosen are probably less important than the attention to careful titration and maintaining hemodynamic stability. The ideal anesthetic drug for children with pulmonary hypertension would have pulmonary vasodilating effects, would not depress cardiac contractility, would maintain systemic vascular resistance and cardiac output, and would be short lasting and easy to titrate. Such an anesthetic agent, unfortunately, does not exist. Most anesthetics are associated with undesirable hemodynamic effects, depending on dosage and speed of administration, by altering heart rate or rhythm, cardiac contractility, systemic vascular resistance, or PVR (**Table 1**). The cardiovascular effects of anesthetic drugs pertinent to a discussion of pulmonary hypertension are summarized here.

Volatile Anesthetics

Volatile anesthetics cause a dose-dependent depression of cardiac contractility and a decrease in systemic vascular resistance (SVR),[34,35] and attenuate hypoxic pulmonary vasoconstriction during one-lung ventilation.[36] The ratio of pulmonary blood flow (Qp)

Table 1
Hemodynamic effects of anesthetic drugs

	Contractility	MAP	SVR	PAP	PVR
Volatile	⇓	⇓	⇓⇓	⇓	⇓
Propofol	⇓	⇓	⇓⇓	⇓	⇓
Ketamine	⇒	⇒	⇑	⇑⇒	⇑⇒
Etomidate	⇒	⇒	⇒	⇑	⇑
Dexmedetomidine	⇒	⇑	⇑	⇒	⇒
Opioids	⇒	⇒	⇒	⇒	⇒
Benzodiazepines	⇒	⇒	⇒	⇒	⇒

Abbreviations: ⇓, decrease; ⇑, increase; ⇒, no significant change; MAP, mean arterial pressure; PAP, pulmonary artery pressure; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance.

to systemic blood flow (Qs) remains unchanged in children with cardiac septal defects in response to halothane, sevoflurane, and isoflurane, so it is assumed that PVR has a similar response to that of SVR.[37]

Nitrous Oxide

Nitrous oxide may increase PVR during prolonged use in adults, but probably has no or little effect in children when it is used for a brief time to perform a mask induction of anesthesia.[38]

Propofol

Propofol causes dose-dependent depression of cardiac contractility.[39] In both adults and children with cardiac disease, propofol is associated with a marked decrease in SVR and mean arterial pressure (MAP), and a slight decrease in PVR and PAP.[40,41] In adults with artificial hearts, propofol causes vasodilation of systemic resistance and capacitance vessels, and a decrease in PAP.[42]

Ketamine

Whereas ketamine is supportive of hemodynamic stability and is frequently recommended as an anesthetic of choice in patients with cardiovascular impairment or instability, its use in patients with PAH is debated because of conflicting results from various studies conducted under a variety of conditions.[43] Study conditions have been varied (spontaneous vs controlled ventilation, natural airway vs endotracheal tube, room air vs added oxygen). A marked increase in PAP and PVR has been observed in children with PAH breathing room air through the natural airway.[44–46] On the other hand, no change in PAP or PVR has been observed in children with PAH during controlled ventilation or while receiving a pulmonary vasodilator, such as oxygen or sevoflurane.[47,48]

Etomidate

Etomidate is known to support systemic hemodynamics, but is associated with significant increases in both SVR and PVR. Despite the observed increase in PVR, etomidate is used as an anesthetic induction drug in patients with PAH because of its support of cardiac contractility and SVR. Only one pediatric study has been performed, which demonstrated a 28% increase in PVR.[49]

Dexmedetomidine

Dexmedetomidine is associated with acutely decreased heart rate and increased MAP and SVR, followed over time by a decrease in MAP.[50,51] These changes appear to be dose dependent. Despite the early significant increase in SVR, a similar pulmonary vasoconstrictor response was not observed in children with pulmonary hypertension.[52]

Opioids

Opioids have minimal hemodynamic effects. PVR remains unchanged in response to fentanyl.[53] Pulmonary vascular responses to remifentanil are clinically insignificant in adults with artificial hearts.[54]

Midazolam

Midazolam exerts clinically insignificant effects on the pulmonary vasculature of adults with cardiac disease.[55]

