Safety and Outcomes of Transcatheter Closure of Patent Ductus Arteriosus

in Children With Pulmonary Artery Hypertension

Arash Salavitabar, MD
Usha S. Krishnan, MD
Mariel E. Turner, MD
Julie A. Vincent, MD
Alejandro J. Torres, MD
Matthew A. Crystal, MD

To investigate whether transcatheter device closure of patent ductus arteriosus (PDA) is safe in children with pulmonary artery hypertension, we retrospectively analyzed our experience with 33 patients who underwent the procedure from January 2000 through August 2015.

Pulmonary artery hypertension was defined as a pulmonary vascular resistance index (PVRI) >3 WU · m². All 33 children (median age, 14.5 mo; median weight, 8.1 kg) underwent successful closure device implantation and were followed up for a median of 17.2 months (interquartile range [IQR], 1.0–63.4 mo). During catheterization, the median PVRI was 4.1 WU · m² (IQR, 3.6–5.3 WU · m²), and the median mean pulmonary artery pressure was 38.0 mmHg (IQR, 25.5–46.0 mmHg). Premature birth was associated with pulmonary vasodilator therapy at time of PDA closure (P=0.001) but not with baseline PVRI (P=0.986). Three patients (9.1%) had device-related complications (one immediate embolization and 2 malpositions). Two of these complications involved embolization coils. Baseline pulmonary vasodilator therapy before closure was significantly associated with intensive care unit admission after closure (10/12 [83.3%] with baseline therapy vs 3/21 [14.3%] without; P <0.001). Of 11 patients receiving pulmonary vasodilators before closure and having a device in place long-term, 8 (72.7%) were weaned after closure (median, 24.0 mo [IQR, 11.0–25.0 mo]).

We conclude that transcatheter PDA closure can be performed safely in many children with pulmonary artery hypertension and improve symptoms, particularly in patients born prematurely. Risk factors for adverse outcomes are multifactorial, including coil use and disease severity. Multicenter studies in larger patient populations are warranted. **(Tex Heart Inst J 2020;47(4):250-7)**

From: Division of Pediatric Cardiology, Department of Pediatrics, New York-Presbyterian Morgan Stanley Children's Hospital, Columbia University Irving Medical Center, New York, New York, 10032

Dr. Salavitabar is now at the University of Michigan Congenital Heart Center at C.S. Mott Children's Hospital, Ann Arbor, Michigan.

Address for reprints:
Matthew A. Crystal, MD, Division of Pediatric Cardiology, Department of Pediatrics, New York-Presbyterian Morgan Stanley Children's Hospital, Columbia University Irving Medical Center, 3959 Broadway, CHN2-253, New York, NY 10032

E-mail: mac2376@ cumc.columbia.edu

The natural history of patent ductus arteriosus (PDA) is well known,[1,2] and transcatheter closure of PDA in children has been well described.[1,3,4] Despite inherent risks, such as device malposition or embolization,[5] transcatheter PDA closure compares favorably with surgical PDA closure; it is associated with similar complication rates but lower costs and shorter hospital stays.[6,7]

One dilemma is how to treat PDA in patients with pulmonary artery hypertension (PAH), given the associated risks of PAH crisis and device-related complications. Most studies of PDA closure in patients with PAH have included adults.[8-18] Pediatric studies have generally involved small patient populations, and varying hemodynamic criteria for diagnosing PAH have been used, most often pulmonary artery pressure (PAP) rather than the PVRI.[8,10,11,13-15,18] The high levels of PAP associated with unrestrictive ductal shunting do not necessarily reflect the high pulmonary vascular resistance associated with pulmonary vascular disease. Moreover, relying on echocardiographic evidence of elevated PAP, including bidirectional shunting through the PDA, to diagnose PAH may miss cases of PAH that would otherwise be diagnosed by cardiac catheterization.[11,19-24] Overall, however, studies of PDA closure in children with PAH have shown relatively positive outcomes and low complication rates.

To evaluate the safety and outcomes of transcatheter PDA closure in children with PAH, we retrospectively examined our center's experience. We also used pulmonary vascular resistance criteria, with or without prior vasodilator therapy, as the basis for diagnosing PAH.

