ISSN 0118-9034

Philippine Heart Center Journal

Vol. 23 No. 2 July - December 2020

PEDIATRIC INTERVENTIONAL CARDIOLOGY RESEARCH & UPDATES

Official Publication of the Philippine Heart Center

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The Philippine Heart Center Journal is published by the Philippine Heart Center.

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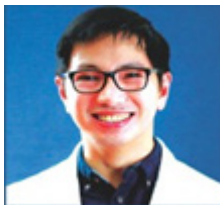

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Foreword

The year 2020 marked the Division of Invasive Pediatric Cardiology's endeavor to publish a journal which would chronicle the experiences and aspirations of pediatric interventional catherization. The journal would focus on this discipline which aims for a nonsurgical approach to children with remediable congenital heart disease.

William Osler, the father of modern medicine, emphasized that medicine should be learned from studying the medical literature and at the bedside. With the advent of modern technology, the medical literature has expanded beyond the medical textbooks and seminal pioneering articles. There are late breaking clinical trials and cutting edge technologies and research that can be explored. This journal hopes to stimulate the curiosity for the journey for knowledge.

The seeds in the field of pediatric cardiology were first planted with the publications of the first editions of textbooks from Dr. Alexander S. Nadas of Boston and Dr. Helen B.Taussig of Baltimore. These served as the foundation for the pioneering research of Drs. Abraham Rudolph, William Rashkind, William Miller and James Lock. Their research then formed the framework for the guidelines of practicing and training interventionalists. The articles in the journal will define clinical approaches, diagnosis, and management as well as innovation in interventional cardiac catherization which would improve survival, minimize risks and reduce hospitalizations days. The articles will help guide pediatric cardiologists in dealing with complex congenital heart disease beyond the scope of the textbooks.

I hope that this journal will be a living legacy for this division that would prove to be a valuable resource for pediatric cardiologists practicing in the country now and in the future. I extend my congratulations to the earnest effort of the staff, especially Drs. Jean Antonio Villareal and Babie Catherine Causapin and to the chairman, Dr. Juan Reganion.

WILBERTO L. LOPEZ, MD
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22 July 2020

Editorial

Facts and Evidences in Pediatric Cardiology... Beyond Limits

JULIET J. BALDERAS, MD

The incidence of Congenital Heart Disease in the country is 5-10/1000 livebirths (PHC Journal, 2015). The whole gamut of heart disease in children extends to acquired heart diseases – with noncardiac manifestations but with chronic (may be progressive) cardiac sequelae - Rheumatic Heart Disease and Kawasaki Disease, to cardiac arrhythmias, and cardiomyopathies. These have made the field of Pediatric Cardiology rich in its subspecialties – which have ramified to Adult Congenital Heart Disease in GUCH, and Fetal Cardiology to include the fetus as the patient. Much more, as every child grows into adulthood, emerging heart disease develops from risk factors that may shape adult non-communicable heart disease. This makes the child a vulnerable cardiac patient- and the challenge is to curb or to detour him from the natural history of untreated heart disease with identifiable risks.

There are gaps in knowledge. Gaps in knowledge can be: (1) evaluation and assessment of cyanosis or heart failure at different age groups; (2) treatment of heart failure, including the fetus, and right heart failure in adolescents with uncorrected heart disease in Eisenmengerization; (3) treatment transcending to surgical correction of simple lesions and challenges met with the complex ones; (4) improvement in the treatment outcomes and short and long-term follow up of corrected and uncorrected heart disease. These gaps in knowledge are a rich source of research agenda that can shape future evidence-based Pediatric Cardiology diagnosis and management, and perhaps, improve survival for the Filipino child.

As a clinician taking care of a young heart patient- where can you contribute? An unusual case with a unique manifestation, or a a new modality treatment – is a case study report. A collection of cases (at least more than 2) with the same unique manifestations but different diagnosis, or same diagnosis with a unique modality treatment – is a case series. There can be a retrospective and a prospective studies, of which experimental researches have the highest level of evidence. Let us continue to learn from each other through evidence based research, and create research agenda so that we may finally know relevant and significant truths with a p value <0.05, at least.

As PHC continues its mandate as the Apex Cardiovascular hospital under the approved Universal Health Care Act (UHC) of 2019, with several cardiovascular care Regional Hospitals under DOH identified as Specialty Centers to work with PHC, we share this Pediatric Cardiology Journal for all taking care of heart disease in children in cooperation with the Department of CV Surgery – Congenital Heart Disease and the Department of Adult Cardiology – Section of Congenital Heart Disease and Grown-up Congenital Heart disease.

More power to all.

Pediatric Invasive Cardiology

Transcatheter Closure of Patent Ductus Arteriosus in Preterm Neonates Using KONAR™ - Multifunctional Occluder: Initial Experience

Ma, Rosita Quitola, MD[1], Jean Antonio Villareal, MD[2]

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Background --- Transcatheter closure of the PDA is a relatively new technique in preterm neonates who have failed pharmacologic therapy; hence, this case series described our initial experience of transcatheter device closure of PDA in pretern neonates using Konar-multifunctional occluder.

Case --- This case series discussed five preterm patients whose weight ranges from 1200-2300 grams who underwent transcatheter PDA device closure. The procedure was accomplished through single venous approach under fluoroscopic and echocardiographic guidance. The size and shape of PDA as well as immediate therapeutic results were recorded by angiography and echocardiography. Procedural successes and adverse events were recorded. All 5 cases had successful device placement with no device embolization. One patent died due to massive pneumothorax two days after the procedure, two patients had small PDA leak within the device, two patients had mild narrowing at the descending aorta, one patient had mild LPA stenosis and one patient had bleeding at the punctured site needing blood transfusion. No other vascular complications were noted like limb ischemia, arterial occlusion or dissection due to the use of a microcatheter delivery sheath and use of venous access only. Echocardiography was used to guide device placement, estimate the blood flow ensuring absence of obstruction to the adjacent vessels and to evaluate for residual ductal shunting prior to device release. The Konar- multifunctional occluder (MFO) used in these patients has the advantages of having a softer delivery cable which allows for much more predictable release of the device and has a unique microcatheter delivery sheath, which is desirable for small infants and increased application to the anatomic variants of PDA in premature infants.

Conclusion --- Transcatheter closure of PDA is feasible as an alternative in the treatment of PDA in preterm and low birth weight infants using venous access only with echocardiographic guidance. Careful patient selection and high degree of technical skills by the interventionalist and echocardiographer are of high considerations. ***Phil Heart Center J 2020;23(2):1-13.***

Key Words: ■ Patent Ductus Arteriosus ■ preterm neonates ■ transcatheter closure ■

The ductus arteriosus is a normal fetal structure that closes spontaneously in majority of term infants within the first week of life. Failure of the arterial duct to close in the weeks following birth accounts for 5-10% of all congenital heart diseases. However, due to the metabolic immaturity, patency of the ductus arteriosus is a common physiological phenomenon in preterm infants who account for as many as 5-7% of all liveborn neonates.[1]

A persistent patent ductus arteriosus (PDA) is associated with an increase in neonatal morbidity which complicates the clinical course of preterm and very low birth weight infants. Hemodynamically significant PDA with left to right flow has been associated with increased incidence of intraventricular hemorrhage, necrotizing enterocolitis, pulmonary hemorrhage, bronchopulmonary dysplasia and poor weight gain.[2]

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Clinically or hemodynamically significant PDAs are currently treated with a combination of supportive approaches, pharmacotherapy, or surgical ligation. Nonselective cyclooxygenase inhibitors, like indomethacin and ibuprofen have an estimated PDA closure rate of 45%-90% in premature and Extremely Low Birth Weight (ELBW) infants;[3,4] however, due to their vasoconstrictive properties, these medications have been associated with renal insufficiency and intestinal perforation. Acetaminophen like paracetamol is a new alternative with similar PDA closure rates and fewer reported side effects. In patients with hemodynamically significant PDA who fail pharmacological therapy, PDA surgery is a second line approach. Despite advancements in surgical technique, surgical ductal ligation in preterm and ELBW infants has complications which includes pneumothorax, vocal palsy, thoracic deformity and misidentification of the ductus resulting to unintentional ligations of the pulmonary artery and the aorta hence a more non-invasive alternative is considered.[2]

Transcatheter PDA closure is the procedure of choice in adults, children, and larger infants with a weight of over 5kg.[5] However, this mode of intervention has not been routinely used in preterm and extremely low birth weight infants due to concerns regarding its safety and feasibility since preterm infants are more medically fragile. Also, there are concerns on possible increased in incidence of procedure-related adverse events, availability of suitable devices and technical challenges in dealing with extremely small infants.

Recently, however, there has been an emergence of several reports of successful transcatheter PDA closure in preterm and extremely low birthweight infants.[6,7]

This case series discussed five preterm infants with low birthweights who underwent transcatheter closure of PDA after medical therapy failure. This is the first PDA device closure done in preterm neonates weighing less than 2.5 kg in the Philippines.

PROCEDURAL DETAILS

PDA Device Closure Procedure

French 4 sheath was placed in the femoral vein before administration of heparin (50U/kg). Arterial access was not established, in an effort to minimize morbidity. A Fr 4 multipurpose catheter with hydrophilic wire with slightly curved tip 0.032 inches in diameter. length of 150cm was manipulated under fluoroscopic guidance into the IVC, RA, RV, MPA, LPA, PDA then into the descending aorta. A descending aortogram (*Figure 1*) at an angle of RAO 30 and lateral views were done to determine the size and shape of the PDA. After that, the occluder in suitable size was selected according to the results of aortography.(*Table 1*)

The diameter was about 1-2 mm larger than the diameter of the narrowest point of the duct. The occluder was inserted through the delivery sheath at the ampulla of the PDA and with the distal end at the pulmonic side to occlude the PDA under fluoroscopic and echocardiographic guidance. (*Figure 2*)

Angiography at the pulmonary artery was again done to determine the position of the occluder and showed occluder in place and with minimal egress of dye thru the occluder. (*Figure 3*) Prior to release from the delivery cable, the left pulmonary artery and descending aorta were assessed by 2-dimensional echocardiography in high parasternal view and suprasternal view to check for the presence of stenosis or obstruction to the said vessels. The device was then released and cineangiography post occlusion of PDA showed the device positioned within the PDA. Following release of the device, echocardiographic evaluation of all pertinent structures was repeated. (*Table 2*)

Procedural Flow

Preterm neonates with hemodynamically significant PDA who failed 2-3 cycles of pharmacological therapy referred by Neonatalogists/ Pediatric cardiologists for PDA device closure

↓

Admitted at intensive care unit
Clearance from infectious service acquired
Co-managed with neonatologist
Referred to CV anesthesia

↓

Pre-procedural laboratory examinations done.
Blood component prepared
Placed on NPO at least 4 hours prior to the procedure

↓

Secure informed consent
Procedure and possible complications explained

↓

At the CV lab: prewarmed blanket applied as mattress.
All fluids to be used for flushing are warmed
Antiseptic solution to be used for skin disinfection are warmed

↓

All patients were intubated and hooked to general anesthesia

↓

PDA device closure procedure

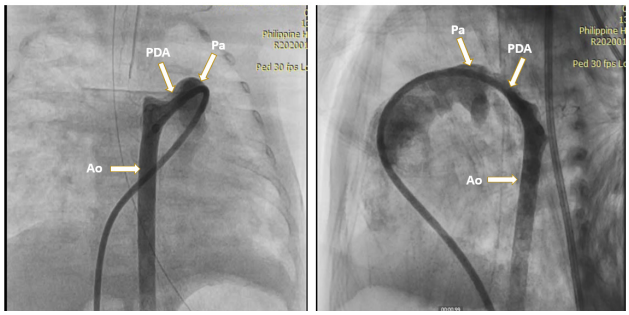

Figure 1. Angiography in descending aorta at RAO 30 and lateral views showing the morphology of a type F patent ductus arteriosus (PDA) in which the PDA is elongated and tubular with minimal tapering at the pulmonic end. Ao indicates descending aorta; Pa, pulmonary artery.