To minimize the undesired hemodynamic effects of a full anesthetic dose of a single anesthetic drug, it is preferable to use a balanced anesthetic technique; that is, administration of subanesthetic doses of several anesthetics. Thus an adequate depth of anesthesia can be achieved without marked hemodynamic changes. For most procedures the authors use midazolam, fentanyl, or remifentanil, and low-concentration sevoflurane or isoflurane. Dexmedetomidine can be added, especially when postoperative sedation is desirable, and high doses of fentanyl can be used if postoperative tracheal extubation is not anticipated. Judicious use of propofol at low infusion rates can be considered, and balancing propofol with ketamine may avoid the undesired effects on SVR of each drug alone. Sometimes hypotension can be observed despite a balanced technique, especially in children who are hypovolemic.

AIRWAY MANAGEMENT

Airway management techniques by the anesthesiologist are chosen as appropriate for the surgical or catheterization procedure. Although case reports have described pulmonary hypertensive crises in association with emergent tracheal intubation, the reports are unclear as to whether intubation caused the pulmonary vascular response or the patients were intubated because of impending cardiac arrest following pulmonary hypertensive crisis. Tracheal suctioning is associated with a significant increase in both PAP and PVR in children with pulmonary hypertension,[56] but with adequate topical and general anesthesia, the authors do not hesitate to intubate when indicated for the type of procedure or condition of the patient. The authors are more inclined to use tracheal intubation for long procedures, interventional cardiac catheterization procedures, or unstable patients.

Alternatively, airway management with a face mask, laryngeal mask airway, or the natural airway (with end-tidal CO_2 monitoring via nasal cannulas) can be chosen when indicated, and the authors often use these for shorter diagnostic catheterization procedures in stable children. It should be remembered that hypoxia and hypercarbia can be associated with a pulmonary hypertensive event, and that airway obstruction or hypoventilation during cardiac catheterization are more likely to occur during sedative techniques with a natural airway than during anesthesia with controlled ventilation.[57] Therefore, the anesthesiologist should consider all options for airway access and ventilatory support.

PULMONARY HYPERTENSIVE CRISIS

Cardiac arrest in children with PAH is often immediately preceded by an acute pulmonary hypertensive crisis, whereby an acute increase in PVR leads to right ventricular failure and a decrease in cardiac output. The self-perpetuating cycle of biventricular failure associated with a pulmonary hypertensive crisis is illustrated in **Fig. 3**. A pulmonary hypertensive crisis can be triggered by several stimuli that directly affect PVR, such as hypoxia,[58,59] acidosis,[60] noxious tracheal stimulation,[56] or events that cause ventricular dysfunction, such as inadequate coronary perfusion associated with systemic hypotension (**Box 7**). Early studies by Rudolph and Yuan[59] suggest that keeping an arterial pH higher than 7.40 and an arterial oxygen pressure (PaO_2) GREATER than 60 mmHg can avoid a severe increase in PVR (**Fig. 4**).

Treatment of a pulmonary hypertensive crisis is directed toward ameliorating the stimulating event and stabilizing hemodynamics (**Table 2**). Early use of a systemic vasoconstrictor, such as epinephrine, norepinephrine, or phenylephrine, or an inotrope, such as epinephrine or dopamine, can improve coronary perfusion and cardiac function, and may avert cardiac arrest. A pulmonary vasodilator should be administered.

