ORIGINAL ARTICLE

Cardiac Catheterization in Children with Pulmonary Hypertensive Vascular Disease

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Abstract The risks associated with cardiac catheterization in children with pulmonary hypertension (PH) are increased compared with adults. We reviewed retrospectively all clinical data in children with PH [mean pulmonary artery pressure (mean PAp) $\geq$25 mmHg and pulmonary vascular resistance index (PVRI) $\geq$3 Wood units m^2] undergoing cardiac catheterization between 2009 and 2014. Our strategy included a team approach, minimal catheter manipulation and sildenafil administration prior to extubation. Adverse events occurring within 48 h were noted. Seventy-five patients (36 males), median age 4 years (0.3–17) and median weight 14.6 kg (2.6–77 kg), underwent 97 cardiac catheterizations. Diagnoses included idiopathic or heritable pulmonary arterial hypertension (PAH) (29 %), PAH associated with congenital heart disease (52 %), left heart disease (5 %) and lung disease (14 %). Mean PAp was 43 $\pm$ 19 mmHg; mean PVRI was 9.7 $\pm$ 6 Wood units m^2. There were no deaths or serious arrhythmias. No patient required cardiac massage. Three patients who suffered adverse events had suprasystemic PAp (3/3), heritable PAH (2/3), decreased right ventricular function (3/3), and pulmonary artery capacitance index <1 ml/mmHg/m^2 (3/3) and were treatment naïve (3/3). No patient undergoing follow-up cardiac catheterization suffered a complication. In 45 % of cases, the data acquired from the follow-up cardiac catheterization resulted in an alteration of therapy. Three percent of children with PH undergoing cardiac catheterization suffered adverse events. However, there were no intra or post procedural deaths and no one required cardiac massage or cardioversion. Follow-up cardiac catheterization in patients receiving pulmonary hypertensive targeted therapy is safe and provides useful information.

Keywords Pulmonary hypertension · Cardiac catheterization · Pulmonary artery capacitance index

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Introduction

Pulmonary hypertensive vascular disease (PHVD) in childhood is a serious, heterogeneous condition that may require cardiac catheterization for diagnostic precision, initiation of therapy and evaluation of therapeutic strategies [6, 20]. Hemodynamic measurements obtained at cardiac catheterization predict outcome and, in some circumstances, may be a pre-requisite for approval of drug prescription and reimbursement of drug costs [2]. Acute vasoreactivity testing with inhaled nitric oxide predicts the responsiveness to calcium channel blocker therapy, and prognosis and, in patients with congenital heart disease or left heart dysfunction, may indicate operability [1, 10, 11, 17]. Indeed absence of a positive response to a short-acting pulmonary vasodilator in the cardiac catheterization laboratory is a contraindication to the use of nifedipine, amlodipine or diltiazem to treat idiopathic or heritable pulmonary arterial hypertension (IPAH) [10]. Accurate assessment of drug effectiveness and prediction of

deterioration is difficult in children because there are no tests of functional capacity that are readily applicable across all patient sizes and neurodevelopmental stages. Children unlike adults may have advanced disease with a paucity of symptoms [2, 13, 20]. Hemodynamic data correlates well with functional assessment and outcomes in clinical trials. It is a useful indicator of disease severity and treatment effect that may be compared across all ages and developmental stages [2, 7, 16]. However, there is a reasonable reluctance to recommend repeated cardiac catheterization in children with pulmonary hypertension (PH) because of a 4–6 % risk of serious adverse outcomes [3, 4, 19, 22]. In 2008, we established a pediatric pulmonary hypertension service, which included a standardized approach to cardiac catheterization in children with pulmonary hypertensive vascular disease. Therefore, we undertook an evaluation of the risks and benefits of cardiac catheterization in children with pulmonary hypertensive vascular disease.

Methods

The study was approved by the institutional ethics review board at the University of Alberta (approval number Pro00038633). The need for individual consent was waived.

We reviewed all available clinical records of children with PHVD defined as mean pulmonary artery pressure (mean PAp) ≥ 25 mmHg and pulmonary vascular resistance index (PVRI) ≥ 3 Wood units m^2 undergoing cardiac catheterization from January 2009 to April 2014.