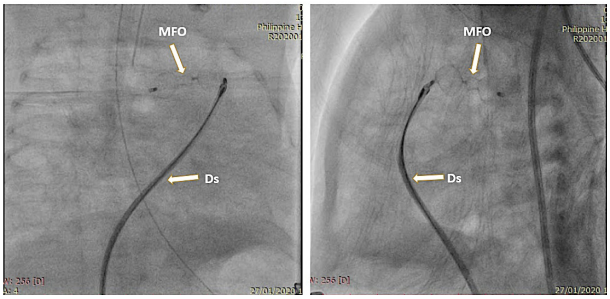

Figure 2. Placement of Konar multifunctional occluder (MFO). The device seems to be in place as the aortic side of the device was seen within the tracheal shadow. Ds indicates delivery sheath.

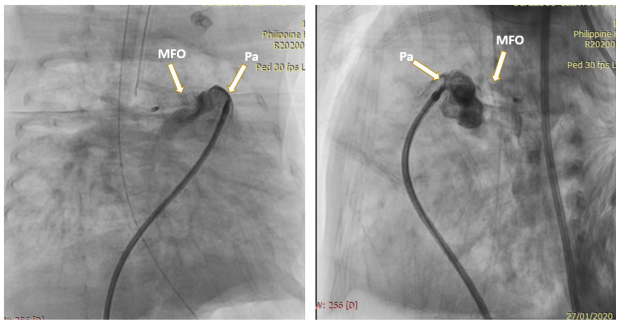

Figure 3. Angiography at the pulmonary artery (Pa) at RAO 30 and lateral views post occlusion showing occluder in place and with minimal egress of dye thru the device. MFO indicates Konar - multifunctional occluder.

Table 1. Patient characteristics

Case	Sex	Gestation Week	Birth Weight (g)	Post natal day	Procedure Weight (g)	PDA Krichenko Type	PDA size Pulmonic end (mm)	Co-morbidities	Device used	Complication
1	F	28	1000	38	1200	A	3	BPD, NP Pneumothorax	MFO 6/4mm	Death PDA leak
2	F	36	2000	25	1800	C	2.4	CHF	MFO 6/4mm	Mild narrowing a the descending aorta
3	F	36	2200	25	2000	C	3	CHF	MFO 5/3mm	Bleeding at punctured site
4	F	31	1700	37	1700	A	2.8	CHF, NP	MFO 5/3mm	Mild LPA stenosis
5	F	33	1300	73	2300	F	2.7	BPD, HCAP, ROP	MFO 6/4mm	Mild narrowing at descending aorta, PDA leak

BPD bronchopulmonary dysplasia, NP neonatal pneumonia, CHF congestive heart failure, HCAP health care associated pneumonia, ROP retinopathy of prematurity, MFO multifunctional occluder.

Table 1 shows clinical characteristics of the 5 preterm neonates who underwent PDA device closure. The corrected age of the patients ranges from 34 weeks - 39 weeks old. The procedural weight ranges from 1200 grams to 2300 grams. Two patients had Krichenko Type A (conical) PDA, two patients who is Type C or tubular, and 1 patient of fetal type of PDA. (*Figure 4*) The PDA size measured thru angiography ranges from 2.4mm to 3mm. Other comorbidities of the patients include bronchopulmonary dysplasia, neonatal pneumonia, healthcare associated pneumonia and retinopathy of prematurity. The immediate complications include one patient died after 48 hours post procedure due to massive pneumothorax, 2 patients had small PDA leak within the device, 2 patients had mild narrowing at the descending aorta,1 patient had mild LPA stenosis and 1 patient who had bleeding at punctured site.

Case Details

Case 1

The infant was born preterm at 28 weeks via cesarean section secondary to abruptio placenta with a birthweight of 1000 grams and APGAR score of 2, 6 and 7. She was managed as a case of hyaline membrane disease secondary to prematurity, extremely low birth weight, congenital heart disease, patent ductus arteriosus and required the administration of surfactant, mechanical ventilation and inotropic support from the time of birth. She was given 3 cycles of Ibuprofen, which failed to close the ductus. She was then referred for transcatheter closure of the PDA at the age of 38 days (32 weeks corrected age) in extremely serious condition where she was dependent on mechanical ventilation, with bronchopulmonary dysplasia, neonatal pneumonia and congenital heart disease, patent ductus arteriosus.

On physical examination, the patient is intubated. Vital signs are the following BP: 67/37 mmHg CR 133 bpm, RR 50 bpm, oxygen saturation of 98-99% on all extremities, weight of 1.2 kg, with adynamic precordium, apex beat at the 4th intercostal space left midclavicular line, S1 normal, S2 physiologically split, normal P2, and Grade 3/6 systolic ejection murmur at the left upper sternal border. Chest radiography revealed increased pulmonary blood flow and LV prominence.

Echocardiography revealed the presence of PDA with a diameter of 3 mm at the pulmonary end, left atrial and left ventricular enlargement with good ventricular function. (*Table 2*)

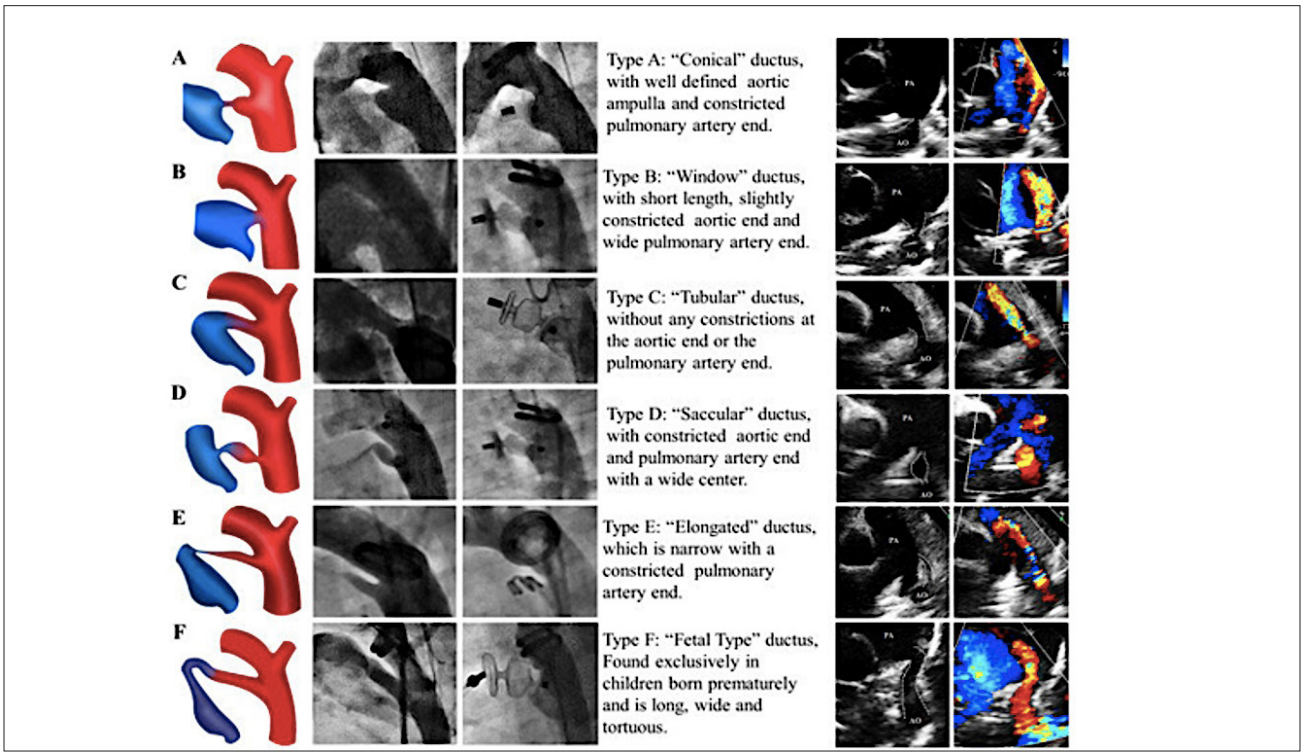

Figure 4. Angiographic Classification of PDA by Krichenko. Adapted from "Angiographic classification of the isolated, persistently patent ductus arteriosus and implications for percutaneous catheter occlusion." By Krichenko A, Benson LN, Burrows P, Moes CA, McLaughlin P, Freedon RM. Am J Cardiol. 1989;63:877-879

Prior to the procedure, the patient had sudden onset of desaturation with bradycardia due to massive right pneumothorax relieved by needling and became stable. Patient then underwent transcatheter closure of the PDA using a Lifetech™ multifunctional occluder size 6/4mm with fluoroscopic and echocardiographic guidance. Prior to the release of the occluder, patient had episodes of desaturation and bradycardia secondary to recurrence of right pneumothorax which was relieved by needling. After which, patient became stable hence PDA device was released. Post-procedure angiography and TTE revealed that the device was in place, with noted minimal residual shunt within the device, (*Figure 5*) with no aortic/pulmonary artery obstruction noted. Patient was then transferred back to PICU for further monitoring. Few hours post procedure, the right pneumothorax persisted with subcutaneous emphysema. CTT was inserted with mild resolution of the pneumothorax. However, on the 3rd post procedure day, patient had persistence of desaturation and bradycardia due to massive tension pneumothorax. Parents signed DNR consent and patient eventually succumbed to death.

Case 2

This is the case of a 25 day old neonate born preterm at 36 weeks by maturity index. First of twin via emergency cesarean section secondary to preterm premature rupture of membranes and malpresentation, APGAR score 9,9, birthweight of 2 kg managed as late prematurity, low birth weight, congenital heart disease, patent ductus arteriosus, mitral regurgitation moderate, and maintained on furosemide and spirolonactone. Patient had 2 cycles of Ibuprofen but the PDA persisted. She was discharged with conservative expectant medical management. However on subsequent follow ups, chest radiography revealed increased pulmonary blood flow and 2D echo revealed persistence of PDA with moderate mitral regurgitation, was admitted for percutaneous closure of PDA the procedure.