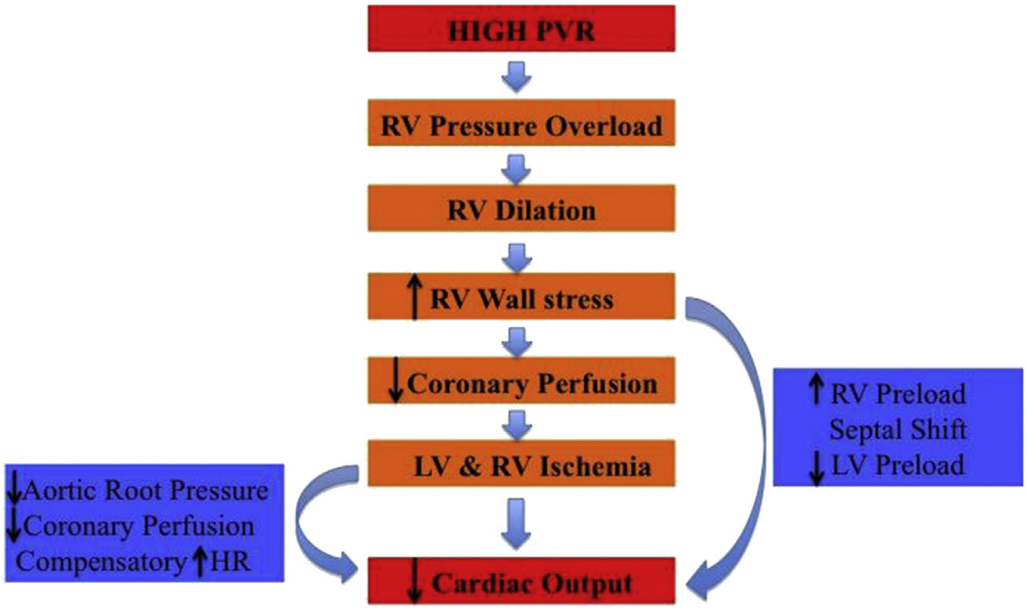

Fig. 3. Pathophysiologic changes during a pulmonary hypertensive crisis. HR, heart rate; LV, left ventricular; PVR, pulmonary vascular resistance; RV, right ventricular.

Because hypotension can be associated with acute administration of an intravenous vasodilator, it is preferable in an urgent setting to give pulmonary vasodilators by inhalation. This approach reduces the risk of systemic hypotension and coronary hypoperfusion by delivering the drug to the target pulmonary vasculature. iNO is the standard for inhaled pulmonary vasodilators, but inhaled prostacyclin analogues may be as effective. Once the cycle of increased PVR and decreased ventricular function begins, however, cardiac arrest may be difficult to prevent. If cardiac arrest occurs, Pediatric Advanced Life Support guidelines for cardiopulmonary resuscitation should be followed.[61] Cardiac arrest associated with pulmonary hypertensive crisis can be difficult to treat, and emergent use of extracorporeal membrane oxygenation (ECMO) may be necessary.[62] If emergent ECMO is required, improved outcomes are associated with shorter duration of cardiopulmonary resuscitation before ECMO, so an institutional protocol that anticipates the need for emergent ECMO in these situations is desirable.[63]

In addition to the avoidance of triggering stimuli, the risk of intraoperative cardiac arrest can be reduced by preoperative treatment with pulmonary vasodilator therapy. The odds ratio for children with PAH to develop a major perioperative complication was only 0.31 if they were chronically treated with a pulmonary vasodilator preoperatively.[26] Although the authors often use prophylactic administration of iNO during the

Box 7
Triggering stimuli for perioperative pulmonary hypertensive crisis

- Hypoxia
- Acidosis
- Hypercarbia
- Agitation and pain
- Tracheal suctioning
- Hypotension

