Long-Term Results of Transcatheter Closure of Large Patent Ductus Arteriosus with Severe Pulmonary Arterial Hypertension in Pediatric Patients

Abstract

Aims: Patent ductus arteriosus (PDA) is one of the most commonly seen congenital heart diseases prevalent today. The aim of this study is to evaluate the safety and efficacy of transcatheter closure of hypertensive ductus at long-term follow-up. **Materials and Methods:** Transcatheter closure was attempted in 52 patients with hypertensive ductus arteriosus. A lateral or right anterior oblique view aortogram was done to locate and delineate PDA. All the patients underwent clinical examination, electrocardiography, chest X-rays, and echocardiography before discharge and at 1, 6, and 12 months after the procedure and yearly thereafter. **Results:** The mean age of patients at procedure was 7.98 ± 4.79 (11 months–17 years), and the mean weight was 17.72 ± 10.81 (4–47) kg. Transcatheter closure of hypertensive ductus was successful in 50 (96.15%) patients. The mean preprocedural pulmonary artery pressure was 81.38 ± 17.31 (range: 55–113) mmHg which decreased to 29.65 ± 8.63 (19-38) mmHg at follow up. The most commonly used device was Amplatzer duct occluder in 63% of the patients followed by Amplatzer muscular ventricular septal defect occluder in 37% of the patients. There were two procedural failures, namely aortic obstruction and left pulmonary artery stenosis, which were managed uneventfully. There were no procedural deaths or device embolization. At median follow-up of 86 months, all the patients are well with no complications. **Conclusion:** The long-term results suggested that transcatheter closure of PDA with severe pulmonary hypertension in pediatric patients is safe and effective with minimal complications.

Keywords: *Device closure, long-term follow-up, patent ductus arteriosus, severe pulmonary arterial hypertension*

Jayal Hasmukhbhai Shah,
Dharmin Khimjibhai Bhalodiya,
Abhishek Pravinchandra Rawal,
Tushar Sudhakarrao Nikam

Department of Cardiology, U.N. Mehta Institute of Cardiology and Research Center, Civil Hospital Campus, Ahmedabad, Gujarat, India

Introduction

With incidence rate of 1:2000 in full-term infants, patent ductus arteriosus (PDA) is one of the most frequent congenital heart defects found in children and is more common in females compared to males.[1] Transcatheter closure of PDA is now the first-line alternative to surgery with excellent results and minimal complications using different devices.[2-14] Children with hypertensive ductus represent a challenging subset of patients in terms of patient selection, techniques, and complications, namely hemolysis, obstruction of the descending aorta, left pulmonary artery (LPA) stenosis, and progressive pulmonary vascular disease.[14-16] We analyzed our experience of transcatheter device closure in children with hypertensive ductus at long-term follow-up.

Materials and Methods

Patients

A total of 52 children of PDA and severe pulmonary arterial hypertension (PAH) underwent transcatheter device closure between 2008 and 2017 at our center. All the patients had large PDA assessed clinically and by transthoracic echocardiography with evidence of left atrial and left ventricular (LV) volume overload prior to the procedure. Data were collected prospectively after due informed consent of parents of all the patients. Complete physical examination, electrocardiogram, chest X-ray, and biochemical investigations were done. Children with associated complex congenital heart defects and those weighing <4 kg were excluded from the study.