On physical examination, patient is awake and with good cry and activity. Vital signs are the following: BP 73/37 mmHg CR 157 bpm, RR 52 bpm, oxygen saturation of 98% on all extremities, weight of 2kg, length of 44 cm with adynamic precordium, apex beat at the 4th intercostal

space left midclavicular line, S1 normal, S2 physiologically split, normal P2, Grade 3/6 systolic ejection murmur at the left upper sternal border. Chest radiography revealed increased pulmonary blood flow and LV prominence. Echocardiography showed a dilated left atrium and left ventricle, PDA with a 2.5 millimeter diameter, showing a left-to-right shunt and a moderate mitral regurgitation. (*Table 2*)

At 25 days old, patient underwent PDA device closure using Lifetech™ multifunctional occluder size 5/3mm with transthoracic echocardiography (TTE) guidance. Post-procedure angiography and TTE revealed that the device was in place and neither residual shunt nor aortic/pulmonary artery obstruction was observed. She was discharged from the hospital after 48 hours. Chest radiography and 2D echocardiography with color Doppler study prior to discharge revealed device in place with no obstruction to adjacent vessels, good function. On subsequent follow ups, patient is thriving well with no signs of congestive heart failure. At one-week, one-month and six-month echocardiography follow-up, the device was in place and there was no residual shunt or flow turbulence in the aorta orpulmonary artery. (*Figure 6*)

Case 3

This is the case of a 25-day old neonate who was born preterm 36 weeks by maturity index via emergency cesarean section secondary to preterm premature rupture of membranie and malpresentation, 2nd of twin, APGAR score 9,9 birthweight of 2.215 kg, AGA, managed as a case of late prematurity 36 weeks AOG, low birth weight, congenital heart disease, patent ductus arteriosus, mitral regurgitation moderate and was maintained on Furosemide and Spirolonactone. Two courses of Ibuprofen were administered however there is persistence of the ductus. Patient was discharged with conservative expectant medical management. However on subsequent follow ups, chest radiography revealed increased pulmonary blood flow and 2D echo revealed persistence of PDA with moderate mitral regurgitation. She was admitted for PDA device closure.

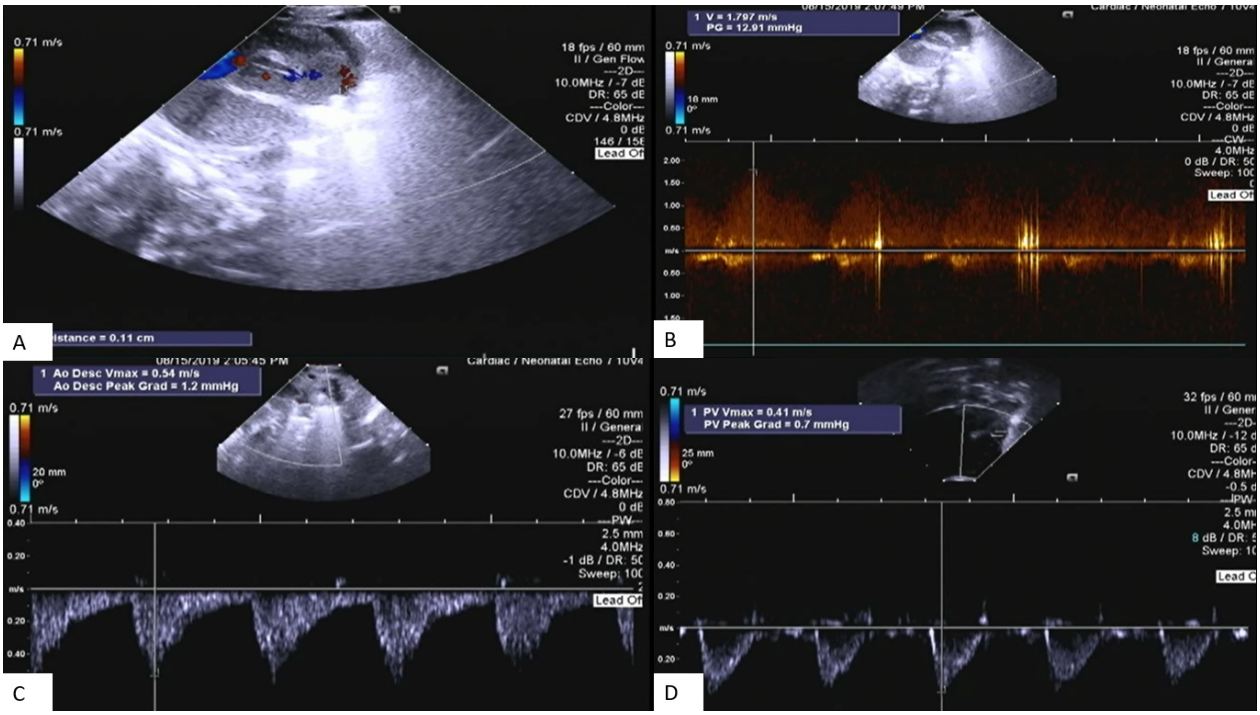

Figure 5. Transthoracic echocardiography images 24 hours after percutaneous closure of PDA. Pictures A and B show the PDA leak within the device measuring 0.11 cm with continuous Doppler signal of 13 mmHg. Pictures C and D show Doppler views in descending aorta and peripheral pulmonary artery, respectively. No pressure gradient was detected in descending aorta and peripheral pulmonary artery.

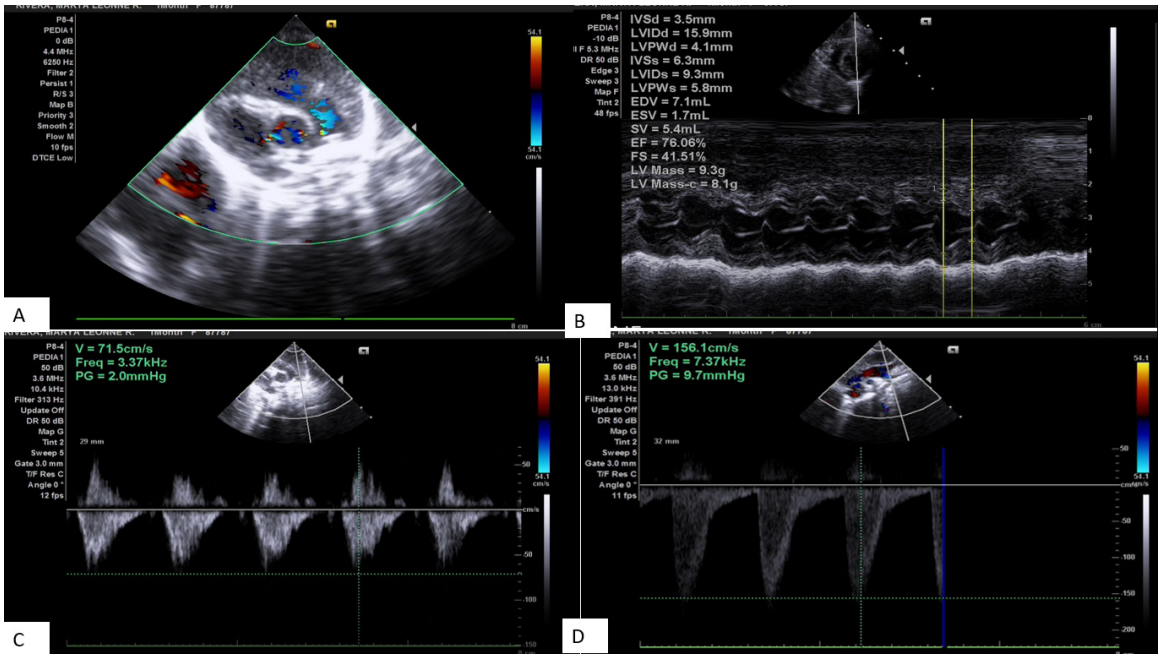

Figure 6. Transthoracic echocardiography images 1 month after percutaneous closure of PDA. Pictures A shows device in place and no leak. Picture B shows a decreased in LVEd at 1.6cm (from 1.8cm pre device closure). Pictures C shows no gradient at the peripheral pulmonary artery while picture D showed a gradient of 10 mmHg at the descending aorta.

On physical examination, patient is awake, with good cry and activity. Vital signs are the following BP: 68/34 mmHg, CR 148 bpm, RR 45bpm, oxygen saturation of 98% on all extremities, weight of 2kg, length of 43 cm with adynamic precordium, apex beat at the 4th intercostal space left midclavicular line, S1 normal, S2 physiologically split, normal P2, Grade 3/6 systolic ejection murmur at the left upper sternal border. Chest radiography revealed increased pulmonary blood flow and LV prominence. Echocardiography showed a dilated left atrium and left ventricle, PDA with a 2.7 millimeter diameter, showing a left-to-right shunt and a moderate mitral regurgitation. (*Table 2*)

On the 25th day of life, patient underwent PDA device closure using Lifetech™ multi-functional occluder device size 6/4 mm and tolerated the procedure well, was brought to NICU for observation. Patient had bleeding at the punctured site which needed PRBC transfusion. Patient was then discharged improved on 5th hospital day. Chest x-ray and 2D echocardiography prior to discharge revealed device in place with no obstruction to adjacent vessels and good ventricular function. On serial follow-up, patient is gaining weight and thriving well and serial echocardiographic evaluation at 1 week, 1 month and 6 months post occlusion showed that the device was in place and no residual shunt or flow turbulence in the aorta or pulmonary artery was observed. (*Figure 7*)

Case 4

This is the case of a 5 weeks old infant born preterm at 31 weeks by Ballard's scoring, via normal spontaneous delivery APGAR score 8,9, birth weight of 1.7 kg managed as prematurity, low birthweight, congenital heart disease, patent ductus arteriosus and maintained on furosemide and spirolonactone. Patient was admitted for 2 weeks and had 2 cycles of Paracetamol but the PDA persisted. Patient was discharged with medical management. However, at 4 weeks of age (35 weeks corrected age) patient presented with heart failure symptoms like tachypnea, subcostal retractions, and crackles. Chest radiography revealed increased pulmonary blood flow and 2D echocardiography revealed persistence of PDA with moderate mitral regurgitation. They were advised for percutaneous closure of PDA.

On physical examination, patient is awake, with good cry and activity. Vital signs are the following BP: 75/38 mmHg CR 147 bpm, RR 52bpm, oxygen saturation of 98% on all

extremities, weight of 1.7 kg, with adynamic precordium, apex beat at the 4th intercostal space left midclavicular line, S1 normal, S2 physiologically split, normal P2, Grade 3/6 systolic ejection murmur at the left upper sternal border. Chest radiography revealed increased pulmonary blood flow and LV prominence. Echocardiography showed a dilated left atrium and left ventricle, PDA with a 2-3 millimeter diameter, showing a left-to-right shunt and a moderate mitral regurgitation (*Table 2*).

At 5 weeks of age, patient underwent PDA device closure using Lifetech™ multifunctional occluder size 5/3mm with transthoracic echocardiography (TTE) guidance. Post-procedure angiography and TTE revealed that the device was in place, with no residual shunt. The gradient across the left peripheral pulmonary artery and descending aorta were 18 mmHg and 5 mmHg, respectively. She was discharged from the hospital after 48 hours. On subsequent follow-ups, patient is thriving well and no signs of congestive heart failure. At one-month echocardiography follow-up, the device was in place and there was no residual shunt with decreased in the gradient at the LPA at 7 mmHg. (*Figure 8*).

CASE 5

The infant was born preterm at 33 weeks via normal spontaneous delivery with a birthweight of 1300 grams and APGAR score of 6 and 7. Patient was admitted initially as a case of prematurity, very low birth weight, neonatal pneumonia and patent ductus arteriosus. Patient was intubated and treated accordingly. Patient underwent 2 courses of Paracetamol to close the PDA; however, it persisted. Patient presented with increased pulmonary blood flow and signs of congestive heart failure; hence, diuretics were continued. However, she had episodes of fever and respiratory distress with noted infiltrates and congestion on chest radiography and was managed as a case of health care associated pneumonia. After appropriate antibiotics, there is resolution of the pneumonia; however, patient had still signs of pulmonary overcirculation due to persistence of the PDA. She was then referred to our institution for transcatheter closure of the PDA at the age of 73 days (*43 weeks corrected age*).

