Published in final edited form as:
Anesth Analg. 2007 March ; 104(3): 521–527.

Perioperative Complications in Children with Pulmonary Hypertension Undergoing Noncardiac Surgery or Cardiac Catheterization

Mario J. Carmosino, MD[*], **Robert H. Friesen, MD**[*], **Aimee Doran, CPNP**[†], and **Dunbar D. Ivy, MD**[†]

***** *Department of Anesthesiology, The Children's Hospital and University of Colorado School of Medicine, Denver, Colorado*

† *Department of Pediatrics (Cardiology), The Children's Hospital and University of Colorado School of Medicine, Denver, Colorado*

Abstract

BACKGROUND—Pulmonary arterial hypertension (PAH) can lead to significant cardiac dysfunction and is considered to be associated with an increased risk of perioperative cardiovascular complications.

METHODS—We reviewed the medical records of children with PAH who underwent anesthesia or sedation for noncardiac surgical procedures or cardiac catheterizations from 1999 to 2004. The incidence, type, and associated factors of complications occurring intraoperatively through 48 h postoperatively were examined.

RESULTS—Two hundred fifty-six procedures were performed in 156 patients (median age 4.0 yr). PAH etiology was 56% idiopathic (primary), 21% congenital heart disease, 14% chronic lung disease, 4% chronic airway obstruction, and 4% chronic liver disease. Baseline pulmonary artery pressure was subsystemic in 68% patients, systemic in 19%, and suprasystemic in 13%. The anesthetic techniques were 22% sedation, 58% general inhaled, 20% general IV. Minor complications occurred in eight patients (5.1% of patients, 3.1% of procedures). Major complications, including cardiac arrest and pulmonary hypertensive crisis, occurred in seven patients during cardiac catheterization procedures (4.5% of patients, 5.0% of cardiac catheterization procedures, 2.7% of all procedures). There were two deaths associated with pulmonary hypertensive crisis (1.3% of patients, 0.8% of procedures). Baseline supra-systemic PAH was a significant predictor of major complications by multivariate logistic regression analysis (OR = 8.1, $P = 0.02$). Complications were not significantly associated with age, etiology of PAH, type of anesthetic, or airway management.

CONCLUSION—Children with suprasystemic PAH have a significant risk of major perioperative complications, including cardiac arrest and pulmonary hypertensive crisis.

Pulmonary arterial hypertension (PAH) is defined as the presence of a mean pulmonary artery pressure (PAP) that exceeds 25 mm Hg at rest or 30 mm Hg during exercise. PAH can be idiopathic (primary) or associated with a variety of underlying causes (1–3). Patients with PAH are generally considered to be at greater risk for the development of life-threatening

Address correspondence and reprint requests to R. H. Friesen, MD, Department of Anesthesiology, The Children's Hospital, 1056 E. 19th Ave., Denver, CO 80218. Address e-mail to friesen.robert@tchden.org.

Presented in part at the meeting of the Society for Pediatric Anesthesia and American Academy of Pediatrics Section on Anesthesiology, Ft. Myers, FL, February, 2006.

Supported by the General Clinical Research Center branch of the National Center for Research Resources, National Institutes of Health Grant M01-RR00069.

perioperative cardiovascular complications. Increases in pulmonary vascular resistance (PVR) will increase right ventricular afterload, and can lead to right ventricular dysfunction. A potentially fatal complication is a pulmonary hypertensive crisis, characterized by a rapid increase in PVR to the point where PAP exceeds systemic blood pressure (BP). The resulting right heart failure leads to a decrease in pulmonary blood flow, decreased cardiac output, hypoxia, and biventricular failure (4). Other perioperative mechanisms associated with right-sided heart failure in patients with PAH include hypovolemia (inadequate preload), right ventricular dilation (compression of the left ventricle), systemic hypotension (decreased coronary perfusion), and hypoxemia. The pathophysiology of PAH, treatment options, and anesthetic considerations have been recently reviewed (1–3). The purpose of this study was to describe the incidence of perioperative complications and associated factors in children with PAH undergoing noncardiac surgery or cardiac catheterization.

