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ORIGINAL STUDIES

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Early experience with the Micro Plug Set for preterm patent ductus arteriosus closure

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Abstract

Objectives: We intend to describe early experience using a new, commercially available Micro Plug Set for preterm neonate and infant transcatheter patent ductus arteriosus (PDA) occlusion.

Background: Transcatheter PDA occlusion in premature neonates and small infants is safe and effective. The procedure is early in its evolution.

Methods: Procedural and short-term outcomes of preterm neonates and infants undergoing transcatheter PDA occlusion with a new, commercially available device were reviewed.

Results: Eight preterm neonates and infants born at median 27 weeks gestation (23–36 weeks) underwent transcatheter PDA device closure with the Micro Plug Set. The device is short (2.5 mm) with a range of diameters (3, 4, 5, 6 mm) and delivered through a microcatheter. Procedures were performed at median 41 days of age (12–88 days) and at 1690 g (760–3,310 g). Transvenous PDA device occlusion was performed with fluoroscopic and echocardiography guidance. All procedures were successful with complete PDA occlusion. There were no procedural or short-term adverse events.

Conclusions: Preterm neonate and infant transcatheter PDA device closure with a new, commercially available short and microcatheter delivered device (Micro Plug Set) was safe and effective in a small, early series of patients.

KEYWORDS

cardiac catheterization, congenital heart disease, patent ductus arteriosus, premature neonate, preterm infant, vascular occlusion

1 | INTRODUCTION

Hemodynamically significant persistent patent ductus arteriosus (PDA) is a common diagnosis among preterm infants that can complicate their postnatal course. Medical, surgical, or transcatheter ductal closure improves outcomes and simplifies clinical management. Transcatheter management is becoming an increasingly accepted practice that has been proven safe and effective.[1-15]

Similar to transcatheter management of older PDA patients[16] and other structural heart lesions (atrial septal defect, transcatheter pulmonary valve, transcatheter aortic valve replacement), there is rapid device evolution early in clinical translation.[17-19] Early on, devices traditionally used for transcatheter PDA device closure in older patients were adapted for use in preterm infants, such as, detachable coils,[1-4] Amplatzer Vascular Plugs (AVPII, *Abbott*, Santa Clara, CA)[6,7] and Amplatzer duct occluders (ADO I, ADO II, *Abbott*, Santa Clara, CA).[3,4,7] Subsequent, a low-profile microcatheter delivered vascular occlusion device, the Medtronic Micro Vascular Plug (MVP, *Medtronic*,

All work performed at Rady Children's Hospital

Minneapolis, MN) garnered more widespread use.[8,9] Most recent, the Amplatzer Piccolo Occluder (formerly the Amplatzer ductal occluder II and additional sizes ADOII-AS, *Abbott*, Santa Clara, CA) has been approved by the United States Food & Drug Administration.[10-13] The latter two devices are favored because they are more suitable for transcatheter device closure of typical tubular PDAs in preterm infants. The ideal device would be short in length for placement in the middle of the tubular ductus minimizing the risk of adjacent vessel (aorta, left pulmonary artery) obstruction. It would not require exchange for a larger, stiffer delivery system; for example, the device could be delivered through a microcatheter. The entirety of the device would be clearly visible by X-Ray fluoroscopy and echocardiography.

A new commercially available vascular occlusion device (Micro Plug Set, *KA Medical*, Minneapolis, MN) is short (2.5 mm), microcatheter deliverable, and X-Ray and ultrasound visible. This device was developed for arterial embolization in peripheral vasculature. The Micro Plug Set is FDA cleared and CE marked. We describe early experience of preterm neonates and infants undergoing transcatheter PDA occlusion with this new, commercially available device for vascular embolization.