On physical examination, vital signs are the following BP: 72/40 mmHg CR 137bpm, RR 64bpm, oxygen saturation of 99% on all extremities, weight of 2.3kg, with adynamic precordium, apex beat at the 4th intercostal space left midclavicular line, S1 normal, S2 physiologically split, normal P2, Grade 3/6 continuous murmur at the left upper sternal border. Chest radiography revealed increased pulmonary blood flow and LV prominence. Echocardiography revealed the presence of PDA with a diameter of 2.9 mm at the pulmonary end, left atrial and left ventricular enlargement with good ventricular function. (*Table 2*).

At 2 months and 2 weeks of age (*43 corrected age)*, patient underwent PDA device closure using Lifetech™ multifunctional occluder size 6/4mm with transthoracic echocardiography (TTE) guidance. Post-procedure angiography and TTE revealed that the device was in place, with minimal PDA leak of 0.18cm with continuous doppler signal of 16 mmHg within the device. No pulmonary artery obstruction was observed however there is a noted gradient of 20 mmHg at the aortic side. We opted not to upsize the device since it may further obstruct the aortic side. We then released the occluder device. Patient tolerated the procedure and was transferred to PICU for post procedural monitoring. During the 1st 24 hours post-procedure, patient had stable vital signs, tolerated weaning from mechanical ventilation set up, no any complications like arrythmia, hematoma or bleeding at punctured site.

Chest radiography 24hr post occlusion revealed significant decreased in pulmonary congestion and mild decreased in heart size. (*Figure 9)*. During stay at the PICU, patient developed septicemia and was treated accordingly. A repeat 2D echocardiography 1 week after the procedure showed persistence of a PDA leak of 0.10cm with continuous doppler signal and decreased in the gradient across the aorta of 16 mmHg (*Figure 10*). She was then transferred back to the referring institution for continuation of medications.

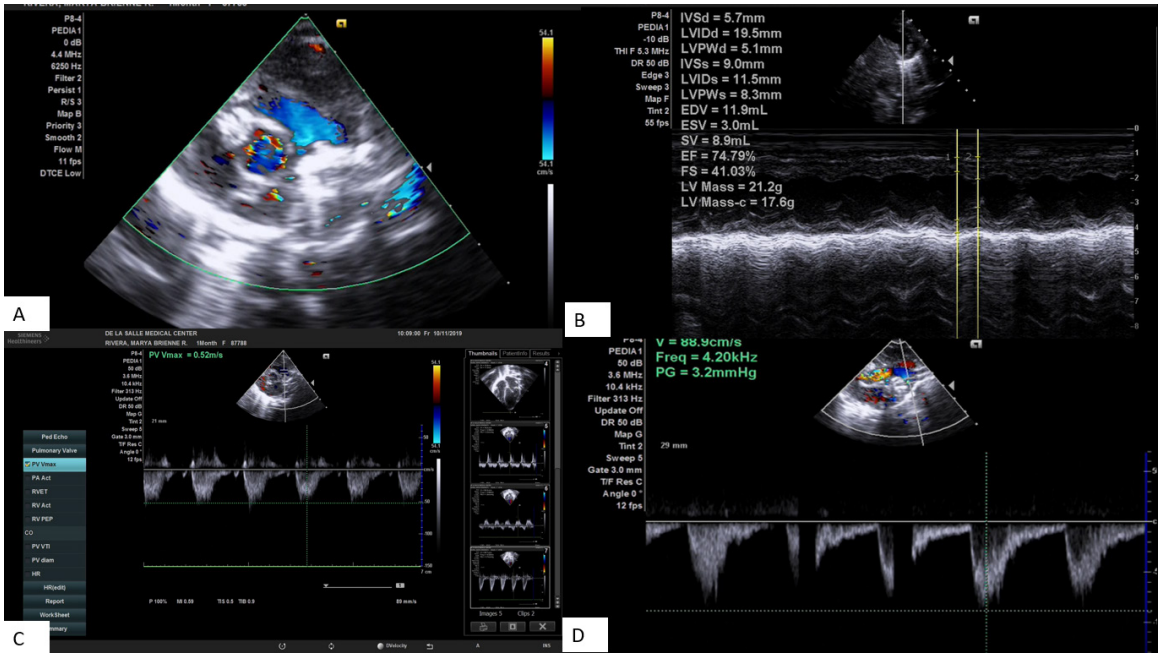

Figure 7. Transthoracic echocardiography images 1 month after percutaneous closure of PDA. Pictures A shows device in place and no leak. Picture B shows a decreased in LVEd at 1.9cm (from 2.2cm pre-device closure). Pictures C and D show Doppler views in peripheral pulmonary artery and descending aorta, respectively. No pressure gradient was detected in descending aorta and peripheral pulmonary artery

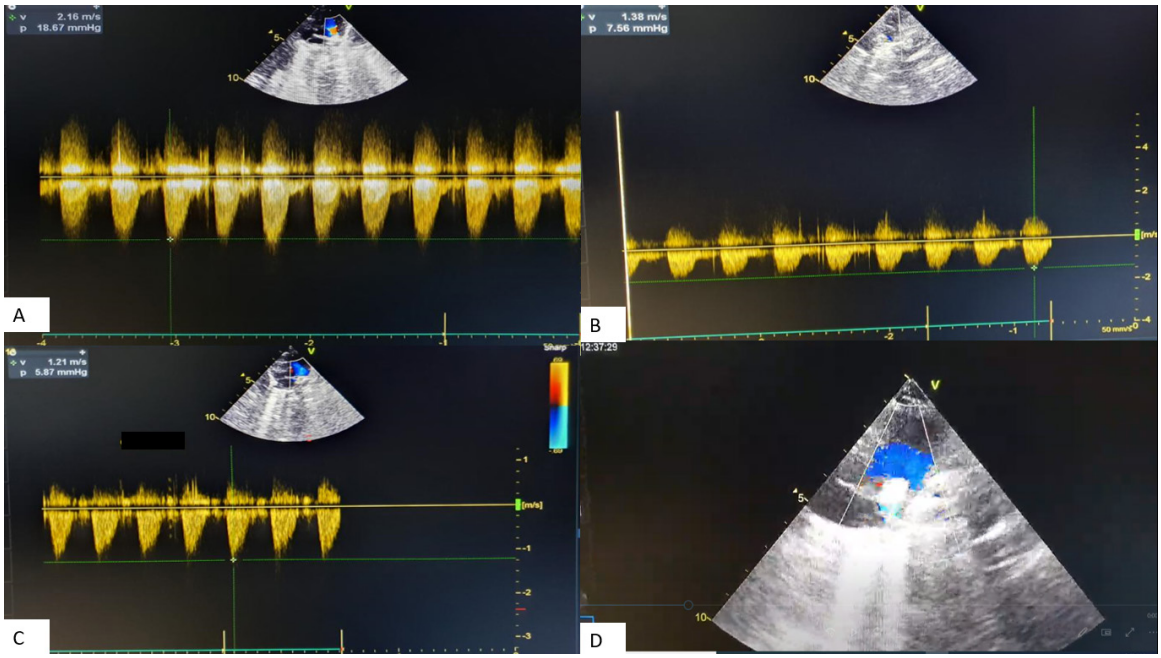

Figure 8. Transthoracic echocardiography images after percutaneous closure of PDA. Pictures A shows a gradient at the LPA at 18 mmHg, 24-hours post closure. Picture B shows a decreased in the gradient at the LPA into 7 mmHg after 1 month post closure. Pictures C and D show Doppler views descending aorta showing no pressure gradient.

Table 2 shows the echocardiographic characteristics of patients pre-closure, 24-hour post closure and after 1 month post-closure. All patients had significant decreased in the LVEd and LA size after 1 month post procedure. There is also a decreased in the PAP of all patients after 1 month. One patient with LPA stenosis immediately after the procedure had resolution of the stenosis after 1 month. The two patients who had mild narrowing at the descending aorta had persistence after 1 month but no significant signs and symptoms of

obstruction was noted.

Table 3 shows the immediate complications post PDA device closure. One patient who had pneumothorax prior to the procedure had recurrence of massive pneumothorax post procedure and evently succumbed. One patient had mild narrowing of the left pulmonary artery but resolved after 1 month. Two patients had mild narrowing at the descedning aorta. One of which had resolution while the other one had decreased in the degree of narrowing after 1 week post procedure. Two patients had small PDA leak within the device wherein one patient had persistence of the leak afer 1 week post procedure. One patient had bleeding at the punctured site needing blood transfusion.

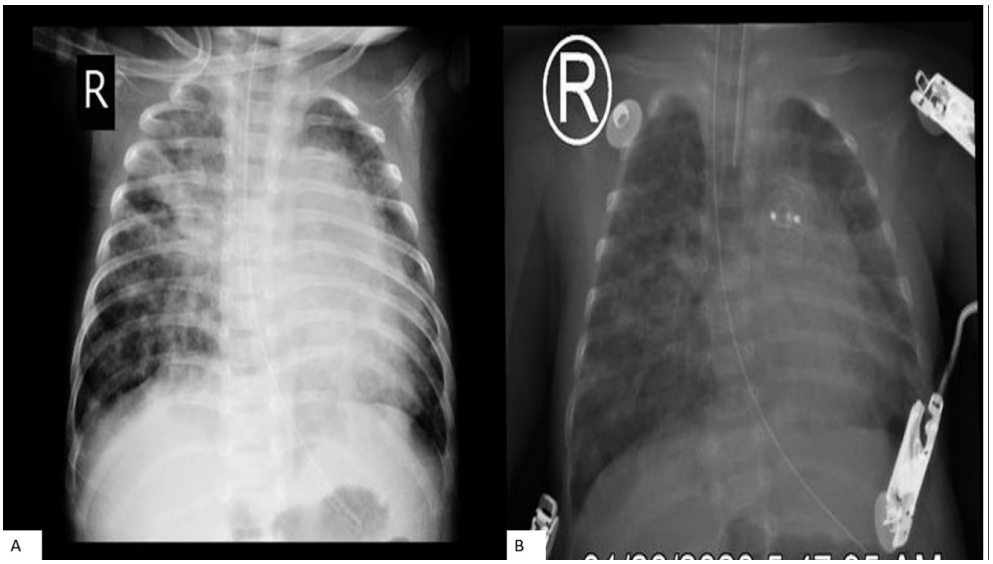

Figure 9. Picture A shows chest radiography prior to device closure. Picture B shows chest radiography 24 hours post device closure with noted significant decreased in pulmonary congestion and heart size. The device was noted to be in place.