METHODS

Data Collection

This retrospective cohort study was approved by the Colorado Multiple IRB. The database of the Pulmonary Hypertension Program at The Children's Hospital was used to identify patients who underwent general anesthesia or sedation from the years 1999 through 2004. Most patients were enrolled in an IRB-approved protocol, "PEACH: A prospective evaluation of adolescents and children with pulmonary arterial hypertension," and all were referred to the Pulmonary Hypertension Program after initial diagnosis of PAH by echocardiogram. Cardiac surgical procedures were excluded. The medical record was reviewed and specific variables from the perioperative record were noted: age, gender, operation or procedure performed, diagnoses and etiology of PAH, the type of anesthetic administered (sedation, general inhaled, total IV anesthesia (TIVA)), anesthetic airway management, vital signs preoperatively and during the procedure, including systemic BP, pulse oximetry (SpO_2), capnography ($PetCO_2$), and cardiac catheterization data when available, including measurements of PAP and PVR. Baseline PAP was defined as the initial PAP measured during cardiac catheterization, before any intentional pharmacologic or ventilatory manipulations of PVR. For noncardiac catheterization procedures, baseline PAP was obtained from the most recent cardiac catheterization or estimated from the preoperative echocardiogram. Severity of baseline PAH was classified as *subsystemic* (PAP <70% of systemic BP), *systemic* (*PAP* = 70%–100% of systemic BP), and *suprasystemic* (PAP >100% of systemic BP) based on mean pressures.

Evidence for incidents and complications occurring intraoperatively through 48 h postoperatively was sought from the anesthetic record, postanesthetic flowsheets, surgical notes, and progress notes. An *incident* was defined as an observed change in monitored values that was transient, had no effect on the patient's condition, and required minimal or no treatment. A *minor complication* was defined as a transient event that had no long-term ill effect on the patient and resolved with specific treatment. A *major complication* was defined as a potentially life-threatening event requiring immediate treatment (5). If a complication was noted, pertinent historical details and laboratory data were recorded.

Anesthetic and Sedation Management

Preoperative assessment in all patients included a recent physical examination by a pediatric cardiologist, a recent electrocardiogram and echocardiogram, and review of the latest cardiac catheterization data. Close communication between the Pulmonary Hypertension Team and anesthesiologist was made in all cases. Inhaled nitric oxide (iNO) was readily available for all procedures.

General anesthesia was administered by pediatric anesthesiologists experienced in cardiac anesthesia. As many anesthetics exhibit mixed hemodynamic effects, and may be unacceptable when used in full anesthetic dosage, we used a balanced anesthetic technique in which subanesthetic doses of several drugs were combined to provide general anesthesia. Oral or IV midazolam was administered for preanesthetic sedation. Induction was cautiously achieved with midazolam, fentanyl, and a small dose of propofol or low concentration of sevoflurane. Inhaled anesthesia was maintained with isoflurane or sevoflurane; TIVA was maintained with infusion of propofol and either intermittent fentanyl or continuous remifentanil. Rocuronium or pancuronium was used for neuromuscular blockade as indicated. We used tracheal intubation in most patients, but used the laryngeal mask airway or facemask when appropriate for the procedure. Infiltration of local anesthetic by the operator at the surgical site helped the anesthesiologist to avoid high doses of general anesthetics.

Sedation was administered by a pediatric cardiologist to selected patients having cardiac catheterizations. Midazolam and fentanyl (rarely meperidine) was the most commonly used combination, and the airway was unaided.

Postoperatively, patients who exhibited signs of right heart failure, were unstable, or were beginning IV epoprostenol therapy were admitted to the pediatric intensive care unit. Stable patients requiring observation, such as those being weaned from intraoperative iNO or beginning oral sildenafil, were admitted to the cardiac ward for overnight observation. Asymptomatic, stable patients who were not changing therapy were discharged after brief procedures.

Statistical Analysis

Statistical analyses were performed using JMP 6 software (SAS, Cary, NC). Patient and procedural characteristics and the incidences of complications and of changes in vital signs were subjected to descriptive statistics. χ^2 analysis was used to compare the incidences of complications among types of procedure, types of anesthetic, methods of airway management, age, etiologies of PAH, and baseline PAP. To assess the association of each nominal variable with the outcome, major complication, bivariate contingency tables were created. Logistic regression analysis was performed to assess the association between each continuous variable and the outcome, major complication. Variables with $P < 0.20$ in the univariate analysis, as well as clinically relevant variables, were then subjected to multivariate logistic regression analysis to determine the individual impact of the variables on the outcome, major complication.