Procedure

The procedure was performed under general anesthesia with inspiratory

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oxygen regulated between 40% and 55% during procedure in infants and those weighing <10 kg. Mild intravenous sedation and local anesthesia were used in older individuals. All the patients were administered preprocedural prophylactic antibiotic cefazolin (30 mg/kg) and two dosages 8 h apart subsequently. The patent duct was delineated in plain lateral and right anterior oblique views on aortic angiography. The ductus was measured at ampulla and its narrowest part to aid in device sizing. The standard procedure for percutaneous closure of PDA was followed. All the children had pulmonary artery systolic pressure (PASP) more than two-third of the systemic arterial pressure on invasive measurements. The balloon occlusion test was performed in all the patients using a Amplatzer sizing balloon (AGA Medical Corporation, Golden Valley, MN, USA) hand inflated with diluted contrast solution till waist appears and duct occlusion was confirmed angiographically. Reactivity of pulmonary arterial bed was ascertained with either fall of PASP by 20% of baseline or increase in pulmonary flow/systemic flow (Qp/Qs) by 20%. The device selection was made primarily on the basis of magnitude in fall of PASP compared to systemic arterial pressure. If PASP decreased under 60% of systemic arterial pressure, then Amplatzer duct occluder-I (ADO-I; AGA Medical Corp., USA) at least 50% larger than the smallest duct diameter was selected. If pulmonary pressures remained over 60% of systemic pressure, then Amplatzer muscular ventricular septal defect occluder (AMVSDO) (AGA Medical Corp., USA) at least 50% larger than the smallest ductal diameter was deployed. Again during device deployment, the chosen occluder was used to occlude the defect for 10 min without oxygen inhalation. The selected device was released only after fulfillment of the following criteria: (a) either pulmonary artery falls or it did not elevate, (b) either aortic pressure rises or it did not fall, and (c) no bradycardia or hemodynamic worsening. Postdeployment aortic angiography was done to confirm the position of occluder and closure of defect. Aspirin was prescribed a dose of 5 mg/kg/day for 6 months. All the procedures in this study were approved by the institutional ethics committee and were in accordance with guidelines provided by the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research involving human beings. All the procedures were in accordance with Helsinki Declaration of 1975, as revised in 2000.

Follow-up

All the children were discharged on the following day after complete clinical and echocardiography evaluation. They were evaluated at 24 h, 1 month, 6 months, and then annually with clinical examination, X-ray, and complete echocardiography evaluation. All the patients were precisely evaluated for residual shunt, pulmonary impingement, and aortic obstruction.

Data analysis

Statistical analysis was performed with statistical software (IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp). Quantitative data were expressed as mean ± standard deviation (SD). A paired *t*-test was performed as indicated to compare two mean values. $P < 0.05$ was taken as a level of statistical significance.

Results

Demographic data

A total of 52 children with hypertensive ductus underwent transcatheter closure which was successful in 50 patients (96.15%). There were 20 male and 32 female patients, with a mean age of 7.98 ± 4.79 years (11 months–17 years). The mean weight of patients was 17.72 ± 10.81 kg (4–47 kg). The New York Heart Association (NYHA) class was I in 3 (11.11%) cases, II in 20 (74.07%) cases, and III in 4 (14.81%) cases [Table 1].

Procedure data

During aortic angiography, the mean smallest PDA diameter was 7.55 ± 2.50 mm (5–14). A balloon occlusion test was performed in all the patients with constant monitoring of pulmonary artery and systemic pressures. PDA in most patients (63%) was closed with ADO-I, whereas AMVSDO was used in remaining (37%) cases. The largest devices used were 18 mm × 16 mm duct occluder and 18 mm AMVSDO. 10 × 8 and 8 × 6 sized duct occluders were most frequently used. The mean preprocedural pulmonary artery and systemic arterial pressures were 81.38 ± 17.31 and 122.22 ± 15.28 mmHg, respectively. The PASP dropped significantly in most of the patients after duct occlusion with mean postprocedure PASP of 29.65 ± 8.63 mmHg. Almost 29.62% of the patients had a mean PASP of more than 45 mmHg at the time of discharge which decreased during subsequent follow-up visits. During final aortic angiogram, six patients had residual shunt which got diminished during follow-up evaluation. The mean fluoroscopy time of all the procedures was 7.43 ± 2.38 (5–11) min, whereas the mean baseline Qp/Qs ratio was 2.67 ± 0.58 [Table 2].