We reviewed in detail using a standard data collection form the demographics, clinical history, physical examination findings, drug therapy, echocardiogram performed within 1 month of the cardiac catheterization and the hemodynamic measurements obtained during cardiac catheterization.

We divided the patients into three groups based on simultaneously measured mean PAp to mean systemic arterial pressure (mSAp) ratio as follows: Group 1 mean PAp/mean SAp < 0.7, Group 2 mean PAP/mean SAp $\geq 0.7 \leq 1$ and Group 3 mean PAp/mean SAp > 1.

All children undergoing cardiac catheterization for PH were evaluated and discussed by a pediatric pulmonary hypertension and pediatric anesthesia specialist. A protocol was established with the following key components:

1. Patients receiving targeted pulmonary hypertension therapy continued their medications according to their usual home schedule both before and during the procedure.
2. A dose of sildenafil (1 mg/kg, max 40 mg) was administered to all the patients through a nasogastric

tube before the end of the case and 20 min prior to tracheal extubation. Exceptions were children already receiving sildenafil or tadalafil as part of their home drug regimen who did not, in general, receive an additional dose.
3. Anesthesia was provided using a regime that generally included ketamine ($\pm$midazolam) with rocuronium for induction and low-dose desflurane or sevoflurane and remifentanil for maintenance. Local anesthesia was administered to sites of proposed vascular access.
4. Anesthetic management included intubation with a cuffed endotracheal tube and mechanical ventilation in all but one patient.
5. End-tidal CO_2 was monitored continuously and maintained between 35 and 45 mmHg.
6. Oxygen consumption was measured by mass spectrometry or the breath-by-breath method (Innocor) (Innovision, Denmark) [8].

The cardiac catheterization protocol varied according to anatomy. We used a modified Seldinger technique to insert percutaneously femoral or radial arterial and femoral or internal jugular venous lines. In patients without intracardiac shunting, a single venous sheath was used through which a thermodilution catheter was positioned with the distal port in the main pulmonary artery. The proximal port was confirmed to be in the right atrium by pressure measurement and used for saline injection to measure cardiac output by thermodilution. To avoid frequent catheter manipulation in subjects with intracardiac or systemic to pulmonary artery shunts, we used an internal jugular vein sheath (one French size larger than the catheter inserted) to measure pre-tricuspid venous saturations and pressures. If there was a shunt at atrial level, then a second catheter was placed via the femoral vein to sample blood and measure pressures in the left atrium or pulmonary veins. Oxygen consumption was measured by mass spectrometry or the breath-by-breath method in all patients [8]. All calculated parameters were indexed to body surface area. Systemic and pulmonary blood flows (L/min/m^2) were calculated from the direct Fick's principle in subjects with cardiac shunts or the indirect Fick's principle by thermodilution in patients without shunts. Systemic and pulmonary vascular resistances (Wood units m^2) were calculated using standard formulas. Pulmonary artery capacitance index (PACI) was calculated from the equation: stroke volume/pulmonary artery pulse pressure (ml/mmHg/m^2). Measurements were recorded at baseline (usually room air) following arterial blood gas analysis demonstrating normal pH and pCO$_2$. Pulmonary vasoreactivity testing was performed with inhaled nitric oxide in all patients undergoing a first cardiac catheterization. We performed additional pulmonary

vasoreactivity testing included hyperoxia, inhaled prostacyclin or sildenafil administered via nasogastric tube depending on the clinical circumstance. Adverse events occurring up to 48 h after the cardiac catheterization were noted. Minor complications were defined as transient events including loss of distal pulse with recovery post-procedure, arrhythmia not requiring medication or electrical cardioversion and post-extubation stridor. We defined major complications as arrhythmias requiring electrical or chemical cardioversion, hypotension (defined as a decrease in systolic blood pressure by 20–30 % [14, 18]) requiring ionotropic support or fluid administration at the discretion of the anesthesiologist, failure to extubate at the end of the cardiac catheterization, need for cardiac massage or cardiopulmonary resuscitation, institution of extracorporeal life support (ECLS) and death.