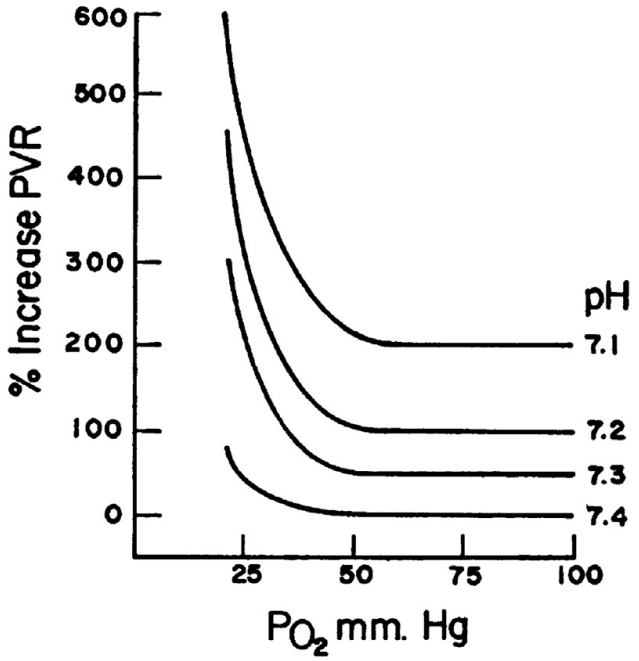

Fig. 4. Pattern of pulmonary vascular responses to changes of pH and Pa_{O_2}. The increases of pulmonary vascular resistance (PVR) are expressed as a percentage of the level at pH 7.4 and Pa_{O_2} 100 mm Hg. The changes in PVR with changes in Pa_{O_2} have been related at different levels of pH. (*From* Rudolph AM, Yuan S. Response of the pulmonary vasculature to hypoxia and H^+ ion concentration changes. J Clin Invest 1966;45:407; with permission.)

perioperative period for noncardiac surgical procedures, this is not usually done for diagnostic cardiac catheterization procedures in children with PAH, in which hemodynamic measurements under baseline conditions are measured.

When administration of a pulmonary vasodilator is indicated, the authors favor perioperative iNO over other pulmonary vasodilators for this purpose because it delivers drug directly to the pulmonary vascular bed, thus avoiding the systemic hypotension that can occur with acute intravenous administration of vasodilators. The authors administer iNO from beginning of induction of anesthesia into the recovery period,

Table 2
Treatment of pulmonary hypertensive crisis

Treatment	Rationale/Therapy
Administer 100% O_2	↑ PA_{O_2} and Pa_{O_2} will ↓ PVR
Hyperventilate	PVR is directly related to Pa_{CO_2}
Exclude pneumothorax	Optimize ventilation
↓ Mean airway pressure	Avoid P_{alv}>P_{art}
Correct metabolic acidosis	PVR is directly related to H^+ level
Administer pulmonary vasodilators	iNO, magnesium
Analgesia	Decrease sympathetic mediated ↑ PVR
Support cardiac output	Phenylephrine, cautious volume, epinephrine
ECMO	Support cardiac output and oxygenation

Abbreviations: ECMO, extracorporeal membrane oxygenation; iNO, inhaled nitric oxide; P_{alv}, alveolar pressure; PA_{O_2}, alveolar oxygen pressure; Pa_{O_2}, arterial oxygen pressure; P_{art}, arterial pressure; PVR, pulmonary vascular resistance.

when it can be administered by face mask or nasal cannulas.[64] Other pulmonary vasodilators that can be effectively administered by inhalation may emerge as satisfactory prophylactic perioperative drug therapy for children with pulmonary hypertension. These agents include the prostacyclin analogues epoprostenol,[65] iloprost,[66] and treprostinil,[67] the phosphodiesterase inhibitor milrinone, and nitroglycerin.[68]

POSTANESTHESIA RECOVERY

Children with PAH are at increased risk of adverse events following anesthesia.[69] Possible causes include increased pulmonary vascular tone, pulmonary hypertensive crisis, pulmonary thromboembolism, cardiac arrhythmia, and fluid shifts. All precautions should be taken to avoid hypoxemia, hypotension, and hypovolemia. Postoperative control of pain should be effective. Any therapy to decrease PVR, such as iNO, should be weaned with caution so as to avoid rebound increases in PVR.[70] It may be necessary to admit the child overnight to a unit where monitoring is available and immediate medical response is possible.

SUMMARY

Children with PAH undergoing cardiac catheterization are at increased risk of perioperative complications. This risk is greatest for those with suprasystemic pulmonary artery pressures and those with PAH who are not yet on any therapy. Although there are many factors that may contribute to the development of PAH, the final common pathway is elevated PAP. All currently available anesthetic agents will have an effect on the cardiovascular system. It is essential for the anesthesiologist to be aware of these effects and how they may change the data being acquired by the cardiologist. It is important to avoid factors that may trigger a pulmonary hypertensive crisis and, if one does occur, it is essential to respond appropriately. The most immediate available help in this situation may be the staff in the cardiac catheterization laboratory, making good communication important.

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