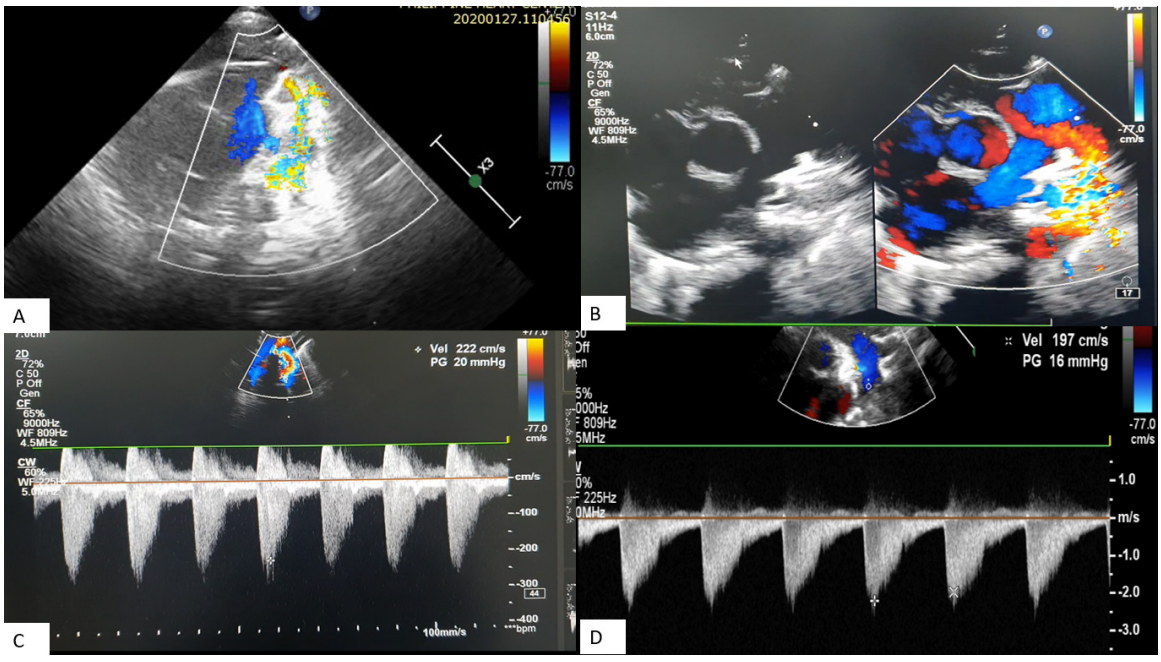

Figure 10. Picture A and B showed PDA leak of 0.18cm on the side of the device post device closure after 24-hours and 1 week respectively. Picture C showed gradient at descending aorta at 20 mmHg 24 hours post device closure. Picture D showed a decreased in the gradient at the descending aorta at 16mmHg after 1 week.

Table 2. Echocardiographic characteristics pre closure, 24-hour post closure and 1-month post PDA device closure

	CASE 1			CASE 2			CASE 3			CASE 4			CASE 5		
	Pre-closure	24-hr post closure	1-mo post closure	Pre-closure	24-hr post closure	1-mo post closure	Pre-closure	24-hr post closure	1-mo post closure	Pre-closure	24-hr post closure	1-mo post closure	Pre-closure	24-hr post closure	1-week post closure
PDA size at pulmonic end (mm)	3	PDA leak 0.11cm	-	2.7	No PDA leak	-	2.5	No PDA leak	-	3.5	No PDA leak	-	2.9	PDA leak 0.18cm	PDA leak 0.18cm
LV ed (cm)	1.87	1.7	-	1.86	1.7	1.6	2.2	1.9	1.7	2.1	1.6	1.5	2.49	2.3	2.1
LA (cm)	1.9	1.85	-	1.5	1.5	1.4	1.6	1.5	1.4	1.4	1.0	1.0	1.2	1.1	1.0
PAT by PAT (mmHg)	43	40	-	74	81	54	47	56	38	48	46	40	68	75	58
LVEF (%)	80	54	-	76	69	76	81	76	79	83	88	86	78	75	80
Tricuspid regurgitation	Jet of 32 mmHg	Jet 20 mmHg	-	Jet 23 mmHg	Jet 14 mmHg	-	-	-	-	Jet 11 mmHg	-	-	-	-	-
Mitral regurgiation	-	-	-	Jet 37 mmHg	Jet 22 mmHg	Jet 18 mmHg	Jet of 68 mmHg	Jet 54 mmHg	Jet 34 mmHg	Jet 19 mmHg	-	-	-	-	-
LPA gradient (mmHg)	-	-	-	-	4	-	-	4	3	-	18	7	-	4	-
Aortic gradient (mmHg)	-	-	-	-	11	10	-	6	3	-	5	-	-	20	16

Table 3. Complications post PDA device closure

	24 Hours Post closure	1-Month Post Closure
Major Complication		
Death		1[a]
Minor Complications		
Mild narrowing of left Pulmonary Artery	1	Resolved after 1 month
Mild narrowing at the Descending Aorta	2	1 - resolved after 1 month 1 - decreased in degree after 1 month
Small PDA leak (within the device)	2	1 - died after 48 hours 1 - decreased PDA leak after 1 week
Bleeding at the punctured site needing blood tranfusion	1	

[a]*Death on 3rd day post closure to massive pneumothorax*

DISCUSSION

Transcatheter PDA closure options have expanded significantly since the first report of this approach in 1979 and currently, percutaneous transcatheter occlusion is standard care beyond the neonatal period with satisfactory results.[1] However, there are reports of its feasibility in premature infants with low birth weight or even extremely low birthweight.[6,7] The problems that are usually encountered in preterm PDA for catheter intervention are technical challenges involved in catheterizing extremely small patients like difficult vascular access and availability of a suitable device due to variable duct sizes and shape and development of adjacent vascular obstruction. Other problem include keeping the small patients thermo-regulated at all times. In our patients, a pre-warmed blankets and mattresses were used, all fluids used for flushing were warmed including the antiseptic solution for skin disinfected were warmed as well.

During transcatheter closure, an arterial access was used for pressure monitoring and also allows initial aortography to be performed without crossing the duct and thus can minimize the risk of ductal spasm and consequent underestimation of the size of the duct. Also, it permits subsequent aortography to locate a good position of the device prior to release and avoid iatrogenic coarctation of the aorta. However, arterial injury has been identified as one of the most significant complications of interventional PDA occlusion especially in those children with lower body weight.[6] Hence, transcatheter closure through single venous approach were done in our patients. Avoiding arterial access by single venous approach could minimize possible major complications associated with arterial puncture like occlusion, embolism, dissection, limb ischemia and bleeding. The disadvantage of this single venous approach lacks precise angiographic view thru an aortography needed prior to the deployment of the device to secure proper location of the occluder and to determine aortic obstruction. Based on a study by Baykan et al[8], good echocardiographic image is sufficient for the safety of the procedure. Echocardiography was used to guide device placement, estimate the blood flow ensuring absence of obstruction to the adjacent vessels and to evaluate for residual ductal shunting prior to device release.

Appropriate occluder selection based on the morphology of the ductus and imaging assessment before and during deployment have proven essential to the success of transcatheter PDA closure in preterm and low birthweight infants. Few devices are particularly suited for PDA closure in small and preterm infants and in our institution, the only available occluder suitable for such is the Konar-multifunctional occluder (MFO). The Konar-multifunctional occluder (MFO) is a soft woven mesh self-expanding device with two discs joined by an articulate. Each disc of the MFO has a hub on the external surface so the device can be either retrogradely or anterogradely positioned. It has a length of 4 mm but it is self-expanding thus can increased application to the anatomic variants of PDA in premature infants. It has a softer delivery cable which allows for much more predictable release of the device and has a unique microcatheter delivery sheath, which is desirable for small infants and increased application to the anatomic variants of PDA in premature infants.

Sathandam et al.[9] described successful echocardiography guided, antegrade PDA occlusion approach via femoral venous access in 12 patients with a median weight of 1210 (range 700-3500 g). In our study, complete ductal occlusion was achieved post procedure in 3 out of 5 patients. One patient who had a small insignificant residual shunt located within the device noted with progressive decreased in size of the PDA leak after 1 week post device closure. Another patient who had small residual shunt died due to massive pneumothorax unrelated to the procedure. In our study, minor complications like iatrogenic coarctation of aorta was noted in two patients. One of which had resolution after 1 month post procedure while the other one had persistence of the narrowing in the descending aorta but with noted decreased in degree after 1 week post procedure. On the other hand, left pulmonary artery branch stenosis was noted in one patient immediate post device closure however become less pronounced after a month post device

closure similar to the study done by Baspinar et al.[10] In our study, no vascular complications were noted due to the use of a microcatheter delivery sheath and the use of venous access only.

CONCLUSION

In summary, our initial experience in transcatheter closure of PDA is feasible as an alternative treatment of PDA in preterm and low birth weight infants. In this study, we described the successful use of venous access procedure with echocardiographic guidance. Careful patient selection, timely referral and high degree of technical skills by the interventionalist and echocardiographer are of high considerations. The Konar-MFO™ is a new self-expanding device that may be useful for the occlusion of PDA in small premature infants.

LIMITATION OF THE STUDY

This is a descriptive case series study with a limited number of patients. There is no established PDA closure algorithm for this group of patients hence questions regarding patient selection and the optimal timing for percutaneous closure remain controversial. The decision to refer the patient for closure was at the discretion of the attending physician. This study reviewed only the short-term results, thus further studies designed to compare long-term improvements in respiratory and other clinically significant outcomes should be done. In the diagnosis of a clinically significant LPA stenosis, we cannot rely on transthoracic echocardiography and a lung perfusion scan may help on follow-up to better understand the natural history of device-related stenosis and the need for reintervention. Another limitation of the sudy is follow-up of the patients for the patency of femoral vessels with doppler ultrasound (doppler scan).

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Editorial Review

An interventional procedure done in a very high risk subset of patients, despite being a relatively low-risk intervention must first and foremost establish the risk-benefit ratio before undertaking such option. First, is to selectively screen those preterm neonates making sure they meet these validation criteria; is the procedure the only option? Are the signs and symptoms primarily due to the PDA or other medical comorbidities? Is the ratio tilted towards the favor of benefit rather than the risk? Second, is the standard and conventional management of surgery comparable to the result of the series done in the institution? Lastly, comparative studies on medical and surgical regimens against transcatheter intervention from other renowned international cardiovascular institutions must have been thoroughly extrapolated. Considering the results of this series, there is a lot to be done answering these credibility issues in the future related papers. But overall, this is a good series sans the validation and comparative analysis. I like this paper because of its novelty and trailblazing approach to a very challenging set of pediatric patients.

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The study of M.S. Quitola, MD and J.A. Villareal, MD shared their experience in transcatheter PDA closure in premature neonates with gestational age between 28 weeks to 33 weeks and whose birth weight was between 1,000 grams to 2,000 grams. The incidence of patent ductus arteriosus (PDA) is prevalent in premature neonates and low birth weight neonates. The management of PDA in these infants is significantly important as complications secondary to left -to-right shunting increases problems such as pulmonary edema, bronchopulmonary dysplasia, necrotizing enterocolitis and intraventricular hemorrhage. This study is a valuable as it has demonstrated the safety and success of transcatheter closure of PDA among premature and low birth weight neonates. The size of the device and protrusion of the disc into the aorta and pulmonary artery are major concerns during the procedure. The closure rate was followed up with echocardiography. Residual leaks and bleeding were the problems seen in the study. Proper choice of the device, such as Konar-Multifunctional Occluder (MFO) plays a pivotal role in interventional catheterization procedures. The study also emphasized the importance of better device and accumulation of experience in interventional pediatric cardiology.

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Pediatric Invasive Cardiology

Comparison of Outcome and Cost of 1-Day versus 3-Day Percutaneous Transcatheter Closure of Isolated Patent Ductus Arteriousus in Children

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Background --- Percutaneous transcatheter occlusion of patent ductus arteriosus has been the standard of care beyond the neonatal period with satisfactory results and low morbidity rates. The aim of this study is to compare a 1-day PDA device closure clinical pathway wherein the procedure and discharge of the patients be done within 24 to the currently being used 3-day PDA device closure pathway in terms of clinical outcome and cost.

Methods --- This is a ambispective cohort study done at the Philippine Heart Center. Consecutive patients for PDA device closure were recruited. Patients were classified according to the clinical pathway into 3 day and 1 day. In-hospital outcomes were recording and costing was computed.