Patients and Methods

We retrospectively identified all patients ≤18 years of age with PDA and PAH who underwent transcatheter closure of the PDA at our center from January 2000 through August 2015. Data were collected by searching our Pediatric Cardiac Catheterization Database for the records of all patients who met the study criteria. All medical records and catheterization reports for qualifying patients were reviewed in accordance with a protocol approved by our Institutional Review Board.

Pulmonary artery hypertension was defined as a PVRI >3 Wood units (WU) · m², according to the 2015 Pediatric Pulmonary Hypertension Guidelines from the American Heart Association (AHA) and American Thoracic Society (ATS).[25] Transcatheter device closure was defined as release of a device in an attempt to close a PDA. Hemodynamic data, medical records, and subsequent catheterizations were reviewed in detail.

We excluded patients older than 18 years, as well as those who had complex congenital heart disease, those whose charts lacked sufficient hemodynamic data to calculate PVRI at the time of PDA closure, and those who did not undergo transcatheter PDA closure.

On the basis of clinical assessment and published recommendations,[26,27] the primary cardiologist in each case decided whether to refer a patient for cardiac catheterization to determine the feasibility of transcatheter device closure, and likewise to refer a patient for recatheterization postoperatively for vasodilator testing when indicated. The decision to attempt transcatheter closure was made at the discretion of the patient's interventional cardiologist on the basis of anatomic variables and hemodynamic measurements calculated according to the Fick principle.

Contraindications to transcatheter closure in patients who underwent diagnostic hemodynamic cardiac catheterization were as follows: a pulmonary-to-systemic vascular resistance ratio of >0.5:1, lack of vasoresponsiveness or decrease in PAP after test occlusion of the PDA, baseline right-to-left or bidirectional shunting across the PDA, and prior evidence of substantial right-to-left shunting as evidenced by clinically substantial pre- and postductal saturation gradients.

The primary outcomes were device-related complications (device embolization or malposition) and death. Secondary outcomes were recatheterization, changes in pulmonary vasodilator and diuretic medications, and readmission after PDA closure for reasons related to PAH.

Demographic variables included sex, weight, age, premature birth (at gestational age <37 wk), and genetic diagnosis of trisomy 21. Anatomic variables included PDA type (types A–E)[28] and minimum PDA diameter. Details of evaluation during catheterization included baseline hemodynamics, angiographic measurement of the PDA, and responses to pulmonary vasodilator testing (defined as a decrease of ≥20% in mean PAP [mPAP] or PVRI after administration of 100% FiO_2, 80 ppm of inhaled nitric oxide, or both)[29] and balloon occlusion testing of the PDA.

Data were analyzed with use of Stata software, version 14 (StataCorp). Clinical and demographic variables were presented as standard summary statistics. Continuous variables were presented as mean ± SD or as median and interquartile range (IQR). Categorical variables were presented as number and percentage. Univariable analyses were performed by using the Student t test or Wilcoxon rank-sum test for continuous variables and the χ^2 test or Fisher exact test for categorical variables. A P value <0.05 was considered statistically significant.

Results

A total of 682 patients with a diagnosis code for PDA underwent a total of 780 cardiac catheterizations for PDA closure in our hospital's pediatric cardiac catheterization laboratory. Of these, 33 patients met the study inclusion criteria (Fig. 1; Table I). Sixteen patients (48.5%) had been born prematurely (mean gestational age at birth, 27.9 ± 4.1 wk), 2 of whom had a device-related complication and one of whom died of a non–device-related complication after transcatheter PDA closure.

At baseline, 12 patients (36.4%) were receiving at least one pulmonary vasodilator (usually oral sildenafil), including 4 patients receiving multiple agents and 2 patients receiving inhaled nitric oxide (one was also receiving iloprost). Six patients (18%) were admitted to
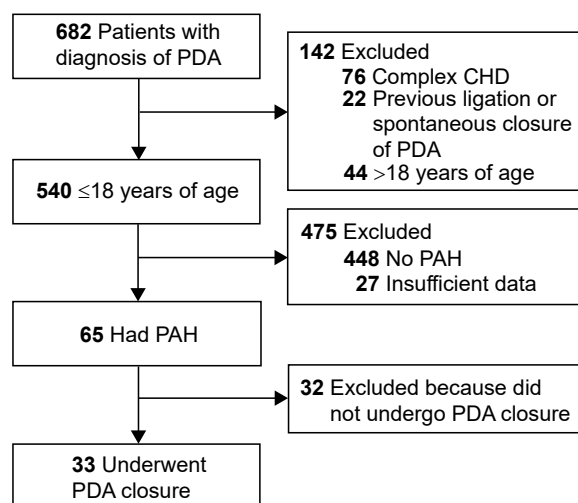

Fig. 1 *Flow chart shows selection of patients included in the study.*

CHD = congenital heart disease; PAH = pulmonary artery hypertension; PDA = patent ductus arteriosus

the intensive care unit (ICU) before device closure, 4 of whom had respiratory insufficiency or failure.