RESULTS

Of 196 patients in the PAH database, 156 patients (Table 1) underwent 256 procedures (Table 2). The most frequent procedure was cardiac catheterization (55%), of which 68% were associated with intentional manipulations of PVR (e.g., hypoxic or hyperoxic challenge and iNO) to investigate the severity of PAH. Central venous access was most frequently performed to provide a port for IV treatment of PAH. Airway procedures included tonsillectomy, adenoidectomy, bronchoscopy, and tracheostomy. Abdominal procedures included gastric fundoplication, open liver biopsy, gastrostomy, cholecystectomy, bowel resection, and splenectomy. Thoracic procedures included open lung biopsy, anterior spinal fusion, and epicardial pacemaker insertion. Other procedures included imaging, dental, posterior spinal fusion, gastrointestinal endoscopy, and myringotomy. Anesthetic techniques and airway management are summarized in Table 2.

Incidents

Clinically significant decreases in SpO_2 (SpO_2 <90% in noncyanotic patients or an absolute decrease >5% in cyanotic patients) occurred during 21% of the procedures. Of these 44% accompanied intentional manipulations of FiO_2 for diagnostic purposes during cardiac catheterization. Clinically significant increases in $PetCO_2$ or $PaCO_2$ (>45 mm Hg) were observed during 22% of the procedures; these were not significantly more frequent during laparoscopic procedures ($n = 9$, $P = 0.11$). Clinically significant decreases in systemic BP (>20% from baseline) were observed in 20% of procedures. Clinically significant increases in PAP (>20% from baseline) occurred during 19% of cardiac catheterization procedures (PAP was not measured during other procedures). The frequency of incidents was not significantly associated with type of procedure, type of anesthetic, method of airway management, etiology of PAH, or severity of baseline PAP.

Minor Complications

Bradycardia responding to treatment with IV atropine occurred in two patients, and supraventricular tachycardia requiring IV adenosine occurred in one patient, all during cardiac catheterization. These were thought to be stimulated by intracardiac manipulation of the catheter. Hypotension associated with remifentanil infusion occurred during cardiac catheterization in a 16-yr-old patient with systemic PAH associated with chronic airway obstruction; the hypotension resolved after discontinuation of the remifentanil.

Two patients had transient decreases of SpO_2 in the postanesthesia care unit that responded immediately to oxygen administration. One was a 3-yr-old child with systemic PAH and history of lung hypoplasia and diaphragmatic hernia who had undergone closure of tracheostomy under inhaled anesthesia with an endotracheal tube. The other was a 30-yr-old patient with suprasystemic PAH associated with Eisenmenger's syndrome and trisomy 21 who had undergone dental extractions under TIVA with an endotracheal tube.

Two patients required unplanned postoperative mechanical ventilation for respiratory issues. One was a 6-mo-old infant with suprasystemic PAH associated with lung hypoplasia who had undergone cardiac catheterization under TIVA with an endotracheal tube. The other was a 5-mo-old infant with subsystemic PAH associated with bronchopulmonary dysplasia and prematurity who had undergone laparoscopic Nissen fun-doplication under inhaled anesthesia.

The frequency of minor complications was not significantly associated with type of procedure, type of anesthetic, method of airway management, etiology of PAH, or severity of baseline PAP.

Major Complications

Cardiac arrest not associated with pulmonary hypertensive crisis occurred in a 9-mo-old infant with subsystemic PAH undergoing device closure of a ventricular septal defect. Resuscitation with external cardiac massage and IV epinephrine was successful within 90 s; there were no sequelae.

Pulmonary hypertensive crisis (defined as an increase in PAP to exceed systemic BP, a decrease in systemic BP, and a decrease in SpO_2) occurred in six patients during cardiac catheterization procedures (3.8% of patients, 4.3% of cardiac catheterization procedures, 2.3% of all procedures). Pulmonary hypertensive crises in two patients resolved with specific treatment intraoperatively. Two patients required postoperative mechanical ventilation and intensive care unit support for 24–48 h before the pulmonary hypertensive crises and hemodynamic instability completely resolved. Two patients with baseline suprasystemic PAH had intractable pulmonary hypertensive crises resulting in postoperative death (1.3% of patients, 1.4% of

cardiac catheterization procedures, 0.8% of all procedures). Details of the pulmonary hypertensive crisis patients are summarized in Table 3.