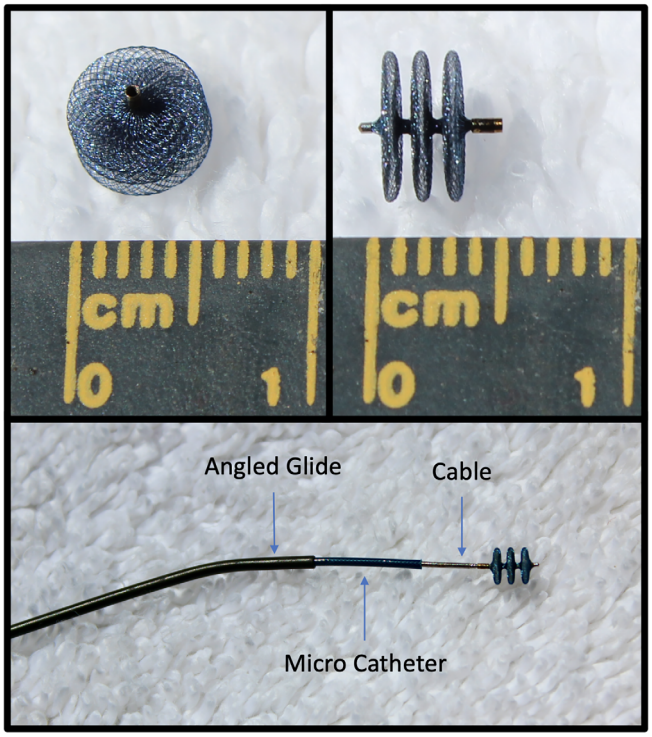

FIGURE 1 Micro Plug Set (unconstrained length 2.5 mm). Device is prepared upon its cable and then loaded into the 2.9 French microcatheter, which is positioned with the 4Fr angled glide catheter for delivery [Color figure can be viewed at wileyonlinelibrary.com]

2 | MATERIALS AND METHODS

2.1 | Patient selection

This is a single-center (Rady Children's Hospital San Diego) retrospective study approved by our Institutional Review Board (University of California, San Diego). As this was a retrospective study, waiver of consent was obtained. All consecutive pre-term patients (March–June 2020) referred for transcatheter device closure of hemodynamically significant patent ductus arteriosus (PDA) were included. Patients were referred by the neonatal intensive care providers due to persistent respiratory requirements and/or failed medical management. All medical records were reviewed. Specific attention was paid to procedural cardiac catheterization, echocardiographic, and post-intervention recovery data. Patients with PDA diameter larger than 4 mm were excluded; PDA length less than 4 mm were excluded.

The Micro Plug Set is composed of self-expanding braided nitinol cylindrical mesh with three equal-sized discs and radiopaque marker bands on each end (see Figure 1). The device is available in four sizes with disc diameters ranging from 3 to 6 mm and an unconstrained length of 2.5 mm. The device is prepared and advanced within the manufacturer microcatheter. This microcatheter can be advanced within a catheter with 0.038″ lumen. There is no device delivery sheath required. KA Medical did not support this research effort.

2.2 | Procedural technique

All procedures were performed in a biplane X-Ray fluoroscopy cardiac catheterization laboratory (*Infinix I*, Toshiba, Tustin, CA) with general anesthesia. Transthoracic echocardiography was performed after patient positioning on the table and prior to vascular access, and then again after device placement prior to release to evaluate for evidence of aortic or left pulmonary artery obstruction. A temperature probe was inserted in the esophagus as a fluoroscopic landmark. We used exclusively transfemoral venous access (4 French sheath) (Cordis, Cardinal Health, Hialeah, Fl) for antegrade approach. As previously described, the 4 French angled glide catheter (*Terumo*, Somerset NJ) and a 0.035″ Wholey wire (*Medtronic*, Minneapolis, MN) were advanced within the sheath into the right atrium.[20] The Wholey wire was exchanged for a Renegade microcatheter (*Boston Scientific*, Marlborough, MA) loaded with an 0.014″ BMW wire (*Abbott*, Santa Clara, CA); the Renegade microcatheter enhances the stability of the coronary wire as it tracks through the heart. Using fluoroscopic landmarks, the Renegade microcatheter and BMW wire were advanced from the right atrium into the right ventricle, the wire was then advanced out the right ventricular outflow tract, across the ductus, and down the descending aorta. The Renegade microcatheter was advanced over the wire. In some cases it was necessary to use the angle on the Renegade microcatheter to manipulate the wire through the PDA. The angled glide was then advanced over the Renegade wire unit (this allowed for smooth advancement of the angled glide into the descending aorta avoiding wire mis-match). The Renegade was then removed, leaving the wire in place and the angled glide catheter was pulled back over it to the aortic end of the PDA, and an angiographic hand injection was performed through a Y-connector

(COPILOT, *Abbott*, Santa Clara, CA) to delineate ductal anatomy. Based on previous experience with other devices utilized for premature PDA occlusion, a Micro Plug Set device at least 1 mm larger than the minimal diameter of the ductus was chosen. The cable and microcatheter catheter completely fill the lumen of the angled glide catheter, so it is not possible to inject through the angled glide to visualize the pulmonary side of the PDA. In order to optimize intraprocedural pulmonary artery angiography the Micro Plug Set microcatheter was cut (90 cm goal microcatheter length) prior to loading the device. Shortening this microcatheter enables withdrawal of the microcatheter over the cable, thus allowing contrast injection through the glide catheter over the delivery cable prior to release of the device to evaluate for pulmonary artery obstruction. The device is back loaded into the microcatheter prior to introduction into the glide catheter through the Y-connector (Video S1).