Catheterization Data

The median PVRI was 4.1 WU · m² (IQR, 3.6–5.3 WU · m²) (Table II); the highest PVRI among individual patients was 11.1 WU · m². The median PVRI was similar between patients who had been born prematurely (4.2 WU · m² [IQR, 3.6–5.1 WU · m²]) and those born full-term (4.1 WU · m² [IQR, 3.4–6.7 WU · m²]) (*P*=0.986). Seven patients (21.2%) underwent pulmonary vasodilator testing, 6 of whom had a marked clinical response in either mPAP or PVRI. Four patients underwent balloon occlusion testing of the PDA and showed a median improvement in mPAP of 33.9% (IQR, 18.0%–47.6%). Of the 4 patients who

TABLE I. Baseline Demographic and Clinical Characteristics of the 33 Patients

Variable	Value
Female	20 (60.6)
Weight (kg)	8.1 (5.7–11.0)
Age (mo)	14.5 (8.8–23.8)
Premature birth*	16 (48.5)
Trisomy 21	5 (15.2)
Pulmonary vasodilator therapy	12 (36.4)
Diuretics use	15 (45.5)
Underlying BPD or CLD	2 (6.1)

BPD = bronchopulmonary dysplasia; CLD = chronic lung disease

*Gestational age <37 weeks

Data are presented as number and percentage or as median and interquartile range.

TABLE II. Hemodynamic Characteristics of the 33 Patients During Catheterization

Variable	Median (IQR)
Qp/Qs ratio	1.5 (1.2–1.8)
Systolic PAP (mmHg)	49.0 (36.0–61.0)
Mean PAP (mmHg)	38.0 (25.5–46.0)
Systolic PAP/systolic AoP (%)	61.6 (45.2–77.1)
PVRI (WU · m²)	4.1 (3.6–5.3)
PVR/SVR	0.32 (0.22–0.37)
Cardiac index (L/min/m²)	3.5 (3.2–4.1)

AoP = aortic pressure; IQR = interquartile range; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; PVRI = pulmonary vascular resistance index; Qp = pulmonary flow; Qs = systemic flow; SVR = systemic vascular resistance

had a device-related complication or died, only one (Patient 4) underwent acute pulmonary vasodilator testing, and none underwent balloon occlusion testing. The median improvement in mPAP immediately after device closure was 24.7% (IQR, 8.5%–35.3%).

The predominant PDA type, according to the Krichenko classification,[28] was type A (16 patients, 48.5%) (Table III). The median minimum ductal diameter was 2.6 mm (IQR, 2.2–4.0 mm). The most frequently used closure device was the Amplatzer Duct Occluder type I (Abbott) (n=17 [51.5%]), followed by embolization coils (n=9 [27.3%]) (Table IV). The time period (or era) in which the procedure was performed had a clear effect on device choice, with a notable decrease over time in the number of PDA closures performed with embolization coils (Fig. 2).

Procedural Outcomes

All 33 patients left the catheterization laboratory with a PDA closure device in place. The median time to last follow-up was 17.2 months (IQR, 1.0–63.4 mo). Three patients (9.1%) had a device-related complication (Table V). Two device-related complications involved embolization or malposition of a coil immediately after release, resulting in a coil-related complication rate of 22.2% (2 of 9 coils placed); in each case, the coil was retrieved and replaced during the same catheterization. The third device-related complication involved a device found to be malpositioned 3 weeks after implantation. One patient (3.0%) experienced a cardiac arrest (likely due to PAH crisis) 4 days after device implantation and died 6 months later of a cardiac arrest secondary to chronic respiratory failure. Of note, this patient had a large PDA and showed signs of high-output failure from left-to-right shunting before transcatheter closure. The median PVRI in our study population was similar between patients who had a device-related complication or died (4.1 WU · m² [IQR, 3.8–4.1 WU · m²]) and those who did not (4.2 WU · m² [IQR, 3.6–5.3 WU · m²]) (*P*=0.294).