Results --- Eighty-eight pediatric patients were included in the study, 33 of which were under 1-day pathway and 55 patients were under 3-day pathway. The 3-day pathway group had a significantly younger age group with a mean of 4 years, the youngest was 2 years old. The 3-day pathway group has lower weight with a mean of 13 (10-20) kgs and has a lower height with a mean of 97 (84-118) cms. There was no significant difference between the two groups in terms of fluoroscopy time, procedural time, PDA size, size and type of PDA occluder used. All of the patients in both groups had successful implantation of the device without embolization. There is no significant difference between the two groups in terms of the presence of complications. The complications after PDA device closure noted were presence of residual shunt, obstruction to adjacent vessels, fair left ventricular function and development of an infection. The 3-day pathway group was more expensive with a median cost of Php 178, 000.

Conclusion --- One-day PDA device closure pathway is comparable to 3-day PDA device closure pathway in terms of safety and has the advantage of lesser costs given with proper screening of patients. ***Phil Heart Center J 2020;22(2):15-21.***

Key Words: Patent ductus arteriosus ■ transcatheter closure ■ 1-day pathway ■ 3-day pathway ■

Patent ductus arteriosus (PDA) accounts for 5% to 10% of congenital heart defects. The presentation of PDA depends upon patient age and the size of the PDA. Patient with moderate to large PDA can present with signs of congestive heart failure, pulmonary vascular disease and endarteritis necessitating closure of the defect. Available treatment modalities include surgical ligation in large ducts not suitable for intervention treatment and transcatheter closure for small to moderate sized ducts whether by coil embolization or occluder devices. Transcatheter PDA closure options have expanded significantly since the first report of this approach in 1979 and currently, percutaneous transcatheter occlusion is standard care beyond the neonatal period with satisfactory results.[1]

Transcatheter PDA closure is now an established procedure and various devices are available in clinical practice to cover almost all types of PDA and generally have satisfactory outcomes but complications happen. According to the report of Faella and Hijazi, 15 (4.7%) of 316 patients experienced complications, including one each patient with sudden death after procedure, hemolysis, transient asystole, ST depression due to blood loss, surgical closure due to device embolization, malpositioning of the device, and blood transfusion due to blood loss.[2]

Since PDA device closure is the most widely used techniques at the present time, the increasing number of PDA patients has led to accumulating logistic constraints.

A reduction in hospital stay and the application of day-case facilities were advocated to reduce procedure-related costs. Also, there would be an increase in the number of PDA patients to be accommodated since there would be an increase in the number of available beds because of shorter hospital stay.

In the Philippine Heart Center, there is an overwhelming number of patients seen at the outpatient department awaiting intervention. Currently, the pediatric cardiology department had formulated a 3-day clinical pathway for transcatheter closure of an isolated PDA in children. In a study done by Paguntalan, et al[3] on the outcome of 537 pediatrics patients who underwent transcatheter device closure of PDA at Philippine Heart Center from year 2007-2017, it was concluded that PDA device closure is a safe and minimally invasive procedure with a 99% success rate and has a risk for adverse events at 8.38%. Among the adverse events noted were residual shunts, blood loss, LPA stenosis, device allergy, device embolization and arrhythmia. In a study done by Villareal, et al[4], safety and cost analysis between transcatheter closure of PDA using ductal occluder device and closed heart surgery in pediatric age group was compared. It was concluded that success of treatment based on immediate occlusion and absence of murmur had no significant difference between the two groups, however complications like presence of pneumothorax and bleeding requiring transfusion was higher in surgery group compared to transcatheter group.

The aim of this study is to compare a 1-day PDA device closure clinical pathway wherein the procedure and discharge of the patients be done within 24 to the currently being used 3-day PDA device closure pathway in terms of clinical outcome and cost. No studies from other foreign countries were published yet regarding 1-day pathway for transcatheter device PDA occlusion.

OBJECTIVES

This study aims to compare the clinical outcomes and the cost of 1-day admission versus the present 3-day protocol of percutaneous transcatheter closure of isolated patent ductus arteriosus in children in this institution.

Specific Objectives

1. To compare the outcome of 1-day versus 3-day percutaneous transcatheter closure of PDA as to the procedural success defined as successful implantation of the device without embolization.
2. To compare the complications (residual shunts, bleeding from punctured sites, infections, arrhythmia, vessel injury) of 1-day versus 3-day percutaneous transcatheter closure of PDA.
3. To compare the actual in-hospital costs between the two groups.

METHODS

This is an ambispective cohort study conducted at the Philippine Heart Center from July 2019 to March, 2020. The study includes pediatric patients ages 1-18 years old with isolated PDA who underwent transcatheter device closure of PDA from September 2019 to February 2020; with hemodynamically significant PDA; and patients with Krichencho Type A (conical) shape as determined by angiography. Excluded were patients with PDA with coarctation of aorta or other assocardiac lesion needing surgical

intervention; PDA with pulmonary arterial hypertension; patients who needs intubation prior, during, or after the procedure; and patients without informed consent.

This study was approved by the Institutional Ethics Review Board (IERB) and consent was obtained from the legally authorized representative of the patient.

Study Maneuver. Consecutive patients for PDA device closure were recruited. The investigator obtained a written informed consent after adequate explanation of the aims, methods, anticipated benefits and potential risks of the study. Patients were classified into 2 groups according to number of hospital days: 1-day protocol group and 3-day protocol group (*Appendix A & B*). The choice of 1-day protocol or 3-day protocol was based on the preference of the attending physician. Both groups underwent standard catheterization protocol for percutaneous transcatheter PDA occlusion. (*Appendix C*).

Demographic data such as age, sex, weight, height and procedural date like fluoroscopy time, procedural time, PDA size and shape, type of PDA occluder and PDA occlude size were recorded and compared.

The primary outcome is procedural success defined as successful implantation of the device without embolization confirmed by 2D-echocardiography. Possible complications post-PDA device closure include residual shunts defined as persistence of PDA murmur and the presence of continuous doppler signal by 2D-echocardiography, bleeding from the punctured sites, infections, arrhythmia, complete heart block requiring intervention, obstruction to adjacent vessels (aorta and pulmonary artery), loss of peripheral pulses, device-related cardiac perforation and death. Complications that occurred immediately after the procedure, during the hospital stay and within 1 month after discharge were recorded.

In the computation of the cost for both procedures, only laboratory and other diagnostics like ECG and chest x-ray done as OPD and in-hospital charges were included. The actual in-hospital charges were gathered through the computer-generated medical records of this institution. The professional charges and the additional diagnostic studies on follow-up were not included. Social costs such as transportation and food were likewise not included.

Sample Size. A minimum of 84 patients from both groups are required for this study based on assumed large effect size between 1-day protocol and 3-day protocol in terms of hospital and procedural cost, 5% level of significance and 95% power.

Statistical Analysis. Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, median and inter quartile range for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. Independent Sample *T*-test, Mann-Whitney U test and Fisher's Exact/Chi-square test were used to determine the difference of mean, rank and frequency, respectively, between patients on 1-day protocol and 3-day protocol. All statistical tests were two-tailed test. Shapiro-Wilk was used to test the normality of the continuous variables. significance. STATA 13.1 was used for data analysis.

RESULTS

Eighty-eight pediatric patients were included in the study, 33 of which were under 1-day protocol pathway and 55 patients were under 3-day protocol pathway. Table 1 shows the characteristics data of pediatric patients with patent ductus arteriosus according to the number of hospital stay days. The 3-day protocol group had a significantly younger age group with a mean of 4 years, the youngest was 2 years old. There was no significant difference between the genders of both groups. There was a significant difference between the weight and height of the patients in both groups. The 3-day protocol group has lower weight with a mean of 13 (10- 20)kgs and has a lower height with a mean of 97 (84-118) cms. There was no significant difference between

the two groups in terms of fluoroscopy time, procedural time, PDA size, size and type of PDA occluder used.

Table 1. Characteristics Data of Pediatric Patients With PDA between 1-Day versus 3-Day Protocol

	1-DAY PROTOCOL	3-DAY PROTOCOL	P-value
	(n=33)	(n=55)	
	Frequency (%); Mean + SD/Median		IGR
Age (years)	8 (3 to 11)	4 (2 to 7)	0.009
Sex			
Male	23 (69.7)	38 (69.09)	0.952
Female	10 (30.3)	17 (30.91)	
Weight (kgs)	21.8 (16 to 30)	13 (10 to 20)	<0.001
Height (cms)	117 (104 to 136)	13 (10 to 20)	<0.001
Fluoroscopy time	4.38 +1.28	5.02 ± 1.66	0.059
Procedural time	27.27 +8.16	30.07 ± 8.85	0.219
PDA size, pulmonic end (mm)	4.39 ± 1.28	4.17 ± 1.83	0.555
PDA occlude size (mm)	11.45 +2.31	10.95 +3.12	0.419
Type of PDA occlude used			0.348
Lifetech™	27 (81.82)	49 (89.09)	
Cocoon™	2 (6.06)	4 (7.27)	
Hyperion™	4 (12.12)	2 (3.64)	

Table 2. Outcome and Complications After PDA Closure Between 1-Day versus 3-Day Protocol

	1-Day Protocol	3-Day Protocol	P-value
	(n = 33)	(n = 55)	
	Frequency (%)		
Primary Outcome Positive	0	0	0.952
Negative	33 (100)	55 (100)	
Complications			0.919
None	26 (78.79)	42 (76.36)	
Residual Shunt	1 (3.03)	2 (3.64)	
Obstruction	2 (6.06)	4 (7.27)	
Low Function	2 (6.06)	5 (9.09)	
Infection	2 (6.06)	1 (1.82)	

Table 3. Comparison of Cost Between 1-Day vs. 3-Day

	1-Day Protocol	3-Day Protocol	P-value
	(n = 33)	(n = 55)	
	Median (IQR)		
Hospital and Procedural cost (by P1000)	166.78 (165 to 168)	178 (175 to 182)	<0.001

Table 2 shows the outcome complications after PDA device closure according to the number of hospital stay days. All of the patients in both groups had successful implantation of the device without embolization. There is no significant difference between the two groups in terms of the presence of complications. The complications after PDA device closure noted were presence of residual shunt, obstruction to adjacent vessels, low left ventricular function, and development of an infection.

Table 3 shows the average cost according to number of hospital stay days. There was a significant difference in the hospital and procedural cost between the two groups. The 3- day protocol group was more expensive with a median cost of Php 178,000.00.

DISCUSSION

Our study showed that 1-day pathway PDA device closure is feasible and can be performed safely with no increase in risk under the clinical conditions defined in this study. A series of criteria was used in the study to include or exclude patients and this leads to the selection of a population with a low risk for clinical complications who would therefore be eligible for rapid discharge. A proper coordination with the involved hospital staff was also done regarding the 1-day pathway set-up to ensure availability of beds, preparation of patient on admission and facilitation of discharge process after the procedure.

All patients who underwent PDA device closure in both groups had successful implantation of the device with no embolization. Patients with Krichencho Type A (conical) shape as determined by angiography were only included because of lower incidence/ chance of embolization as compared to other types of PDA morphology.

The complications associated with transcatheter PDA device closure based on a study done by Paguntalan, et al.[3] were residual shunts, blood loss, LPA stenosis, device allergy, device embolization and arrhythmia.