2.3 | Data analysis

This is a descriptive study. Categorical data are summarized as count (percentage), and continuous data are summarized as median and range. All statistical analyses were performed using the Excel (*Microsoft* 2010, Redmond, WA). The authors had full access to the data and take responsibility for data integrity. All authors have read and agree to the manuscript as written.

3 | RESULTS

Eight consecutive preterm subjects meeting inclusion criteria underwent transcatheter PDA device closure with the Micro Plug Set (Figure 1, Video S1 and Video S2). Patient data are summarized in Table 1. Median cohort gestational age was 27 weeks (23–36 weeks), procedural age was 41 days (12–88 days), and procedural weight was 1,690 g (760–3,310 g). 63% (n = 5) required pre-procedure ventilatory support. Five patients had been treated medically with ibuprofen, indomethacin, or acetaminophen unsuccessfully. One patient, with additional cardiac comorbidities was on diuretic therapy.

All procedures were successful (Figures 2, 3). All patients had documented PDA closure with no residual shunt on intraprocedural echocardiography. Procedure data are summarized in Table 2. Angiography based PDA measurements are noted. Median procedure time was 49 min (39–69 min). Median fluoroscopy time was 8.2 min (range: 3.1–16.7). Median dose area product (DAP) 56.2 cGy.cm2 (range: 19.2–177.8). Mean respiratory severity score (RSS) (calculated from mean airway pressure multiplied by fraction of inspired oxygen) at 48 hr post procedure improved from mean value of 2 to 1.8.

There were no procedural complications. In follow-up [median = 78 days (28–101 days)], there was no mortality and no device or procedural related adverse events. Specifically, there was no left pulmonary artery (LPA) stenosis, coarctation of the aorta (CoA), tricuspid valve injury, or aortic wall injury on follow up echocardiograms. Immediately following device deployment, in four patients there was transient mild, self-resolving increased echocardiographic left pulmonary artery velocity (median 11 mmHg, range 9-16 mmHg) without 2-dimensional abnormality. Subsequent follow-up echocardiograms demonstrated resolution with normal left pulmonary artery velocity.

4 | DISCUSSION

We report early experience of preterm patent ductus arteriosus transcatheter device closure using the new, commercially available Micro Plug Set. All procedures were successful without complications or short-term adverse events. In our early series, which included an infant as small as 760 g, we found that the Micro Plug Set was well suited for typical premature ductus morphology and size. Notably, the device is short (2.5 mm) in length to fit within the premature ductus without encroaching or obstructing neighboring vessels (left pulmonary artery, aorta). Devices, in their entirety, were clearly visible on X-Ray fluoroscopy and transthoracic echocardiography. Device delivery was straightforward through a microcatheter without the need for a stiffer delivery system (i.e., sheath) in these small preterm infants.

TABLE 1 New device for preterm infant PDA device closure: patients

Patient	Gestational age (weeks)	Age at procedure (days)	Birthweight (g)	Procedure weight (g)	Respiratory support	Associated cardiac diagnoses
1	27	12	930	1,100	Nasal CPAP	None
2	23	14	630	760	SIMV	None
3	27	88	1,040	2,930	None	None
4	36	69	2,240	3,310	None	Complete atrioventricular canal
5	28	63	850	1940	None	None
6	26	22	860	1,030	SIMV	None
7	27	60	1,000	2075	Nasal CPAP	None
8	28	23	1,450	1,440	Nasal CPAP	None
Median	27	41	965	1,690	n/a	n/a

Abbreviations: CPAP, continuous positive airway pressure; SIMV, synchronized intermittent mandatory ventilation.