Statistical analyses were performed with IBM SPSS version 21. We used the ANOVA test to compare means of continuous variables and the Chi-square test to compare the nominal variables between the three groups. Multiple Fischer's exact t tests were used to compare variables between patients with and without major adverse events. $p < 0.05$ was considered significant.

Results

During the study period, 75 patients (36 males), median age 4 years (3 months to 17 years) and median weight 14.6 kg (2.6–77 kg), underwent 97 cardiac catheterization procedures. Diagnostic groups included IPAH ($n = 22$, 28 %), PAH associated with repaired or unrepaired congenital heart disease ($n = 39$, 52 %), acquired left heart disease ($n = 4$, 5 %) and lung disease ($n = 10$, 14 %). Arterial access was through the femoral artery ($n = 86$) and radial artery ($n = 11$). Venous access was right and left femoral vein ($n = 23$), right internal jugular vein and femoral vein ($n = 28$) and femoral vein only ($n = 46$). The mean PAp overall was 43 ± 19 mmHg, mean PVRI was 9.7 ± 6 Wood units m^2, and mean PACI was 2.1 ± 0.8 ml/mmHg/m^2.

Table 1 describes the clinical characteristics of the patients subdivided into three groups by severity of pulmonary hypertension. All three groups were comparable in height weight, body surface area and World Health Organization (WHO) functional class. Mean PAp was 38 ± 7, 48 ± 11 and 76 ± 14 mmHg in groups 1, 2 and 3, respectively ($p < 0.001$). The mean PVRI was 5.6 ± 2.4 Wood units m^2, 11.4 ± 5.1 and 19.6 ± 7.9 in groups 1, 2 and 3, respectively ($p < 0.001$). The mean PACI in Group 1 was 1.5 ± 0.6 ml/mmHg/m^2, in Group 2 was 1 ± 0.5 ml/mmHg/m^2 and in Group 3 was 0.8 ± 0.2 ml/mmHg/m^2 ($p = 0.06$).

Complications occurred in 6/97 (6.2 %) cardiac catheterization procedures. Major complications occurred in 3/97 (3.1 %). All three children had suprasystemic pulmonary artery pressures and moderate-to-severe right ventricular dysfunction and were undergoing a first diagnostic cardiac catheterization before initiation of specific therapy. 2/3 patients had heritable PAH and carried mutations of BMPR2 and Alk 1. In 2/3 of these children, systemic hypotension during the procedure required treatment. One patient received a fluid bolus in response to a 20 % decrease in systolic blood pressure. The other patient had a 50 % decrease in systolic blood pressure and required inotropic support transiently during the case. Both patients were observed overnight on the pediatric cardiac intensive care unit. A third patient was re-admitted 36 h after cardiac catheterization with progressive right heart failure. Hemodynamic instability persisted despite treatment with intravenous prostacyclin, milrinone, epinephrine and tracheal intubation. She was resuscitated with ECLS and underwent lung transplantation 7 weeks later. There were no deaths.

Minor complications occurred in 3/97 (3.1 %). All three patients suffered transient loss of the foot pulses on the side used for arterial access. The clinical characteristics of the patients who suffered minor or no adverse events versus those who suffered major adverse events are summarized in Table 2. Risk factors for a major adverse event were WHO functional class 3–4, moderate or severe right ventricular dysfunction, suprasystemic pulmonary artery pressure and decreased PACI (Table 3).

Follow-up catheterization was performed in 22 children. In 10/22 (45 %) cases, the data acquired from the follow-up cardiac catheterization resulted in a decision to alter therapy. In 3/22 children, an additional oral agent was added. In 2/22, sildenafil was replaced by long-acting tadalafil because breakthrough pulmonary hypertension was documented during the cardiac catheterization. In 5/22 children continuously infused, subcutaneously administered treprostinil was added to therapy. In the remaining 12/22 cases, the results of cardiac catheterization confirmed treatment efficacy. None of the patients undergoing a follow-up cardiac catheterization while receiving specific pulmonary hypertension targeted therapies suffered a complication.

Discussion

Our programmatic approach to the cardiac catheterization of children with pulmonary hypertension resulted in a 2 % risk of transient inotrope use with overnight observation in the cardiac intensive care unit, but no intraprocedural deaths, cardioversion or need for cardiac massage.