The 2 patients who had the most severe adverse events related to PDA device closure (Patients 2 and 3; Table V)

TABLE III. Frequency of Patent Ductus Arteriosus by Krichenko Classification

Type	No. (%)*
A	16 (48.5)
B	2 (6.1)
C	4 (12.1)
D	5 (15.2)
E	5 (15.2)

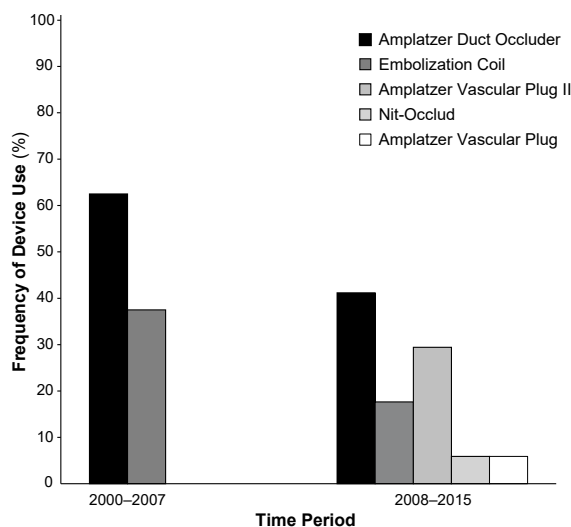*One patient had unknown ductal morphology and was not included in the frequency counts.

Fig. 2 *Graph shows frequency of device use in the study population by time period, with a notable decrease in use of embolization coils over time.*

TABLE IV. Devices Used for Transcatheter PDA Closure in the 33 Patients

Device	No. (%)
Amplatzer Duct Occluder*	17 (51.5)
Embolization coil	9 (27.3)
Amplatzer Vascular Plug II*	5 (15.2)
Nit-Occlud PDA**	1 (3)
Amplatzer Vascular Plug*	1 (3)

PDA = patent ductus arteriosus

 * Abbott
** PFM Medical

had also been admitted to the ICU before device closure. Patient 2 needed endotracheal intubation and milrinone infusion in the ICU before device closure. Thirteen patients (39.4%) were admitted to the ICU after closure for a median stay of 3.5 days (IQR, 1.0–5.3 d), most often for close monitoring without further changes in therapy. Patients receiving baseline pulmonary vasodilator therapy before closure were more often admitted to the ICU afterward (10/12; 83.3%) than were patients not receiving such therapy (3/21; 14.3%) (P <0.001).

Eight patients were referred for recatheterization during the postprocedural follow-up period. One needed stent implantation to treat pulmonary vein stenosis, and another needed confirmation of device malposition into the aorta (Patient 2, Table V). The remaining 6 patients needed recatheterization primarily for pulmonary vasodilator testing, which was first performed a median of 16 months (IQR, 11.8–20.3 mo) after device placement. At the time of their most recent recatheterization (a median of 28.5 months [IQR, 15.8–39.8 mo] after device placement), these 6 patients showed clinically relevant, but not statistically significant improvement in median mPAP from 37.5 mmHg (IQR, 28.5–50.3 mmHg) at baseline to 24.0 mmHg (IQR, 22.3–25.0 mmHg) (P=0.074); they showed no statistically significant change in median PVRI from baseline (5.0 WU · m² [IQR, 4.1–8.1 WU · m²]) to the time of their most recent recatheterization (5.2 WU · m² [IQR, 4.6–5.3 WU · m²]) (P=0.593).

Clinical Outcomes

Of the 12 patients who were receiving pulmonary vasodilator therapy before device closure, 10 had an uncomplicated closure, and 11 ultimately had a device in place for the long term (excluding Patient 2, who eventually underwent surgical closure). Eight of the 11 patients (72.7%) had their vasodilator dose, number of medications, or both decreased at a median time of 7 months (IQR, 3.6–8.5 mo) or were completely weaned from therapy by a median time of 24.0 months (IQR, 11.0–25.0 mo) after closure. Premature birth was significantly associated with pulmonary vasodilator therapy at the time of PDA closure: 11 of 16 patients (68.8%) born prematurely compared with 1 of 17 patients (5.9%) born full-term (P=0.001). All 8 patients who were weaned from pulmonary vasodilator therapy after closure had been born prematurely. Of the 15 patients receiving diuretic medications before closure, 11 (73%) had the dosing frequency decreased or were weaned from therapy during the study period.