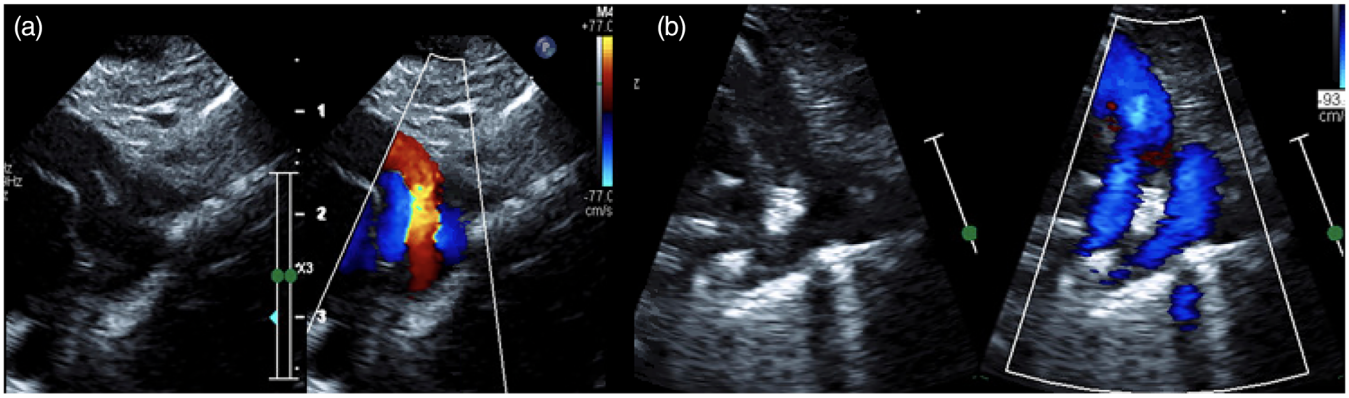

FIGURE 2 Transcatheter patent ductus arteriosus (PDA) occlusion with Micro Plug Set: echocardiography. Intra-procedural echocardiography: Suprasternal views of the PDA (red) and left pulmonary artery (blue) prior to device placement in 2D and color (panel a). Subsequent echocardiography, post PDA device (echo-bright) occlusion, showing unobstructed color flow in the LPA and descending aorta (panel b) [Color figure can be viewed at wileyonlinelibrary.com]

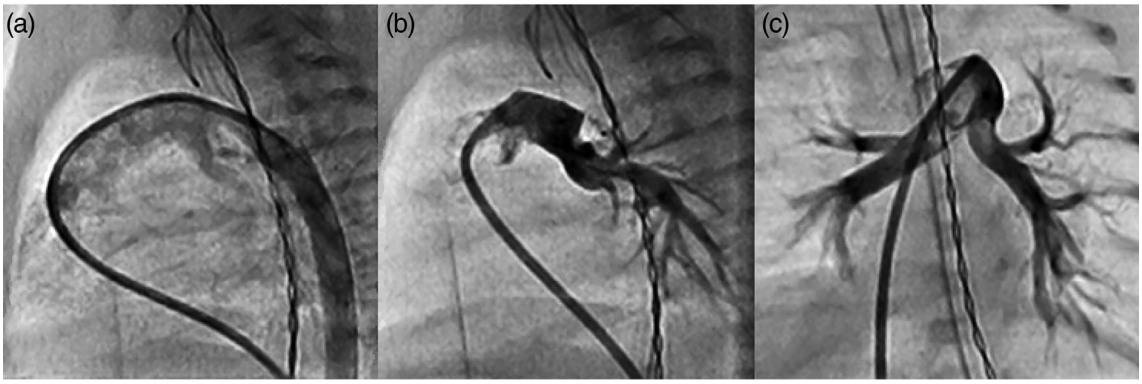

FIGURE 3 Transcatheter patent ductus arteriosus occlusion with the Micro Plug Set: X-Ray angiography. Intra-procedural X-Ray angiography: Initial lateral plane angiogram with 4 French glide catheter within the ductus to delineate ductal anatomy (a). Repeat angiogram in straight lateral projection (b) and extreme caudal projection (c) through glide catheter, positioned in the main pulmonary artery following device deployment demonstrating unobstructed flow to the branch pulmonary arteries and occluded ductus with device in stable position