Table 1 Clinical and echocardiographic characteristics of patients grouped according to severity of pulmonary artery hypertension

Groups	Group 1 ($n = 48$) (mPAp/ mSAp < 0.7)	Group 2 ($n = 35$) (mPAp/ mSAp $\geq 0.7 \leq 1.0$)	Group 3 ($n = 14$) (mPAp/ mSAp > 1.0)
Age in years [median (range)]	3.9 (0.3–14)	4.1 (0.7–16)	4 (0.8–17)
Gender (M/F)	20:28	22:13	5:8
Height (cm)	96 ± 42	101 ± 33	115 ± 36
Weight (kg)	21 ± 6	21.9 ± 7.2	24.8 ± 6.8
Body surface area (m²)	0.7 ± 0.5	0.7 ± 0.4	1 ± 0.5
WHO functional class			
Class I/II	46	34	7
Class III/IV	2	1	7
Septal position			
Normal/flat	47	32	3
Concave into the left ventricle	0	3	11
Right ventricular function			
Normal/mild RV dysfunction	38	18	4
Moderate-to-severe RV dysfunction	8	17	10

Right ventricular dysfunction; mild = Tricuspid annular plane systolic excursion distance (TAPSE) Z score <−2 and ≥−2.5, Moderate-to-severe right ventricular dysfunction = TAPSE Z score <2.5. All values are in mean ± 2 SD unless specified otherwise

mPAp mean pulmonary artery pressure, *mSAp* mean systemic artery pressure

Table 2 Comparison of clinical, ECG and echocardiographic findings of children with major adverse events within 48 h of the procedure and those without significant adverse events

Variable	No major adverse event ($n = 94$)	Major adverse event ($n = 3$)	p value
WHO functional class			
Class I/II	86	1	
Class III/IV	8	2	0.05
Genetic syndrome			
No identifiable genetic syndrome	70	2	
Genetic syndrome present	24	1	0.48
Septal position			
Normal/flat	83	0	
Concave into the left ventricle	11	3	0.05
Right ventricular function			
Normal/mild RV dysfunction	79	0	
Moderate-to-severe RV dysfunction	15	3	0.04

Right ventricular dysfunction; mild = Tricuspid annular plane systolic excursion distance (TAPSE) Z score <−2 and ≥−2.5, Moderate-to-severe right ventricular dysfunction = TAPSE Z score <2.5

Furthermore, follow-up cardiac catheterization to assess the effects of treatment was accomplished safely, without any adverse events, and yielded information resulting in therapeutic changes in 45 % of cases. Our results compare favorably with other reports in children [3, 4, 9, 12, 19, 22].

The three patients who suffered adverse events during or after cardiac catheterization had suprasystemic pulmonary artery pressures (3/3), heritable PAH (2/3), decreased right ventricular function (3/3), and pulmonary capacitance index <1 ml/mmHg/m² (3/3) and were treatment naïve (2/3). This suggests that children with some or all of these characteristics may be served better by delaying cardiac catheterization until therapy has been started providing that they have diagnostic echocardiograms and chest CT scans

Table 3 Cardiac catheterization data in patients with and without a major adverse event

Cardiac catheterization findings	No major adverse events	Patient 1	Patient 2	Patient 3
Systolic pulmonary artery pressure (mmHg)	61 ± 25	78	106	58
Mean pulmonary artery pressure (mmHg)	42.4 ± 19.5	56	89	45
Systolic systemic artery pressure (mmHg)	83 ± 16	69	90	56
Mean systemic artery pressure (mmHg)	61 ± 12	49	64	43
Cardiac index (L/min/m^2)	3.5 ± 1.6	3.9	2.8	2.7
PVRI (Wood units m^2)	9.7 ± 6.3	12.3	29.5	9.5
SVRI (Wood units m^2)	18.5 ± 7.3	18.1	9.4	12
PACI (ml/mmHg/m^2)	2.1 ± 0.8	0.8	0.8	0.7
Mean PAp > mean SAp (n)	11	Yes	Yes	Yes