Only one patient needed readmission, for exacerbation of PAH, 4.5 months after PDA closure. The patient was transferred to our institution after a cardiopulmonary arrest that followed surgical repair of an incarcerated hernia. Initial treatment with inhaled nitric oxide, iloprost, milrinone, and sildenafil was later changed to subcutaneous treprostinil. By study's end, this patient had been weaned from all medications, and his hemodynamic status was normal.

Discussion

To our knowledge, this is the first evaluation of transcatheter PDA closure in a pediatric population in which the primary inclusion criterion was PVRI >3 WU · m², as established by the 2015 AHA/ATS Guidelines for Pediatric Pulmonary Hypertension.[25] We contend that PVRI is more specific than PAP for identifying patients who have true pulmonary vascular disease and are therefore at risk for adverse outcomes of PDA closure.

Our results indicate that transcatheter PDA closure is safe. A closure device was successfully implanted in all patients, and only 2 (6.1%) had acute procedural complications (device embolization or malposition upon release). That the 2 patients with the most severe device-related adverse events had needed ICU admis-

TABLE V. Clinical Characteristics of the 4 Patients Who Had Device-Related Complications or Died

Variable	Patient 1	Patient 2	Patient 3	Patient 4
Age (mo) at baseline, sex	14, F	14, F	10, F	13, M
Weight (kg) at baseline	10	5.3	5.7	8
Premature birth (<37 wk)	No	Yes (35 wk)	Yes (26 wk)	Yes (24 wk)
Diagnosis	Asymptomatic moderate PDA, left-sided heart dilation	Small-to-moderate VSD, large PDA	CLD, restrictive VSD, moderate PDA	PDA
ICU admission before catheterization	No	Yes (H1N1 influenza–related ARDS, endotracheal intubation)	Yes (respiratory distress, aspiration pneumonia, CHF)	No
Pulmonary vasodilators before catheterization	No	Inhaled nitric oxide, then sildenafil	No	Sildenafil, bosentan
Krichenko PDA classification	A	B	D	E
Minimum PDA diameter (mm)	2.2	6	3.7	2
Hemodynamics at baseline				
Qp/Qs ratio	1.6	1.7	0.8	1
PVRI (WU · m^2)	3.2	4.3	4	4.1
Systolic PAP (mmHg)	38	55	60	30
Mean PAP (mmHg)	29	48	46	22
Systolic PAP, % systemic	40	77	88	37
Device	Embolization coil	Amplatzer Duct Occluder	Amplatzer Vascular Plug II	Embolization coil
Adverse event	Immediate embolization to LPA	Malposition of device into aorta 3 wk after closure with substantial residual shunting and failed extubation	Bradycardic arrest (× 2) 4 d after catheterization in presence of *Pseudomonas* tracheitis (received inhaled nitric oxide, sildenafil, and bosentan after PDA closure) Bradycardic arrest 6 mo after catheterization, secondary to chronic respiratory failure	Malposition of coil into aorta
Outcome	Successful coil retrieval; replacement with 2 embolization coils	Surgical device removal; surgical closure of PDA and VSD	Death	Successful coil retrieval; replacement with Amplatzer Vascular Plug II
Recatheterization	No	Yes (3 wk after PDA closure, to confirm device malposition in aorta)	No	No

ARDS = acute respiratory distress syndrome; CHF = congestive heart failure; CLD = chronic lung disease; F = female; ICU = intensive care unit; LPA = left pulmonary artery; M = male; PAH = pulmonary artery hypertension; PAP = pulmonary artery pressure; PDA = patent ductus arteriosus; PVRI = pulmonary vascular resistance index; VSD = ventricular septal defect

sion before the procedure makes it reasonable to assume that the severity of PAH at presentation is a potential risk factor because the procedure acutely alters hemodynamics. Embolization coils were involved in both cases (a coil-specific complication rate of 22.2%); therefore, device choice was likely a major contributor to the overall rate of adverse events. Nonetheless, the coils were easily retrieved and replaced without further problems. As in most centers, coils were used relatively frequently at our hospital in the first half of our study period and less frequently in the second half when newer technologies became available. The Amplatzer Duct Occluder was used in our patient population as frequently as in other studies; notably, however, those studies also reported frequent use of the Amplatzer Muscular VSD Occluder (Abbott) to treat PDAs with large ductal diameters.[8,10,11,13,14,17,18]