In our study, patients were observed for the occurrence of possible complications after PDA device closure immediately post procedure, prior to discharge then within 1 month post procedure. Minor complications were noted in 22.7% of the total patients and these include presence of residual shunt, LPA stenosis, fair ejection fraction and development of infection. Three patients had small residual shunts less than 2 mm in diameter, which was considered small and needs no further intervention except follow-up. All three patients had complete closure of the residual shunt 1 month after the procedure determined through echocardiography. Left pulmonary stenosis was observed in 6 (6.8%) patients however it was not considered as significant obstruction. Patients who developed LPA stenosis are those with low body-weight with a large PDA requiring a larger device. These patients will be followed-up clinically and through echocardiogram since doppler flow acceleration may resolve spontaneously with the patient's growth. There were 3 patients who developed a fair LV function but had improved to normal function 1 week. Three patients developed pneumonia within 1 week after discharge and was treated accordingly. Generally, in this study, manageable minor complications were recorded and did not outweigh the benefits of transcatheter closure of patent ductus arteriosus.

In this study, more patients had lower weight and height in the 3-day pathway because this group of patients belonged to a younger group. Even though, there is no significant difference of both groups in terms of the success of the procedure and presence of minor complications. In our study, it was found out that 1-day pathway leads to a cost reduction of around Php10,000.00 per patient. Next to minor cost reduction, this 1-day pathway renders substantial logistic benefits for the hospital as to the increase in the number of available beds and hospital staff to accommodate more patients.

Transcatheter closure of PDA using 1-day pathway is a viable option with no major risks for patients. In the presence of favorable characteristics of patients such as absence of pulmonary arterial hypertension and considering the PDA morphology to lessen the risk for embolization, this 1-day pathway shortened hospital stay and cost. This may be one way of adapting to the increasing demand for transcatheter PDA closure. More PDA patients will be accommodated since there would be more available beds due to shorter hospital stay for procedure.

STUDY LIMITATION AND RECOMMENDATION

This is a short-term study as it monitored patients until 1-month post device closure only. It is recommended to include long-term efficacy and morbidity. For a more accurate cost benefit study, indirect costs such as the cost of patients' care giver and the loss of productivity in the family should be put into consideration. Because this is an ambispective study we wre not able to incorporate the indirect cost.

APPENDICES

Appendix A
Process flow for the 1-day protocol

OPD screening of patients suitable for PDA device closure

↓

Within 1 week prior to the scheduled procedure:

1. Pre-procedural diagnostic examination including CBC PT, APTT, creatinine, Chest X-ray and 15 lead ECG will be done.
2. Patient will be preliminary examined / evaluated by CV Anesthesia for the pre-procedural instruction including NPO time.

↓

Day of Admission:

1. Patient will be admitted by 6am and the procedure will start at 10am
2. Final evaluation of CV Anesthesia prior to procedure
3. PDA device closure procedure
4. Post-procedure monitoring at the ward

↓

The following day:

1. CXR and 2D echocardiography, post-prodecure
2. Discharge patient if no problem

Appendix B
Process flow for the 3-day protocol

OPD screening of patients suitable for PDA device closure

↓

Day 1

1. Patient will be admitted.
2. Pre-procedural diagnostic examination including CBC, PT, APTT, creatinine, CXRay and 15 Lead ECG will be done.
3. Patient will be examined / evaluated by CV Anesthesia for the pre-procedural instruction including NPO time.

↓

Day 2

1. Patient will undergo PDA Device Closure
2. Post-procedure monitoring at the ward

↓

Day 3

1. CXR and 2D echo post-procedure
2. Discharge patient if no problems

***Appendix C**: *PDA device procedure process*

The PDA device closure procedure will be done at the cardiac catheterization laboratory. Patients will be referred to anesthesiology service for IV sedation during the procedure. All patients will receive prophylactic antibiotic therapy prior to catheterization. During the procedure, arterial and venous access will be established. Aortic and pulmonary pressures will be collected to determine presence of pulmonary arterial hypertension. Descending aortogram then will be done to determine the size and shape of the PDA and assess the diameter of the ampulla and the pulmonary end as well as the length of the duct to determine appro-

priate size of the device. There are three (3) local brands of PDA occlude available in our institution: Lifetech Scientific, Cocoon and Hyperion. The availability of the devices at operation day will be the main factor in the choice of device to be used.

Prior to the deployment of the PDA device, a repeat descending aortogram will be done to check if the device is properly placed and presence of device leak. After successfully deploying the device, patient will be transferred to the ward for post procedure monitoring. All patients will undergo chest x-ray and 2D-echocardiography with CFDS prior to discharge. Any factors that will be seen that compromises patient safety or needs further observation, the patient will not be discharged. Patients will be discharged if there are no contraindications.

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Editorial Review

Patent Ductus Arteriosus (PDA) Device Closure has indeed made a breakthrough in the management of isolated PDA. In the Philippine Heart Center (PHC) setting, PDA device closure has surpassed the census of surgical closure in 2018. The outcome has so far been commendable with over-all procedural success rate of 99% and complication rate of only 8.38% (Paguntalan, Kristine MD, 2020). Because of the growing popularity of the modality, it has become the procedure of choice in PDA closure in most centers like the PHC.

This study made a comparison between 1-day and 3-day protocols for PDA Device Closure. The term 1-day in this research actually corresponds to a 24-hour overnight stay in the hospital and not a whole day admission-discharge protocol. It particularly compared the procedural success rate, complications and cost of hospitalization/procedure between the two groups. The result was comparable between the two groups except for the procedural and hospitalization cost which was lower in the 1-day protocol.

The attempt to compare the two protocols is indeed commendable because the results would definitely aid in the recommendation to use the 1-day protocol for isolated and uncomplicated PDA. However, I would suggest that in future studies, age should be standardized in both groups. It was noted that older patients were analyzed in the 1-day protocol. Many will be interested as well to find out how the younger age will fare in the 1-day protocol. As has been suggested by the author, the computation of the productivity loss of caretakers should likewise be taken into consideration. This will put more weight on the cost incurred if the 3-day protocol is followed. The study did not mention if there were different operators involved but since the success rate for both protocols was 100% and the complication rate was not significant between 2 groups, I think that operator factor would not have that much bearing in this research.

Over all this is a good study to show that for isolated and uncomplicated PDA, the number of days of hospitalization will not greatly affect the outcome. In developing countries like the Philippines, the 1-day protocol is a judicious option considering its cost and the unremarkable rate of complications. This protocol will greatly improve the number of patients served, especially those lined-up for the procedure for many years at the outpatient department and the turn-around of patients admitted at the ward. This will equate to a better service and more satisfied clientle.

Nothing to disclose.

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Editorial Review

The 3-day clinical pathway for transcatheter closure of an isolated Patent Ductus Arteriosus (PDA) in children of the Philippine Heart Center was revisited and tested for both cost as well as procedural and clinical outcome in this paper titled, "Comparison of Outcome and Cost of 1-day versus 3-day Percutaneous Transcatheter Closure of Isolated PDA in Children".

Clinical pathways are standardized, evidence-based multidisciplinary management plans, which identify an appropriate sequence of clinical interventions, time frames, milestones and expected outcomes for a homogenous patient group.[1] Clinical pathways generally aims to support the implementation of evidence-based practice, improve clinical processes by reducing risk, reduce duplication through the use of a standardized tool, and reduce variation in health service process delivery.[1]

In this paper, the proposed 1-day clinical pathway for percutaneous duct closure was compared to the previously accepted institutional protocol. The objectives were simple, direct, and clear. The problem is in the homogeneity of the general sample population characteristics that were not achieved, as well as the inequitable distribution into each treatment arm protocol. The more challenging and technically difficult patients in terms of younger age and smaller size were placed in the "safer" 3-day treatment protocol. This group of patients benefitted the most in terms of closer monitoring and longer post-procedural observation inside the hospital.

It was very clear even without the benefit of statistical analysis that the 3-day treatment arm will cost more than the 1-day treatment protocol. What was promising and proven remarkably in this paper were the hospitalization and procedural cost could be reduced with good success in outcome and safety in selected patients.

Nothing to disclose.

REFERENCE:

[1]https://clinicalexcellence.qld.gov.au/resources/clinicalpathways

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Transcatheter Trial Occlusion of Patent Ductus Arteriosus with Pulmonary Arterial Hypertension

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Background --- Transcatheter occlusion of a patent ductus arteriosus (PDA) in pediatric patients with pulmonary arterial hypertension (PAH) carries some challenges and risks. This descriptive study aims to project the short-term course and outcome of pediatric patients with pulmonary hypertension who have undergone transcatheter patent ductus arteriosus closure.

Methods --- Pediatric patients 0-18 years old with patent ductus arteriosus and pulmonary hypertension who have undergone transcather PDA trial occlusion at the Philippine Heart Center from March 2015 to February 2018 were included in this study. Charts were reviewed and data were gathered. Measurement of the PDA sizes, pulmonary pressure before and after trial occlusion, short term course and outcome were obtained and tabulated.

Results --- Out of the 27 patients with PDA and PAH who have undergone trial PDA occlusion, 33% were aborted and only 66% occlusions were completed. Immediate complications noted were migration of the PDA device and pulmonary hypertensive crisis and 1 reported mortality.

Conclusion --- Patients with patent ductus arteriousus and pulmonary hypertension carry more risks when undergoing transcatheter device closure. The decision to proceed with the occlusion of the ductus arteriosus is based on the hemodynamics of the patients and their overall response to the procedure. Careful patient preparation, timely intra-procedural decision making whether to proceed or to abort occlusion of the shunt, post-procedural management of pulmonary hypertension and prevention of other possible complications are imperative in achieving a good outcome. ***Phil Heart Center J 2020;22(2):24-29.***

Key Words: Patent ductus arteriosus ■ pulmonary hypertension ■ trial occlusion ■ transcatheter closure

The ductus arteriosus is a normal fetal structure that is essential in providing adequate cardiac output in the fetus.[1] Being an important and obligatory shunt required in the fetal circulation, its persistence immediately after birth is almost universal.[2] Normally, constriction of the ductus after birth will lead to its functional and anatomical closure but it is reported to remain patent in approximately 0.05% of all live births.[1] Patent Ductus Arteriosus (PDA) is considered a form of congenital heart disease if it is still patent beyond the third month of life in term infants. It can either be an isolated lesion or associated with other various congenital heart diseases.[2] Sympomatic PDA accounts for 5-10% of congenital heart defects and may present with a murmur, symptoms of increased pulmonary blood flow, volume overload of the left side of the heart and pulmonary hypertension.[1] Before the use of echocardiography in the diagnosis of patent ductus arteriosus, angiography through cardiac catheterization was the gold standard.[1] Through the years, the use of cardiac catheterization in patients with PDA has shifted from making the diagnosis to establishing operability through hemodynamic studies and at present, transcatheter closure of the shunt. Patients with pulmonary hypertension secondary to a PDA can now undergo hemodynamic studies and then proceed to occlusion of the ductus arteriosus in a single procedure.

The reactivity of the pulmonary vascular bed and the hemodynamics of a patient after

device occlusion of a large PDA with pulmonary hypertension is better observed and can be aborted immediately once the patient presents with pulmonary hypertensive crisis during trial occlusion. Since the introduction of transcatheter device closure in the 1960-1970s, the use of several approaches and devices has been reported. Transcatheter occlusion of PDA is a well-established alternative to surgical ligation or transection. Even in the presence of a calcified ductus arteriosus with pulmonary hypertension, transcatheter closure is frequently preferred over surgical repair.[3] Quiang reported that transcatheter closure in an adult with PDA and pulmonary hypertension is generally safe but the risk for pulmonary hypertensive crisis or acute right heart failure is still present which may even result to irreversible pulmonary vascular disease.[4]

In the pediatric population, proper screening of patients and timely intervention is essential in the success of any interventional procedure. Patients who have already developed pulmonary hypertension may still benefit from transcather device closure of a PDA. This descriptive study aims to project the demographic profile, short term course and outcome of patients with a patent ductus arteriosus and pulmonary hypertension who underwent cardiac catheterization and trial occlusion of the PDA.