Major complications were significantly more frequent in patients with baseline suprasystemic PAH ($P = 0.014$) (Fig. 1), but were not significantly associated with type of anesthetic, method of airway management, or etiology of PAH. All major complications occurred during cardiac catheterization procedures. Death occurred significantly more frequently in patients with baseline suprasystemic PAH ($P = 0.015$).

Variables that were significantly associated with major complications by univariate analyses were severity of baseline PAH, duration of procedure, and a clinically significant intraoperative decrease in SpO_2 (Table 4). The multivariate predictor of major complications was suprasystemic baseline PAH (Table 5).

DISCUSSION

Our data demonstrate that children with PAH have a significant risk of major perioperative cardiovascular complications, including cardiac arrest, pulmonary hypertensive crisis, and death, when undergoing sedation or anesthesia for cardiac catheterization procedures. Overall complications were more frequent in children with systemic or suprasystemic PAH, but were not associated with patient age, etiology of PAH, type of anesthetic, or airway management techniques.

The incidence of perioperative cardiac arrest that we found to be associated with PAH is much greater than published incidences of perioperative cardiac arrest in all children. The initial findings of the Pediatric Perioperative Cardiac Arrest (POCA) Registry report an overall incidence of perioperative cardiac arrest of 0.0265%, an incidence of anesthesia-related cardiac arrest of 0.014%, and an incidence of anesthesia-related death of 0.0036% (6). The overall incidences of perioperative cardiac arrest and death in a pediatric teaching hospital without open cardiac or neurosurgical services were reported to be 0.033% and 0.004%, respectively (7). Our institution's unpublished overall incidence of perioperative cardiac arrest from 2001 through 2004 was 0.024% (Quality Assurance Program, Department of Anesthesiology, The Children's Hospital, Denver). In comparison, the three cardiac arrests that occurred during our 256 procedures in children with PAH represent an incidence of 1.17%, and the two deaths 0.78%.

Major complications are more frequent in association with pediatric cardiac catheterization. A leading pediatric cardiac center reported the incidences of perianesthetic cardiac arrest and death associated with cardiac catheterization to be 0.49% and 0.08%, respectively (5). Our institution's incidence of intraoperative cardiac arrest and perioperative death associated with cardiac catheterization (excluding PAH patients) from 2000 through 2004 was 0.07% and 0.11%, respectively (Quality Assurance Program, Division of Cardiology, The Children's Hospital, Denver). In comparison, the three cardiac arrests that occurred during our 141 catheterization procedures in children with PAH represent an incidence of 2.1%, and the two deaths 1.4%.

There is not a significant body of literature about PAH and its associated complications in children who require anesthesia care. Studies of adults demonstrate that the presence of PAH significantly contributes to adverse outcomes after both cardiac and noncardiac surgery (8,9). Reich et al. (8), in a retrospective analysis of computerized intraoperative databases, determined that pulmonary hypertension was a predictor of perioperative myocardial infarction and death in a large cohort of adult patients undergoing coronary artery bypass grafting. Ramakrishna et al. (9) performed a retrospective analysis of adult patients with PAH who had undergone noncardiac surgery and reported a high incidence of early postoperative morbidity

and a mortality rate of 7%, indicating the serious impact of PAH. In a retrospective study of 276 pediatric and adult patients with congenital heart disease undergoing noncardiac surgery, Warner et al. (10) found that PAH, cyanosis, congestive heart failure, and age <2 yr was a predictor of perioperative morbidity.

Studies of adults with PAH have reported other perioperative factors that have varying importance in predicting morbidity. Long duration of anesthesia was a significant independent predictor of morbidity in adults with PAH (9). Although long duration of the procedure achieved significance in our univariate analysis, it did not prove to be an independent predictor of major complications when subjected to multivariate logistic regression (long duration was due to the time taken to resuscitate and/or stabilize children with PAH crises before transfer to the pediatric intensive care unit). Similar to the findings of Warner et al. (10), our data suggest that general anesthesia versus nongeneral anesthesia is not a significant factor associated with complications.