The distribution of PDAs by morphologic classification in our patient population was similar to that in other studies, although the 49% prevalence of classic type A PDA in our study was relatively lower than the 60% to 80% prevalence reported by others in similar populations.[9,12,14,17,18]

Several previous studies incorporated PVRI data into confirming the presence of severe PAH.[9-12,16,18] However, almost all of those studies included adult patients, limited inclusion to patients with large, unrestrictive PDAs, or both. Although the PVRI inclusion criterion in our study successfully identified patients with true pulmonary vascular disease, the baseline PVRI value was not significantly higher in patients who had device-related complications than in those who did not. This analysis was limited by the small population size inherent to this disease; however, the results indicate that risk factors for complications within this population are multifactorial.

One dilemma interventionists face is how best to determine which patients are at high risk for complications beyond what clinical data the care team has provided. Acute pulmonary vasodilator testing has been well described in patients with PAH undergoing evaluation for PDA device closure,[10,12,15,16,18,30] and balloon occlusion testing of PDA has been used in previous studies, either as part of an institutional protocol or simply in selected patients.[8-11,13,14,17,18] At our institution, the interventionist decides whether to perform these tests at the time of device placement. Nearly all the patients in our cohort who underwent acute pulmonary vasodilator testing responded, and those who underwent balloon occlusion testing showed an overall improvement in mPAP in response. Although not analyzed within the scope of this study, the severity of pulmonary vascular disease was included in our individualized risk stratification process and was strongly considered in deciding whether to implant a device in patients who underwent hemodynamic testing without device closure.

As in previous studies,[10-13,16,17] most of our patients showed clinical improvement during the study period. Few investigators have reported baseline use of pulmonary vasodilators before device closure. Niu and colleagues[11] described baseline use of pulmonary vasodilators in 5 of 6 patients who eventually underwent transcatheter PDA device closure; 2 of them were given multiple agents, including inhaled nitric oxide. Similarly, our center often uses pulmonary vasodilator therapy to attenuate pulmonary vasoreactivity before procedures that can exacerbate PAH; however, this therapy is individualized. Many patients in our study underwent recatheterization, as is our institution's practice, to help manage pulmonary hypertension therapy as the treatment team decides. Nearly 75% of our patients who were receiving baseline pulmonary vasodilator therapy were weaned from or had their medications discontinued within several months of device closure, indicating a clinically important improvement in the status of their PAH. This was particularly true of patients born prematurely, who constituted all who were weaned from pulmonary vasodilator therapy.

As a result of this study, our institution has standardized its approach to patients with coexisting PDA and PAH. Our inpatient nursing team charts pre- and postductal saturations for 7 to 10 days, paying special attention during activities that can cause stress or Valsalva maneuvers (for example, stooling, bathing, and suction). Similar monitoring is performed during outpatient visits. If there is no substantial postductal desaturation and if the PDA shunts mostly left-to-right and is considered severe enough to warrant closure, the child is referred for catheterization and possible PDA closure. We now routinely perform acute pulmonary vasodilator or balloon occlusion testing (or both) in children with a PDA and a PVRI >3 WU · m². If the patient responds to testing, meets other indications for PDA closure, and has a favorable ductal anatomy, we proceed with device closure.

When substantial right-to-left shunting or a preductal-to-postductal saturation gradient is noted, any associated ventilatory factors are optimized; risks associated with gastroesophageal reflux, infection, and atelectasis are minimized; and targeted therapy including phosphodiesterase inhibitors, endothelin receptor antagonists, or both is initiated. If the right-to-left shunting improves or resolves, the patient can be referred for transcatheter PDA closure. Delayed response to acute pulmonary vasodilator testing is now a contraindication for PDA closure, although closure may be reconsidered after prolonged therapy.