PVRI pulmonary vascular resistance index, *PACI* pulmonary artery capacitance index, *SVRI* systemic vascular resistance index

sufficient to exclude pulmonary veno-occlusive disease [15]. We agree that a full diagnostic evaluation including cardiac catheterization is important before starting targeted or specific pulmonary hypertensive therapy in most cases [10]. However, we would defer cardiac catheterization in patients who present in overt right heart failure and/or requiring mechanical ventilation and inotropic support until a measure of stability is achieved which may include the use of specific pulmonary hypertensive drugs. Ensuring the availability of rapidly deployed ECLS to salvage deteriorating patients with pulmonary hypertension during or after cardiac catheterization seems prudent. We do start oral therapy with sildenafil without cardiac catheterization in children who are weaning from inhaled nitric oxide on the intensive care unit and in ex-premature infants without cardiac shunts, pulmonary vein stenosis or aortopulmonary collaterals who have been recently extubated. In the latter patients, before starting therapy, we obtain a complete echocardiogram, CT scan, and pulmonology consult and optimize non-invasive ventilation strategies, oxygen therapy and treatment for aspiration. However, if they require prolonged pulmonary hypertensive therapy, then cardiac catheterization is performed later in their course.

We suggest that follow-up cardiac catheterizations yield important information particularly about treatment efficacy and may be performed without adverse events. Cardiac catheterization is one of the few tests that can be applied uniformly across all ages and neurodevelopmental stages to provide prognostic information or to asses the effect of therapy [2]. Hemodynamic data obtained at cardiac catheterization particularly pulmonary artery pressure, capacitance and pulmonary vascular resistance correlate well with functional class, exercise capacity and the effect of therapy [2, 7, 16, 20].

We have chosen to perform cardiac catheterizations using general anesthesia and endotracheal intubation to reduce inadvertent hypercarbia, acidosis, hypoxia and agitation that may precipitate acute, and potentially, lethal increases in pulmonary artery pressure, as well as, confound the baseline hemodynamics and the effects of pulmonary vascular reactivity testing. Nevertheless, we are cognizant that cardiac catheterization may be performed safely using local anesthesia and sedation without tracheal intubation depending on local expertise and resource availability [22]. Certainly, general anesthesia could be avoided in adolescent patients who are cooperative and willing to undergo cardiac catheterization with local anesthesia with or without mild sedation (as in one of our patients). The median age of our patients with PH undergoing cardiac catheterization was 4 years and so few patients in our cohort were in this category. There remains an on-going discussion whether the hemodynamics obtained during cardiac catheterization with general anesthesia or sedation are reflective of the awake hemodynamics outside of the cardiac catheterization laboratory. Our review cannot answer this question, and while our approach has been to favor general anesthesia to avoid the confounding effects of hypercarbia and agitation on the hemodynamics and the interpretation, as stated above we are cognizant that cardiac catheterization can be undertaken safely with a more permissive use of local anesthesia and sedation without tracheal intubation. However, whichever approach is taken, we suggest that a key component of ensuring the safety of children with pulmonary hypertension during cardiac catheterization is discussion with the anesthesiologist before, during and after the procedure. The development of a standardized anesthetic approach encourages safety and reduces the confounding effects of different anesthetic regimens on the hemodynamics and their interpretation. In treatment naïve patients, a dose of sildenafil before the end of the procedure may reduce the pulmonary vascular lability surrounding tracheal extubation and the early recovery period. Ketamine with or without inhalation agents has been shown by others to be safe in pediatric patients with pulmonary hypertension undergoing general anesthesia [21, 22]. We routinely use ketamine with or without inhalation anesthetic for induction and maintenance of anesthesia. In addition, we have found an infusion of remifentanil helpful to maintain anesthesia with minimal hemodynamic change and rapid recovery, once the infusion is ended.

We prefer to secure additional central venous access to minimize catheter manipulation with each new testing

condition. We suggest that this approach reduces the risk of provoking an arrhythmia and shortens the study time. In contrast to previous reports, none of the patients in our series developed an arrhythmia or required cardioversion during the procedure [3, 9, 19, 22]. We monitor arterial pressure and blood gases throughout the procedure.