Compared to the published studies of PAH in adults, ours is limited by a relatively small number of subjects; thus, our ability to identify a significant association between some variables and complications may have been limited by inadequate power, or a Type II statistical error. A further limitation of retrospective studies is that details of clinical management and other data can be incomplete or lacking; thus, some complications or other important information can be missed. We anticipate that both outcomes and contributing factors such as anesthetic management and surgical techniques will be more precisely defined as experience grows.

Several mechanisms can be associated with hemodynamic deterioration in patients with PAH. Of critical importance among these mechanisms is a rapid increase in PVR related to pulmonary arterial vasoreactivity. Hypercarbia, hypoxia, acidosis, and noxious stimuli such as pain and airway instrumentation can trigger a rapid increase in PVR (1,11–14) that can lead to a pulmonary hypertensive crisis and/or right heart failure. It was not apparent during this retrospective review that hypercarbia, acidosis, pain, or airway instrumentation contributed to any complications; SpO_2, $PetCO_2$, and arterial blood gases were generally well documented. However, one pulmonary hypertensive crisis that responded quickly to iNO appeared to be associated with exposure to subambient FiO_2 during evaluation of pulmonary vasoreactivity. Unrecorded noxious stimuli, including catheter stimulation of the heart or pulmonary vasculature, could have contributed.

Anesthesiologists should be aware that other mechanisms can also contribute to right-sided heart failure in patients with PAH. Hypovolemia can provide inadequate preload to the right ventricle, leading to decreased stroke volume, cardiac output, and pulmonary blood flow. Systemic hypotension or a decrease in systemic vascular resistance can cause a decrease in coronary artery blood flow, leading to biventricular ischemia. Compensatory right ventricular hypertrophy or dilation can compress the septal wall of the left ventricle, leading to inadequate filling of the left ventricle, decreased stroke volume, and decreased cardiac output. Hypoxemia related to problems with ventilation, lung disease, or decreased pulmonary blood flow can further impair ventricular function.

The hemodynamic and pulmonary vascular effects of anesthetic drugs have been reviewed elsewhere (2,15–20) and should be considered in the anesthetic care of children with PAH. Sedation without general anesthesia is a common technique for cardiac catheterization of selected patients and was used in 56 of the 141 cardiac catheterization procedures in this series. Fentanyl and midazolam were the most commonly used combination and are thought to have little direct effect on the pulmonary vasculature. Oversedation does occur during procedural sedation, however (21), and can be associated with hypercarbia, hypoxemia, and airway obstruction in patients managed with a natural airway and spontaneous ventilation (22). These

clinical problems can also occur during general anesthesia and must be avoided in patients with PAH.

Selective pulmonary vasodilators are frequently used perioperatively, even in the absence of hemodynamic deterioration. During cardiac catheterization procedures for evaluation of PAH, iNO is administered to test pulmonary vasoreactivity. For other surgical procedures, iNO is usually administered prophylactically intraoperatively and continued postoperatively via nasal cannulae (23). Postoperative withdrawal of iNO or other pulmonary vasodilators can be associated with life-threatening rebound pulmonary hypertension; this must be anticipated and can be attenuated by administration of other pulmonary vasodilators (24,25). Treatment of pulmonary hypertensive episodes involves 100% oxygen, hyperventilation, attenuation of noxious stimuli, and pharmacologic pulmonary vasodilators. Such treatment and drugs have been reviewed elsewhere (1–3).

In summary, our data indicate that children with suprasystemic PAH have a perioperative risk of major complications, including cardiac arrest, pulmonary hypertensive crisis, and death that is many times greater than that reported for the general pediatric population. It is important that anesthesiologists be aware of this increased risk, understand the pathophysiology of PAH, form an appropriate anesthetic management plan, and be prepared to treat cardiovascular deterioration.

Acknowledgements

The authors thank Jane Gralla, PhD, and Zhaoxing Pan, PhD, for their assistance with statistical analysis.