Complications

There were major complications in two of the patients, namely aortic obstruction in one and stenosis of LPA

Table 1: General characteristics	
Variables	**Data***
Gender (female/male)	32/20 (61.53/38.47)
Age (years)	7.98±4.79 (11 months-17 years)
<6	16 (30.76)
6-12	26 (50)
12-18	10 (19.23)
Weight (kg)	17.72±10.81 (4-47)

*Data are expressed as *n* (%) or mean±SD (range) wherever applicable. SD: Standard deviation

in the other patient. The deployment of a 16-mm large AMVSDO in one of the patients leads to significant impingement of LPA with a notable pullback gradient which was subsequently managed with device removal and surgical ligation. The second patient developed a significant gradient in the descending thoracic aorta due to large 18-mm AMVSDO. The device was later removed, and the patient was successfully managed by surgical approach. Minor complications included fever, transient vascular complications, and transient LV dysfunction which were managed conservatively. Loss of peripheral pulse at the site of puncture was reported in 12 (23.07%) patients, which was successfully managed with heparin and streptokinase infusion. All these patients had large defects with the use of bulky devices and hardware. There was no incidence of worsening of pulmonary hypertension, device embolization, or mortality in any of the patients. Transient LV systolic dysfunction with reduced ejection fraction was noted in 4 (7.7%) patients immediately after procedure which recovered with angiotensin-converting enzyme inhibitors and diuretics. Transient hemolysis was observed in two (3.8%) patients 12 h after the procedure, but it subsided spontaneously in both the cases on the 2nd day [Table 3].

Follow-up

Barring some cases of procedural failure, all the patients fared well at long-term up with no clinical worsening or progression in pulmonary disease. There were no cases of residual shunting, aortic obstruction, or pulmonary impingement at median follow-up of 86 months. The mean pulmonary artery pressure recorded in children at follow-up was 18 ± 4.32 (13–23) mmHg which was significantly lower than immediate postprocedure pulmonary pressures. There was a reduction or stabilization in LV size on serial transthoracic echocardiography in all the patients. With exception of one patient suffering from bronchial asthma, all the patients reported improvement in their clinical symptoms from NYHA 2–4 to NYHA 1 [Table 4].

Discussion

Due to paucity of awareness and delay in diagnosis, patients with large PDA and severe PAH are more often reported in developing world. Nonsurgical modalities for closure of large hypertensive ductus have largely replaced surgical options, especially beyond infancy.[9-13] Children with hypertensive ductus represent a special subset primarily due to severe pulmonary hypertension, mismatch between size of device and patient, and third, hardware required to deliver bulky devices through small vascular anatomy. Patients with established Eisenmenger syndrome should not undergo closure of ductus as the defect vents into systemic circulation and helps in maintaining cardiac output albeit with desaturation. However, children with high pulmonary artery pressures and small left-to-right or bidirectional shunt need detailed evaluation to determine

Table 2: Procedural data and devices used

Variables	Data*
Fluoroscopy time (min)	7.43±2.38 (5-11)
Qp/Qs	2.67±0.58 (1.1-3.8)
Duct diameter (mm)	7.55±2.50 (5-14)
Preprocedure PASP (mmHg)	81.38±17.31 (55-113)
Postprocedure PASP (mmHg)	29.65±8.63 (19-38)
Procedural time (min)	25±3.2 (18-31)
Follow-up (months)	89.5±22.5 (52-120)
Types of devices used	
ADO-I	33 (63)
AMVSDO	19 (37)

*Data are expressed as *n* (%) or mean±SD (range) wherever applicable. SD: Standard deviation; Qp: Pulmonary flow; Qs: Systemic flow; ADO-I: Amplatzer duct occluder; AMVSDO: Amplatzer muscular ventricular septal defect occluder; PASP: Pulmonary artery systolic pressure

Table 3: Adverse events

Events	*n* (%)
Major adverse events	2 (3.84)
Aortic obstruction that required surgery	1 (1.92)
Pulmonary artery stenosis that required surgery	1 (1.92)
Minor adverse events	32 (61.53)
Groin hematoma	1 (1.92)
Fever	8 (15.38)
Transient loss of peripheral pulse	12 (23.07)
Transient LV dysfunction that required medication	4 (7.69)
Residual shunting	5 (9.61)
Transient hemolysis	2 (3.84)

LV: Left ventricle

Table 4: Follow-up

Variable	Data*
Follow-up period (months)	89.5±22.5 (52-120)
Clinical improvement	51 (98.07)
Device embolization	0
Freedom from infective endocarditis	52 (100)
Device infection	0
Pulmonary pressures at follow-up (mmHg)	18±4.32 (13-23)
Residual shunting (postprocedure)	
Day 1	5 (9.61)
Day 30	3 (5.76)
Day 180	0

*Data are expressed as *n* (%) or mean±SD (range) wherever applicable. SD: Standard deviation

pulmonary vascular reactivity and reversibility, especially in early stages to benefit from closure of the defect.