Two of the three patients who suffered important adverse events had heritable PAH but in the setting of advanced disease. Although heritable forms of PAH may carry a poorer prognosis and may be less responsive to therapy than IPAH [5], our numbers are too small to suggest that they have an increased risk during cardiac catheterization. It seems more likely that the baseline suprasystemic pulmonary artery pressures, right ventricular dysfunction and degree of tricuspid valve regurgitation are more indicative of the probability of a complication.

We limit the use of angiography in patients with PH to those in whom CT scan, MRI or echocardiography has failed to image important structures adequately. We do not perform routinely pulmonary artery wedge angiography to assess operability in children with congenital heart disease. We perform pulmonary artery wedge angiograms in patients with suspected pulmonary vein stenosis and selective pulmonary artery angiograms if chronic thromboembolic pulmonary hypertension is suspected from CT scan or nuclear ventilation and perfusion scans.

Study Limitations

The limitations of a retrospective analysis are present in our review. However, the data are collected concurrently with the diagnosis of pulmonary hypertension and provide useful information to caregivers and families about the risks and benefits of cardiac catheterization in this group of patients.

Conclusion

Cardiac catheterization in children with pulmonary hypertensive vascular disease was performed with a 3 % risk of important adverse events. There was no intraprocedural death and no one required cardiac massage. We found that the three patients who suffered adverse events during or after cardiac catheterization had suprasystemic pulmonary artery pressures (3/3), heritable PAH (2/3), decreased right ventricular function (3/3), and PACI <1 ml/mmHg/m^2 (3/3) and were treatment naïve (3/3). Close collaboration with pediatric anesthesia, a standardized approach with minimal catheter manipulation and the use of sildenafil before the end of the procedure may have contributed to the decreased frequency of arrhythmias and pulmonary hypertensive events. Follow-up cardiac catheterization in patients receiving specific pulmonary hypertensive targeted therapy is safe, often results in a change in management, and can be accomplished without adverse events.

References

1. Adatia I, Perry S, Landzberg M, Moore P, Thompson JE, Wessel DL (1995) Inhaled nitric oxide and hemodynamic evaluation of patients with pulmonary hypertension before transplantation. J Am Coll Cardiol 25:1656–1664
2. Adatia I, Haworth SG, Wegner M, Barst RJ, Ivy D, Stenmark KR, Karkowsky A, Rosenzweig E, Aguilar C (2013) Clinical trials in neonates and children: report of the pulmonary hypertension academic research consortium pediatric advisory committee. Pulm Circ 3:252–266
3. Beghetti M, Berger RM, Schulze-Neick I, Day RW, Pulido T, Feinstein J, Barst RJ, Humpl T, Investigators TR (2013) Diagnostic evaluation of paediatric pulmonary hypertension in current clinical practice. Eur Respir J 42:689–700
4. Carmosino MJ, Friesen RH, Doran A, Ivy DD (2007) Perioperative complications in children with pulmonary hypertension undergoing noncardiac surgery or cardiac catheterization. Anesth Analg 104:521–527
5. Chida A, Shintani M, Yagi H, Fujiwara M, Kojima Y, Sato H, Imamura S, Yokozawa M, Onodera N, Horigome H, Kobayashi T, Hatai Y, Nakayama T, Fukushima H, Nishiyama M, Doi S, Ono Y, Yasukouchi S, Ichida F, Fujimoto K, Ohtsuki S, Teshima H, Kawano T, Nomura Y, Gu H, Ishiwata T, Furutani Y, Inai K, Saji T, Matsuoka R, Nonoyama S, Nakanishi T (2012) Outcomes of childhood pulmonary arterial hypertension in BMPR2 and ALK1 mutation carriers. Am J Cardiol 110:586–593
6. del Cerro MJ, Abman S, Diaz G, Freudenthal AH, Freudenthal F, Harikrishnan S, Haworth SG, Ivy D, Lopes AA, Raj JU, Sandoval J, Stenmark K, Adatia I (2011) A consensus approach to the classification of pediatric pulmonary hypertensive vascular disease: report from the PVRI pediatric taskforce, Panama 2011. Pulm Circ 1:286–298
7. Douwes JM, Roofthooft MT, Bartelds B, Talsma MD, Hillege HL, Berger RM (2013) Pulsatile haemodynamic parameters are predictors of survival in paediatric pulmonary arterial hypertension. Int J Cardiol 168:1370–1377
8. Guo L, Cui Y, Pharis S, Walsh M, Atallah J, Tan MW, Rutledge J, Coe JY, Adatia I (2014) Measurement of oxygen consumption in children undergoing cardiac catheterization: comparison between mass spectrometry and the breath-by-breath method. Pediatr Cardiol 35:798–802
9. Hill KD, Lim DS, Everett AD, Ivy DD, Moore JD (2010) Assessment of pulmonary hypertension in the pediatric catheterization laboratory: current insights from the Magic registry. Catheter Cardiovasc Interv 76:865–873
10. Ivy DD, Abman SH, Barst RJ, Berger RM, Bonnet D, Fleming TR, Haworth SG, Raj JU, Rosenzweig EB, Schulze Neick I, Steinhorn RH, Beghetti M (2013) Pediatric pulmonary hypertension. J Am Coll Cardiol 62:D117–D126