References

1. Fischer LG, Van Aken H, Bürkle H. Management of pulmonary hypertension: physiological and pharmacological considerations for anesthesiologists. Anesth Analg 2003;96:1603–16. [PubMed: 12760982]
2. Blaise G, Langleben D, Hubert B. Pulmonary arterial hypertension: pathophysiology and anesthetic approach. Anesthesiology 2003;99:1415–32. [PubMed: 14639158]
3. Rashid A, Ivy D. Severe paediatric pulmonary hypertension: new management strategies. Arch Dis Child 2005;90:92–8. [PubMed: 15613526]
4. Jones ODH, Shore DF, Rigby ML, et al. The use of tolazoline hydrochloride as a pulmonary vasodilator in potentially fatal episodes of pulmonary vasoconstriction after cardiac surgery in children. Circulation 1981;64 (Suppl II):134–9.
5. Bennett D, Marcus R, Stokes M. Incidents and complications during pediatric cardiac catheterization. Pediatr Anesth 2005;15:1083–8.
6. Morray JP, Geiduschek JM, Ramamoorthy C, et al. Anesthesia-related cardiac arrest in children. Initial findings of the pediatric perioperative cardiac arrest (POCA) registry. Anesthesiology 2000;93:6–14. [PubMed: 10861140]
7. Murat I, Constant I, Maud'Huy H. Perioperative anaesthetic morbidity in children: a database of 24,165 anaesthetics over a 30-month period. Pediatr Anesth 2004;14:158–66.
8. Reich DL, Bodian CA, Krol M, et al. Intraoperative hemodynamic predictors of mortality, stroke, and myocardial infarction after coronary artery bypass surgery. Anesth Analg 1999;89:814–22. [PubMed: 10512249]
9. Ramakrishna G, Sprung J, Ravi BS, et al. Impact of pulmonary hypertension on the outcomes of noncardiac surgery. J Am Coll Cardiol 2005;45:1691–9. [PubMed: 15893189]
10. Warner MA, Lunn RJ, O'Leary PW, Schroeder DR. Outcomes of noncardiac surgical procedures in children and adults with congenital heart disease. Mayo Clin Proc 1998;73:728–34. [PubMed: 9703297]
11. Rudolph AM, Yuan S. Response of the pulmonary vasculature to hypoxia and H^+ ion concentration changes. J Clin Invest 1966;45:399–411. [PubMed: 5904557]

12. Hickey PR, Hansen DD, Wessel DL, et al. Blunting of stress responses in the pulmonary circulation of infants by fentanyl. Anesth Analg 1985;64:1137–42. [PubMed: 4061893]
13. Morray JP, Lynn AM, Mansfield PB. Effect of pH and PCO_2 on pulmonary and systemic hemodynamics after surgery in children with congenital heart disease and pulmonary hypertension. J Pediatr 1988;113:474–9. [PubMed: 3137318]
14. Hickey PR, Retzack SM. Acute right ventricular failure after pulmonary hypertensive responses to airway instrumentation: effect of fentanyl dose. Anesthesiology 1993;78:372–6. [PubMed: 8439035]
15. Friesen RH, Veit AS, Archibald DJ, Campanini RS. A comparison of remifentanil and fentanyl for fast track paediatric cardiac anesthesia. Pediatr Anesth 2003;13:122–5.
16. Chanavaz C, Tirel O, Wodey E, et al. Haemodynamic effects of remifentanil in children with and without intravenous atropine. An echocardiographic study. Br J Anaesth 2005;94:74–9. [PubMed: 15486003]
17. Hickey PR, Hansen DD, Wessel DL, et al. Pulmonary and systemic hemodynamic responses to fentanyl in infants. Anesth Analg 1985;64:483–6. [PubMed: 3994009]
18. Williams GD, Jones TK, Hanson KA, Morray JP. The hemodynamic effects of propofol in children with congenital heart disease. Anesth Analg 1999;89:1411–16. [PubMed: 10589618]
19. Morray JP, Lynn AM, Stamm SJ, et al. Hemodynamic effects of ketamine in children with congenital heart disease. Anesth Analg 1984;63:895–9. [PubMed: 6486488]
20. Wolfe RR, Loehr JP, Schaffer MS, Wiggins JW Jr. Hemodynamic effects of ketamine, hypoxia and hyperoxia in children with surgically treated congenital heart disease residing ≥1200 metres above sea level. Am J Cardiol 1991;67:84–7. [PubMed: 1986509]
21. Motas D, McDermott NB, Vansickle T, Friesen RH. Depth of consciousness and deep sedation attained in children as administered by nonanaesthesiologists in a children's hospital. Pediatr Anesth 2004;14:256–60.
22. Friesen RH, Alswang M. Changes in carbon dioxide tension and oxygen saturation during deep sedation for paediatric cardiac catheterization. Pediatr Anesth 1996;6:15–20.
23. Ivy DD, Griebel JL, Kinsella JP, Abman SH. Acute hemodynamic effects of pulsed delivery of low flow nasal nitric oxide in children with pulmonary hypertension. J Pediatr 1998;133:453–6. [PubMed: 9738734]
24. Ivy DD, Kinsella JP, Ziegler JW, Abman SH. Dipyridamole attenuates rebound pulmonary hypertension after inhaled nitric oxide withdrawal in postoperative congenital heart disease. J Thorac Cardiovasc Surg 1998;115:875–82. [PubMed: 9576224]
25. Atz AM, Wessel DL. Sildenafil ameliorates effects of inhaled nitric oxide withdrawal. Anesthesiology 1999;91:307–10. [PubMed: 10422958]