Limitations

Our study has limitations. First, it was retrospective, which precluded our determining any causal relationships between patient characteristics, catheterization data, or practice variation and outcomes of PDA closure

in children with PAH. Second, because this study was not designed as an intention-to-treat analysis, we cannot recommend a general approach to patients with coexisting PDA and PAH, but can only comment on our particular approach to those patients that our care team deemed clinically amenable to PDA closure. Therefore, this study cannot be used to determine the safest PVRI at which device closure can be attempted. Last, given the relative infrequency of children with true pulmonary vascular disease and a PDA, as well as complications associated with PDA closure, our ability to find significance in the statistical analyses was limited.

Conclusion

Transcatheter PDA closure can be performed safely and successfully in certain children with PAH, and it can improve PAH symptoms over time, particularly in patients born prematurely. Acute respiratory illness and severity of presentation should be considered before attempting device implantation because these factors can increase the risk of adverse hemodynamic effects. Acute pulmonary vasodilator and balloon occlusion testing can be used effectively to triage high-risk patients who can be treated medically and reevaluated at a future date. Choosing an appropriate device can help to mitigate embolization risks, taking into consideration the rate of embolization or malposition when using coils and the interim advances in device technology. Multicenter studies with larger patient populations are needed to overcome the inherent limitations of a single-center study.

References

1. Schneider DJ, Moore JW. Patent ductus arteriosus. Circulation 2006;114(17):1873-82.
2. Moore P, Brook MM. Patent ductus arteriosus and aortopulmonary window. In: Allen HD, Driscoll DJ, Shaddy RE, Feltes TF, editors. Moss and Adams' heart disease in infants, children, and adolescents: including the fetus and young adult. 8th ed. Philadelphia: Lippincott Williams & Wilkins; 2013. p. 722-45.
3. Backes CH, Rivera BK, Bridge JA, Armstrong AK, Boe BA, Berman DP, et al. Percutaneous patent ductus arteriosus (PDA) closure during infancy: a meta-analysis. Pediatrics 2017;139(2):e20162927.
4. Al-Hamash SM, Wahab HA, Khalid ZH, Nasser IV. Transcatheter closure of patent ductus arteriosus using ADO device: retrospective study of 149 patients. Heart Views 2012;13(1):1-6.
5. Ewert P. Challenges encountered during closure of patent ductus arteriosus. Pediatr Cardiol 2005;26(3):224-9.
6. Wang K, Pan X, Tang Q, Pang Y. Catheterization therapy vs surgical closure in pediatric patients with patent ductus arteriosus: a meta-analysis. Clin Cardiol 2014;37(3):188-94.
7. Prieto LR, DeCamillo DM, Konrad DJ, Scalet-Longworth L, Latson LA. Comparison of cost and clinical outcome between transcatheter coil occlusion and surgical