11. Kulik T, Mullen M, Adatia I (2009) Pulmonary arterial hypertension associated with congenital heart disease. Prog Pediatr Cardiol 27:25–33

12. Lin CH, Hegde S, Marshall AC, Porras D, Gauvreau K, Balzer DT, Beekman RH 3rd, Torres A, Vincent JA, Moore JW, Holzer R, Armsby L, Bergersen L (2014) Incidence and management of life-threatening adverse events during cardiac catheterization for congenital heart disease. Pediatr Cardiol 35:140–148

13. Moledina S, Hislop AA, Foster H, Schulze-Neick I, Haworth SG (2010) Childhood idiopathic pulmonary arterial hypertension: a national cohort study. Heart (British Cardiac Society) 96:1401–1406

14. Nafiu OO, Voepel-Lewis T, Morris M, Chimbira WT, Malviya S, Reynolds PI, Tremper KK (2009) How do pediatric anesthesiologists define intraoperative hypotension? Paediatr Anaesth 19:1048–1053

15. Palmer SM, Robinson LJ, Wang A, Gossage JR, Bashore T, Tapson VF (1998) Massive pulmonary edema after prostacyclin infusion in a patient with pulmonary veno-occlusive disease. Chest 113:237–240

16. Sajan I, Manlhiot C, Reyes J, McCrindle BW, Humpl T, Friedberg MK (2011) Pulmonary arterial capacitance in children with idiopathic pulmonary arterial hypertension and pulmonary arterial hypertension associated with congenital heart disease: relation to pulmonary vascular resistance, exercise capacity, and survival. Am Heart J 162:562–568

17. Sitbon O, Humbert M, Jais X, Ioos V, Hamid AM, Provencher S, Garcia G, Parent F, Herve P, Simonneau G (2005) Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. Circulation 111:3105–3111

18. Sury MR, William Broadhead M (2009) Hypotension during anesthesia before surgery. Paediatr Anaesth 19:1037–1040

19. Taylor CJ, Derrick G, McEwan A, Haworth SG, Sury MR (2007) Risk of cardiac catheterization under anaesthesia in children with pulmonary hypertension. Br J Anaesth 98:657–661

20. van Loon RL, Roofthooft MT, Hillege HL, ten Harkel ADJ, van Osch-Gevers M, Delhaas T, Kapusta L, Strengers JL, Rammeloo L, Clur SAB, Mulder BJ, Berger RMF (2011) Pediatric pulmonary hypertension in the Netherlands. Epidemiology and characterization during the period 1991 to 2005. Circulation 124:1755–1764

21. Williams GD, Philip BM, Chu LF, Boltz MG, Kamra K, Terwey H, Hammer GB, Perry SB, Feinstein JA, Ramamoorthy C (2007) Ketamine does not increase pulmonary vascular resistance in children with pulmonary hypertension undergoing sevoflurane anesthesia and spontaneous ventilation. Anesth Analg 105:1578–1584

22. Williams GD, Maan H, Ramamoorthy C, Kamra K, Bratton SL, Bair E, Kuan CC, Hammer GB, Feinstein JA (2010) Perioperative complications in children with pulmonary hypertension undergoing general anesthesia with ketamine. Paediatr Anaesth 20:28–37