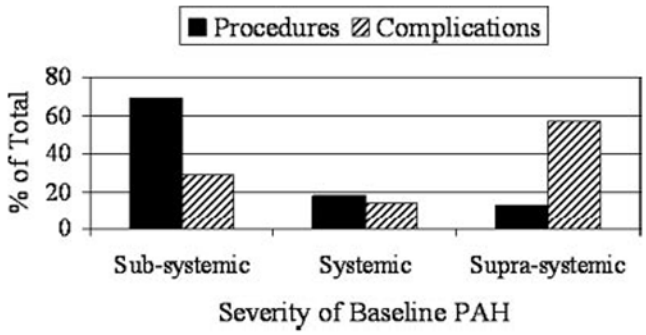

Figure 1.
The frequency of major complications was significantly associated with the severity of baseline pulmonary artery hypertension (PAH) ($P = 0.014$ by χ^2 analysis).

Table 1

Characteristics of 156 Children with Pulmonary Hypertension

Median age (range)	4 yr (4 d–30 yr)
Gender (male/female)	73/83
PAH etiology (*n*)	
Idiopathic PAH	88
Congenital heart disease	32
Chronic lung disease	22
Chronic airway obstruction	7
Chronic liver disease	7
Baseline mean PAP (*n*)	
Subsystemic (<70% of systemic BP)	106
Systemic (70%–100% of systemic BP)	30
Suprasystemic (>100% of systemic BP)	20

PAH = pulmonary arterial hypertension; PAP = pulmonary artery pressure. BP = blood pressure.

Table 2

Characteristics of 256 Procedures in Children with Pulmonary Hypertension

	n
Procedures	
Cardiac catheterization	141
Central venous access	31
Airway	28
Abdominal	20
Thoracic	8
Other	28
Anesthetic type	
Sedation	56
General volatile	148
General TIVA	52
Airway management	
Natural unaided airway	54
ETT	192
LMA	7
Face mask	3

TIVA = total intravenous anesthesia; ETT = endotracheal tube; LMA = laryngeal mask airway.