TABLE 2 New device for preterm infant PDA device closure: procedures

Patient	1	2	3	4	5	6	7	8	Median
PDA minimal diameter (mm)	1.9	2.3	1.7	2	2.7	2.4	1.1	1.8	2
Mid PDA diameter (mm)	2.7	2.3	2.7	2.3	3.6	2.4	1.1	1.8	2.4
PDA aortic diameter (mm)	4.4	4.4	3.8	2.5	3.8	3.4	1.1	2.1	3.6
PDA length (mm)	12.8	8.7	10.7	6	12.9	10	6.7	9	9.5
Device deployed	4 mm	4 mm	5 mm	3 mm	5 mm	4 mm	3 mm	3 mm	n/a
Procedure time (min)	43	50	69	49	61	42	39	68	49
Fluoroscopy time (min)	8.6	7.7	5.7	9.2	11.4	6.2	3.1	16.7	8.2
Fluoroscopy dose (DAP cGy.cm2)	19.2	28.4	59.6	177.8	59	28.7	53.4	63.4	56.2
Fluoroscopy dose (mGy)	9.1	12.8	17.6	45.8	21.4	28.7	19.7	28.2	20.5
LPA obstruction (PSIG; mmHg) (intraprocedure)	9	16	None	None	10	None	None	13	4.5
LPA obstruction (follow-up)	None	None	None	None	None	None	None	None	None
Aortic obstruction (intraprocedure)	None	None	None	None	None	None	None	None	None

Abbreviations: DAP, dose area product; mm, millimeter; min, minutes; PDA, Patent ductus arteriosus; PSIG, peak systolic instantaneous gradient.

Tremendous progress has been made toward addressing the previously unmet need for transcatheter PDA device closure in the fragile premature neonatal population. Little more than a decade ago studies, such as, Roberts et al (2007) and Francis et al (2010) successfully used coils in preterm infants with small PDAs.[1,2] An interval leap in procedural evolution came with exclusive transvenous approach (avoiding potential of arterial injury) and limited X-Ray angiography in lieu of adjunctive echocardiography for implanting commercially available devices. Zahn et al (2015) used AVPII devices.[5] Sathanandam et al (2017) and Wang-Giuffre et al (2017) reported the potential benefits of less rigid, more accommodating microcatheter delivery systems with the MVP device.[8,9] The Amplatzer Piccolo Occluder device was approved by the United States Food & Drug Administration for infants at least 700 g.[13]

The Micro Plug Set addresses limitations of contemporary devices used for transcatheter PDA device closure in premature infants. First, the device is shorter in length (2.5 mm). The short length is well suited to sit in the middle of the tubular ductus frequently encountered in premature or neonatal infants. Second, the device is delivered through a soft, low profile (2.9 French) microcatheter. It does not require a catheter exchange for a stiffer delivery catheter or sheath. The latter can alter intra-procedural hemodynamics by propping open multiple valves and risks tricuspid valve injury.[8]

We report early procedural and short-term success of transcatheter preterm and neonate PDA closure. Our patient population, procedural characteristics, and results were similar to comparable early, small sized (n = 6, 8, 15, respectively) preterm PDA device closure reports.[5,8,9] Procedure success was 100% and there was no residual PDA flow. There were no mortalities or procedural/short-term adverse events. Thus far, we have noted transient trivial to mild LPA aliasing on transthoracic echocardiogram (PSIG <15 mmHg) in half of the patients immediately following device deployment resolving on follow-up echocardiography. This is not an uncommon finding in these patients irrespective of implanted device. Some report transient LPA stenosis from ductal spasm[1] or device obstruction both which improve with somatic growth and time.[21] We acknowledge direct comparison of our early report of a small series of patients to larger [n = 22 (median); 10–200], predecessor reports may be flawed. Nevertheless, we found the following noteworthy. We did not see previously reported failure modes precluding device implantation [PDA too short, LPA stenosis] with the short Micro Plug Set.[4,6,9] Similarly, we did not experience short-term significant LPA stenosis[1,3,4,6,7,10-12] or coarctation of the aorta[4,7,12,13] requiring close surveillance or even transcatheter/surgical rescue. There was no device migration or embolization as has been previously reported.[4,7,8,13] The microcatheter (transvenous) delivery system likely mitigated against previously encountered cardiac perforation,[4,11] tricuspid injury/regurgitation,[12,13] or arterial injury/complications.[1,7]

4.1 | Limitations

This is a retrospective study with a small sample size. Future, larger studies are needed and may even compare available preterm infant and neonate PDA occlusion devices. It is a promising, but early report (shortest follow-up = 1 month). Early in procedural evolution, early small sized studies are important.[5,8,9]

5 | CONCLUSIONS

The Micro Plug Set is a promising transcatheter device option for preterm infants and neonates. It addresses current available device limitations. Our early reported experience shows the device can be safely implanted with no significant procedural complications or adverse events.