8. closure of isolated patent ductus arteriosus. Pediatrics 1998;101(6):1020-4.
8. Vijayalakshmi IB, Setty N, Narasimhan C, Singla V, Manjunath CN. Percutaneous device closure of patent ductus arteriosus with pulmonary artery hypertension: long-term results. J Interv Cardiol 2014;27(6):563-9.
9. Ji Q, Feng J, Mei Y, Wang X, Cai J, Sun Y, et al. Transcatheter closure of adult patent ductus arteriosus with severe pulmonary hypertension. Hypertens Res 2008;31(11):1997-2002.
10. Sadiq M, Rehman AU, Hyder N, Qureshi AU, Kazmi T, Qureshi SA. Intermediate- and long-term follow up of device closure of patent arterial duct with severe pulmonary hypertension: factors predicting outcome. Cardiol Young 2017;27(1):26-36.
11. Niu MC, Mallory GB, Justino H, Ruiz FE, Petit CJ. Treatment of severe pulmonary hypertension in the setting of the large patent ductus arteriosus. Pediatrics 2013;131(5):e1643-9.
12. Yan C, Zhao S, Jiang S, Xu Z, Huang L, Zheng H, et al. Transcatheter closure of patent ductus arteriosus with severe pulmonary arterial hypertension in adults. Heart 2007;93(4):514-8.
13. Bhalgat PS, Pinto R, Dalvi BV. Transcatheter closure of large patent ductus arteriosus with severe pulmonary arterial hypertension: short and intermediate term results. Ann Pediatr Cardiol 2012;5(2):135-40.
14. Thanopoulos BD, Tsaousis GS, Djukic M, Al Hakim F, Eleftherakis NG, Simeunovic SD. Transcatheter closure of high pulmonary artery pressure persistent ductus arteriosus with the Amplatzer muscular ventricular septal defect occluder. Heart 2002;87(3):260-3.
15. Khositseth A, Wanitkun S. Patent ductus arteriosus associated with pulmonary hypertension and desaturation. Cardiol J 2012;19(5):543-6.
16. Froehle M, Haas NA, Sandica E, Happel C, Laser KT. Percutaneous closure of a gigantic patent ductus arteriosus (PDA) with pulmonary hypertension with an atrial septal defect occluder in a 35-year-old woman. Clin Res Cardiol 2014;103(4):319-23.
17. Hokanson JS, Gimelli G, Bass JL. Percutaneous closure of a large PDA in a 35-year-old man with elevated pulmonary vascular resistance. Congenit Heart Dis 2008;3(2):149-54.
18. Zabal C, Garcia-Montes JA, Buendia-Hernandez A, Calderon-Colmenero J, Patino-Bahena E, Juanico-Enriquez A, Attie F. Percutaneous closure of hypertensive ductus arteriosus. Heart 2010;96(8):625-9.
19. D'Alto M, Romeo E, Argiento P, D'Andrea A, Vanderpool R, Correra A, et al. Accuracy and precision of echocardiography versus right heart catheterization for the assessment of pulmonary hypertension. Int J Cardiol 2013;168(4):4058-62.
20. Lafitte S, Pillois X, Reant P, Picard F, Arsac F, Dijos M, et al. Estimation of pulmonary pressures and diagnosis of pulmonary hypertension by Doppler echocardiography: a retrospective comparison of routine echocardiography and invasive hemodynamics. J Am Soc Echocardiogr 2013;26(5):457-63.
21. Greiner S, Jud A, Aurich M, Hess A, Hilbel T, Hardt S, et al. Reliability of noninvasive assessment of systolic pulmonary artery pressure by Doppler echocardiography compared to right heart catheterization: analysis in a large patient population. J Am Heart Assoc 2014;3(4):e001103.
22. Janda S, Shahidi N, Gin K, Swiston J. Diagnostic accuracy of echocardiography for pulmonary hypertension: a systematic review and meta-analysis [published erratum appears in Heart 2011;97(13):1112]. Heart 2011;97(8):612-22.

23. Farber HW, Foreman AJ, Miller DP, McGoon MD. REVEAL Registry: correlation of right heart catheterization and echocardiography in patients with pulmonary arterial hypertension. Congest Heart Fail 2011;17(2):56-64.

24. Groh GK, Levy PT, Holland MR, Murphy JJ, Sekarski TJ, Myers CL, et al. Doppler echocardiography inaccurately estimates right ventricular pressure in children with elevated right heart pressure. J Am Soc Echocardiogr 2014;27(2): 163-71.

25. Abman SH, Hansmann G, Archer SL, Ivy DD, Adatia I, Chung WK, et al. Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic Society. Circulation 2015;132(21): 2037-99.

26. Allen HD, Beekman RH 3rd, Garson A Jr, Hijazi ZM, Mullins C, O'Laughlin MP, Taubert KA. Pediatric therapeutic cardiac catheterization: a statement for healthcare professionals from the Council on Cardiovascular Disease in the Young, American Heart Association [published erratum appears in Circulation 1998;97(23):2375]. Circulation 1998;97(6):609-25.

27. Feltes TF, Bacha E, Beekman RH 3rd, Cheatham JP, Feinstein JA, Gomes AS, et al. Indications for cardiac catheterization and intervention in pediatric cardiac disease: a scientific statement from the American Heart Association. Circulation 2011;123(22):2607-52.

28. Krichenko A, Benson LN, Burrows P, Moes CA, McLaughlin P, Freedom RM. Angiographic classification of the isolated, persistently patent ductus arteriosus and implications for percutaneous catheter occlusion. Am J Cardiol 1989(12);63:877-80.

29. Rich S, Kaufmann E, Levy PS. The effect of high doses of calcium-channel blockers on survival in primary pulmonary hypertension. N Engl J Med 1992;327(2):76-81.

30. McLaughlin VV, Archer SL, Badesch DB, Barst RJ, Farber HW, Lindner JR, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. J Am Coll Cardiol 2009;53(17):1573-619.