Patients with hypertensive ductus present with unique hemodynamics compared to other patients with left-to-right shunts, because in these patients in addition to left-to-right shunt, there is a direct transmission of aortic pressures into pulmonary bed during systolic and diastolic phases of cardiac cycle. This leads to difficulty in determining the

reversibility of pulmonary hypertension using conventional invasive assessment tools. Different modalities such as clinical examination, X-ray chest, arterial saturation of all extremities, and echocardiography may be conclusive in assessing operability in majority of children with hypertensive ductus arteriosus. However, in equivocal cases, cardiac catheterization and hemodynamic evaluation may be confirmatory. There is a small subset of patients with large patent ductus and severe pulmonary artery hypertension who remain operable until adulthood and benefit most from this approach. In this study, we determine the effect of balloon occlusion of ductus on pulmonary pressures and magnitude of change in shunting across the defect to delineate the operability of the defect. A fall in PASP by 20% from the basal state, with systemic pressure remaining constant, indicates significant left-to-right shunting across ductus and was selected as one of the criteria for reversibility of pulmonary hypertension. In our study, there was a transient LV dysfunction immediately after procedure in four (7.7%) patients. All these patients had large defects and excessive left-to-right shunting leading to increased LV preload. The increased in LV preload leads to increased stretching of LV muscle fibers which according to Starling's law leads to increased contractility of the left ventricle. Closure of the defect leads to sudden reduction in LV preload and increase in LV afterload due to closure of low resistance pulmonary shunting through PDA leading to LV dysfunction in some patients.

Yan *et al*. reported 29 adult patients with PDA and severe PAH in which trial occlusion with the device was done for 30 min, without unscrewing the device. They followed the delineated criteria for selection of patients: (a) a fall in the PASP or no elevation, (b) no decrease in the systemic aortic pressure, and (c) no worsening of clinical signs and symptoms. If all parameters were satisfied, then PAH was considered to be reversible and occluded with device. Otherwise, the device closure was abandoned considering PAH irreversible. Successful device closure with both ADO-I and AMVSDO devices was done in twenty patients, whereas seven patients failed trial balloon occlusion due to worsening clinical symptoms or increase in PA systolic pressures.[17] A detailed comprehensive evaluation to identify operability in borderline cases is must to combat limitations of individual technique. ADO-I is a self-expanding conical device composed of nitinol wire mesh and thrombogenic polyester fabric with a single aortic retention skirt. It is fully retrievable and available in wide range of sizes and delivered percutaneously through 6–8 Fr sheath.[13] Thanopoulos *et al*. described the first-ever successful use of AMVSDO in seven patients of hypertensive ductus with substantial reduction of pulmonary pressures.[18] Szkutnik *et al*. narrated their experience of successful deployment of ADO in all 13 patients with severe PAH in high-altitude environment.[19] Viswanathan and Kumar reported on 21 patients with large PDA and

severe PAH in which almost 12% of the patients continued to have raised pulmonary arterial pressures on follow-up due to nonregression of pulmonary pressures after closure and subsequently worsened clinically.[20]

Although excellent short-term and midterm outcomes have been reported of percutaneous closure of large hypertensive ductus, long-term results are lacking.[17,18,21-25] This study tries to delineate the long-term outcomes of transcatheter closure of large hypertensive ductus in terms of regression of pulmonary pressures and clinical improvement.

Conclusion

Transcatheter closure in children with large PDA and severe PAH is safe and effective at long-term follow-up. Thorough knowledge about different devices including retrieval techniques is vital before attempting percutaneous closure in this high-risk subset of patients. The use of bulkier devices in patients with severe PAH necessitates a lower threshold for surgery in cases of device embolization. A comprehensive evaluation of borderline cases before device closure of hypertensive ductus is inevitable for successful outcomes.

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Conflicts of interest

There are no conflicts of interest.

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