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None.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

1. Roberts P, Adwani S, Archer N, Wilson N. Catheter closure of the arterial duct in preterm infants. Arch Dis Child Fetal Neonatal Ed. 2007;92(4):F248-F250.
2. Francis E, Singhi AK, Lakshmivenkateshaiah S, Kumar RK. Transcatheter occlusion of patent ductus arteriosus in pre-term infants. JACC Cardiovasc Interv. 2010;3(5):550-555.
3. Narin N, Pamukçu Ö, Baykan A, et al. Transcatheter closure of PDA in premature babies less than 2 kg. Anatol J Cardiol. 2017;17(2):147-153.
4. Baspinar O, Sahin DA, Sulu A, et al. Transcatheter closure of patent ductus arteriosus in under 6 kg and premature infants. J Interv Cardiol. 2015;28(2):180-189.
5. Zahn EM, Nevin P, Simmons C, Garg R. A novel technique for transcatheter patent ductus arteriosus closure in extremely preterm infants using commercially available technology. Catheter Cardiovasc Interv. 2015;85(2):240-248.
6. Zahn EM, Peck D, Phillips A, et al. Transcatheter closure of patent Ductus Arteriosus in extremely premature newborns: early results and midterm follow-up. JACC Cardiovasc Interv. 2016;9:2429-2437.
7. Backes CH, Cheatham SL, Deyo GM, et al. Percutaneous patent Ductus Arteriosus (PDA) closure in very preterm infants: feasibility and complications. J Am Heart Assoc. 2016;5(2):1-10.
8. Wang-Giuffre EW, Breinholt JP. Novel use of the medtronic micro vascular plug for PDA closure in preterm infants. Catheter Cardiovasc Interv. 2017;89(6):1059-1065.
9. Sathanandam S, Justino H, Waller BR, Radtke W, Qureshi AM. Initial clinical experience with the Medtronic micro vascular plug™ in transcatheter occlusion of PDAs in extremely premature infants. Catheter Cardiovasc Interv. 2017;89(6):1051-1058.

10. Narin N, Pamukcu O, Baykan A, Sunkak S, Ulgey A, Uzum K. Percutaneous PDA closure in extremely low birth weight babies. J Interv Cardiol. 2016;29(6):654-660.
11. Morville P, Akhavi A. Transcatheter closure of hemodynamic significant patent ductus arteriosus in 32 premature infants by amplatzer ductal occluder additional size-ADOIIAS. Catheter Cardiovasc Interv. 2017;90(4):612-617.
12. Malekzadeh-Milani S, Akhavi A, Douchin S, et al. Percutaneous closure of patent ductus arteriosus in premature infants: a French national survey. Catheter Cardiovasc Interv. 2020;95(1):71-77.
13. Sathanandam SK, Gutfinger D, O'Brien L, et al. Amplatzer piccolo Occluder clinical trial for percutaneous closure of the patent ductus arteriosus in patients ≥700 grams. Catheter Cardiovasc Interv. 2020. https://doi.org/10.1002/ccd.28973. [Epub ahead of print].
14. Sathanandam S, Balduf K, Chilakala S, et al. Role of transcatheter patent ductus arteriosus closure in extremely low birth weight infants. Catheter Cardiovasc Interv. 2019;93(1):89-96.
15. Almeida-Jones M, Tang NY, Reddy A, Zahn E. Overview of transcatheter patent ductus arteriosus closure in preterm infants. Congenit Heart Dis. 2019;14(1):60-64.
16. Schneider DJ, Moore JW. Patent ductus arteriosus. Circulation. 2006;114(17):1873-1882.
17. Moore J, Hegde S, El-Said H, et al. Transcatheter device closure of atrial septal defects: a safety review. JACC Cardiovasc Interv. 2013;6(5):433-442.
18. Ghawi H, Kenny D, Hijazi ZM. Transcatheter pulmonary valve replacement. Cardiol Ther. 2012;1(1):5.
19. Eleid MF, Holmes DR. Transcatheter aortic valve replacement: state of the art and future directions. Annu Rev Med. 2017;14(68):15-28.
20. Agrawal H, Waller BR, Surendan S, Sathanandam S. New patent Ductus Arteriosus closure devices and techniques. Interv Cardiol Clin. 2019;8(1):23-32.
21. Tomasulo CE, Gillespie MJ, Munson D, et al. Incidence and fate of device-related left pulmonary artery stenosis and aortic coarctation in small infants undergoing transcatheter patent ductus arteriosus closure. Catheter Cardiovasc Interv. 2020. https://doi.org/10.1002/ccd.28942. [Epub ahead of print].

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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