Table 3

Summary of Pulmonary Hypertensive Crises

Patient	Procedure	Event	Treatment and outcome
6-yr-old male	Cardiac catheterization, PAH study	PAP 24 → 70 mm Hg	Immediate response to oxygen, iNO. Discharged after overnight observation. Chronic diltiazem begun
Subsystemic PAH	Sedation: fentanyl, midazolam	PVR 4.4 → 13.4 Wood u/m^2	
History of HAPE No chronic medications	Natural airway Exposure to subambient FiO_2	MAP 64 → 58 mm Hg SpO_2 97 → 68%	
14-yr-old male	Cardiac catheterization, PAH study	PAP 90 → 115 mm Hg	Immediate response to oxygen, iNO. Discharged after overnight observation
Suprasystemic idiopathic PAH Meds: epoprostenol, oxygen	Anesthesia: isoflurane Endotracheal tube	MAP 70 → 50 mm Hg SpO_2 90 → 77%	
2-yr-old female	Cardiac catheterization, PAH study	PAP 67 → 102 mm Hg	Oxygen, iNO, epoprostenol, atropine, dopamine. Mechanical ventilation for 48 h in CICU. Discharged day 12
Systemic PAH	Anesthesia: sevoflurane, isoflurane	PVR 20.5 → 29.7 Wood u/m^2	
Bronchopulmonary dysplasia VSD Meds: epoprostenol, oxygen, coumadin, furosemide	Endotracheal tube	MAP 79 → 55 mm Hg SpO_2 92 → 72% PaO_2 46 mm Hg, $PaCO_2$ 37 mm Hg Bradycardia	
1.8-yr-old female	Cardiac catheterization, PAH study	PAP 72 mm Hg	Oxygen, iNO, bicarbonate. Mechanical ventilation for 24 h in CICU. Discharged day 8. Chronic bosentan and dipyridamole begun
Suprasystemic PAH Branch pulmonary artery stenosis Meds: digoxin, oxygen	Anesthesia: isoflurane Endotracheal tube	MAP 52 mm Hg PaO_2 96 → 44 mm Hg Metabolic acidosis	
1.9-yr-old female Suprasystemic PAH	Cardiac catheterization Sedation: meperidine, midazolam	PAP 84 mm Hg PVR 27.8 Wood u/m^2	External cardiac massage, epinephrine, iNO, oxygen, epoprostenol. Mechanical ventilation. Continuing PAH crises, RV failure. Death at 48 h
Repaired VSD, ASD Trisomy 21 Meds: furosemide, oxygen	Natural airway	MAP 54 mm Hg $PaCO_2$ 48 mm Hg, PaO_2 91 mm Hg Cardiac arrest	
2-yr-old female	Cardiac catheterization	PAP 75 → 88 mm Hg	External cardiac massage, epinephrine, iNO, oxygen, milrinone, bicarbonate. Not resuscitatable. Placed on ECMO. Death at 19 h
Hospitalized in acute respiratory distress. New diagnosis of suprasystemic PAH and coarctation of aorta	TIVA: fentanyl, midazolam	MAP 51 → 35 mm Hg	
Meds: oxygen, iNO	Endotracheal tube	SpO_2 98 → 50% $PaCO_2$ 39 mm Hg, PaO_2 23 mm Hg Cardiac arrest	

PAH = pulmonary arterial hypertension; HAPE = high altitude pulmonary edema; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; MAP = mean systemic arterial blood pressure; iNO = inhaled nitric oxide; CICU = cardiac intensive care unit; VSD = ventricular septal defect; ASD = atrial septal defect; RV = right ventricle; ECMO = extracorporeal membrane oxygenation; TIVA = total IV anesthesia.

Table 4

Univariate Association of Patient and Procedural Characteristics with Major Complications

Variable	*P*
Age	0.327
Gender	0.302
PAH etiology	0.434
Baseline PAH severity	0.014
Type of anesthesia	0.877
Airway management	0.904
Type of procedure	0.129
Duration of procedure	0.023
Decrease in SpO_2[a]	0.032
Increase in PCO_2[b]	0.915

Nominal variables were analyzed with χ^2 tests, and continuous variables were analyzed with logistic regression.

PAH = pulmonary arterial hypertension.

[a] SpO_2 <90% during procedure in noncyanotic patients or an absolute decrease >5% in cyanotic patients.

[b] $PetCO_2$ or $PaCO_2$ >45 mm Hg during procedure.

Table 5

Multivariate Predictors of Major Complications

Variable	Odds ratio	95% CI	*P*
PAH etiology = Idiopathic	1.3	0.2–10.6	0.74
Baseline PAH = Systemic	0.8	0.04–9.0	0.87
Baseline PAH = Suprasystemic	8.1	1.3–67.4	0.02
Cardiac catheterization procedure	NC		
Decrease in SpO_2[a]	3.6	0.7–20.6	0.13
Long duration of procedure[b]	5.1	0.7–103	0.10

Variables were dichotomized (yes or no) and analyzed with multivariate logistic regression.

PAH = pulmonary arterial hypertension; NC = not calculable because all major complications occurred during catheterization procedures.

[a] SpO_2 <90% during procedure in noncyanotic patients or an absolute decrease >5% in cyanotic patients.

[b] Greater than median duration of 133 min.