OBJECTIVES

To describe the short term course and outcome of patients with a PDA and pulmonary hypertension who have undergone cardiac catheterization for trial occlusion.

Specific Objectives

1. To review the sizes of the ductus arteriosus of patients prior to undergoing device trial occlusion
2. To review the pulmonary pressure on 2D echocardiography of patients prior to and after undergoing PDA device closure.
3. To determine the presence of any immediate complications in patients with PDA and pulmonary hypertension who have undergone PDA trial occlusion.

METHODS

This is a descriptive study done at the at the Philippine Heart Center. Included in the study were pediatric patients from 0 to less than 19 years old, diagnosed with PDA and pulmonary hypertension who have undergone transcatheter trial occlusion at the Philippine Heart Center from March 2015 to February 2018. Excluded in the study were patients with incomplete data during chart review.

Study Maneuver. The list of all pediatric patients from age 0 to less than 19 years old with diagnosis of PDA and pulmonary hypertension who underwent cardiac catheterization and PDA trial occlusion was obtained. Chart review was done and data were collected. Measurement of the size of the PDA prior to the procedure, the pulmonary pressure before and after the procedure by 2D-echocardiography, as well as any immediate complications after the procedure were noted.

Statistical Analysis. All data collected were entered and tabulated in Microsoft Excel. Quantitative variables were summarized into mean and standard deviations.

RESULTS

The study included 25 patients diagnosed with PDA and pulmonary arterial hypertension from 0 to less than 19 years old from March 2015 to February 2018. Two of the patients underwent a second PDA trial occlusion after an aborted first attempt and were entered twice as subjects in this study (total of 27 cases of PDA trial occlusion).

Table 1. Basic Demographic Profile on Age, Sex, Other Associated Cardiac Lesion and Type of Procedure Done

Basic demographic profile	Frequency (n=27)
Sex	
Male	8
Female	19
Age	
<5 years old	4
5-10 years old	5
>10 years old	18
Diagnosis	
PDA only	24
PDA + VSD doubly committed	1
PDA + VSD perimembranous	1
PDA + ASD secundum	1
Procedure done	
PDA occluded	18
Procedure aborted	9

PDA - Patent Ductus Arteriosus; VSD - Ventricular Septal Defect; ASD - Atrial Septal Defect

Table 1 shows the basic demographic profile of all patients included in the study. Seventy percent of the patients are females. The youngest patient included in the study is 1 month old but most of the patients are more than 10 years of age with a mean age of 12.2 years. Eighty-nine percent of the patients have an isolated PDA while 11% or 3 subjects have other associated lesions. 1 patient had a peri-membranous ventricular septal defect, another had a doubly committed ventricular septal defect and 1 patient had a secundum atrial septal defect. Majority of the subjects completed the procedure while 33% of the procedures were aborted.

Table 2 lists down the ages, diagnoses, PDA size, pulmonary arterial pressure before and after occlusion measured by 2D echocardiography, immediate complications and outcome

Table 2. Measurement of PDA size, PA pressure before and after PDA occlusion, presence of immediate complications and outcome

Subjects (n=18)	Age	Diagnosis	Measurement of the PDA size before trial occlusion	Pulmonary arterial pressure before PDA occlusion	Pulmonary arterial pressure after PDA occlusion	Immediate complications	Outcome
1	17	PDA	0.5 - 0.8	76	50	None	Improved
2	3	PDA	0.5 - 0.8	39	25	None	Improved
3	1 mo	PDA	0.2	50	No data	Aspiration pneumonia	Died
4	4	PDA	0.4 - 0.8	62	84	Device migration to RPA	Underwent surgical device retrieval and PDA transection
5	18	PDA	0.8 - 1.0	124	84	None	Improved
6	17	PDA	0.7 - 0.9	56	50	None	Improved
7	15	PDA	0.8	46	25	None	Improved
8*	10	PDA	0.8 -.1.1	62	57	None	Improved*
9	13	PDA + ASD	0.3 - 0.5	50	43	None	Improved
10	7	PDA	0.6	76	45	None	Improved
11	14	PDA	0.7	67	56	None	Improved
12	1	PDA + VSD	0.5	70	83	None	Underwent surgical VSD closure
13	14	PDA	0.5	60	24	None	Improved
14	18	PDA	0.7 - 1.0	60	25	None	Improved
15	12	PDA	1.1	60	50	None	Improved
16*	14	PDA	1.0	63	25	None	Improved*
17	14	PDA	0.6 - 1.0	86	50	None	Improved
18	10	PDA	1.0	63	45	None	Improved

*Second attempt of PDA trial occlusion (first attempt was aborted)

of subjects who completed the transcatheter PDA occlusion. Mean age of this group of patients is 12.4 years. Majority of the patients were noted to improve and were discharged from the hospital with a mean hospital stay of 4 days. Two patients had another intracardiac shunt present. Most of the patients had a significant decrease in the pulmonary arterial (PA) pressure as measured by echocardiography which were done within 3 days from the procedure. The patient with concomitant VSD was noted to have increased PA pressure immediately after device closure. He was maintained on sildenafil and was able to undergo successful surgical closure of the VSD after 5 months. Another patient with increased PA pressure post procedure is a 4 year old female whose device migrated to the right pulmonary artery and documented with 2D-echocardiography which was done immediately post procedure. This patient underwent surgical device retrieval and PDA transection.

There was 1 reported mortality. The patient is a 1 month old infant who developed aspiration pneumonia 3 days after the procedure and eventually died.

Out of the 27 subjects who underwent PDA trial occlusion, 9 procedures were aborted. Patients in this group has a higher mean age (14.3 years) with ages ranging from 8 to 18. Only 1 patient had another shunt present which is a doubly committed VSD. This patient had hypertensive crisis during the procedure and eventually died within 24 hours. A total of 3 patients had pulmonary hypertensive crisis. The other 2 patients were given sedation and paralysis at the Pediatric ICU postprocedure and were eventually extubated within 48 hours. Out of the 9 aborted procedures, 2 of them eventually underwent PDA device closure after 2-3 months. All the patients who were discharged were given pulmonary dilators as part of their maintenance medications.

DISCUSSION

Transcatheter closure of a patent ductus arteriosus in the pediatric population is a safe and well tolerated procedure but performing this in a patient with pulmonary hypertension has many challenges. In this study, 37% of patients were not able to complete the PDA occlusion procedure due to pulmonary hypertensive crisis or observed unacceptable hemodyamic changes. There is a higher mean age in the group with aborted PDA occlusion. This is probably due to the higher incidence of pulmonary hypertension in older children with PDA. Sixty-six percent completed the device occlusion but with a reported complication of PDA device migration to the right pulmonary artery. There were 2 reported mortalities, 1 is due to pulmonary hypertensive crisis which began during the procedure and 1 late complication due to aspiration pneumonia which was brought about by other conditions in the patient. Two patients whose procedures were aborted previously eventually underwent successful PDA device occlusion after a few weeks.

A similar study done in India reported transcatheter PDA closure in 65 patients with pulmonary arterial hypertension. Around 5% were reported to have immediate post-procedure complications but resolved prior to discharge – one patient with a residual shunt had acute hemolysis that lasted for 48 hours and was managed conservatively, and 4 patients had transient loss of limb pulses. Around 10% of patients still had a pulmonary artery pressure recording of >50 mmHg by 2D-echocardiogram although the values were significantly lower than the pre-procedure PA pressures.

None of the patients had worsening symptoms of pulmonary hypertension on follow-up.[5] Another study done in China described 9 patients with pulmonary arterial hypertension who underwent transcatheter PDA closure. All 9 subjects showed >20% decrease in the pulmonary artery pressure but long term follow-up (mean follow up of 3.6 years) revealed that 4 out of the 9 patients still had increasing pulmonary artery pressure and worsening symptoms of PAH where in 1 patient eventually died from acute right heart failure triggered by pulmonary infection.[6] None of the mentioned studies on PDA occlusion with pulmonary arterial hypertension mentioned complications of embolization of the PDA device.

Table 3. Measurement of PDA Sizes and Pulmonary Artery Pressure of Patients Who Underwent PDA Trial Occlusion But Was Eventually Aborted

Subjects (n=18)	Age	Diagnosis	PDA size before trial occlusion	Pulmonary arterial pressure before trial occlusion	Complications during the procedure	Hospital course	Outcome
1	17	PDA	1.1	109	None	No events	Discharged
2	17	PDA	0.8 - 1.1	57	None	No events	Discharged
3	17	PDA	0.6 - 0.8	80	None	No events	Discharged
4	15	PDA + VSD doubtly committed	1.0	88	Pulmonary hypertensive crisis during the procedure (desaturation and hypotension)	Intractable acidosis and pulmonary hypertensive crisis	Died
5	13	PDA	0.8 - 1.0	56	Pulmonary hypertensive crisis during the procedure (desaturation and hypotension)	Extubated after 1 day	Discharged
6	8	PDA	0.7 - 0.9	50	None	No events	Discharged
7	18	PDA	0.8	67	None	No events	Discharged
8	10	PDA	0.8 - 1.1	63	Pulmonary hypertensive crisis during the procedure (desaturation and hypotension)	Extubated after 2 days	Underwent successful PDA occlusion after 3 months
9	14	PDA	1.0	63	None	No events	Underwent successful PDA occlusion after 3 months

Generally, the overall success of PDA trial occlusion from 2015 to 2018 is acceptable and has allowed patients who have very high risk for surgical transection or ligation to be given appropriate treatment.

One limitation of the study is the variability in the measurement of the pulmonary pressure in each patient. The measurements were based on the echocardiographic reports done before and after the procedure wherein variable parameters were used (PDA gradient and pulmonary acceleration time). It is recommended for future studies to acquire other hemodynamic data such as the measurement of pulmonary vascular resistance prior and after occlusion.

CONCLUSION

Patients with a large left to right shunt and pulmonary hypertension carry more risks when undergoing invasive procedures. One way of decreasing this risk is through trial occlusion by cardiac catheterization. This allows the operator to observe for the hemodynamic changes in the patient once the shunt is removed. The decision to proceed with the occlusion of the ductus arteriosus is based on the hemodynamics of the patients and their overall response to the procedure. Transcatheter occlusion of the PDA in patients with pulmonary hypertension has greater risks and challenges but careful patient preparation, appropriate intra-procedural decision making on whether to proceed or to abort occlusion of the shunt, post-procedural management of pulmonary hypertension and prevention of other possible complications are imperative in achieving a good outcome.

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Editorial Review

The result of transcatheter trial occlusion of PDA with pulmonary hypertension are encouraging as reported in the present study. 18 of the 27 (66%)patients had successful occlusion. Of the 9 procedures aborted, all of the cases were adolescents with large PDA with pulmonary pressure ranging from 60- 109 mmHg ,the reason to abort was development of pulmonary hypertensive crises in 4 patients of which one patient died and 3 were successfully treated. There was patient where the PDA device migrate to the distal pulmonary artery. To avoid this complication it would be prudent to oversize 4-10 mm size the duct occluder to increase occlusion rate. Trial PDA occlusion was tried in a one month old infant which unfortunately died. It is well known that neonate with large PDA is almost always associated with flow related PAH and PVR is slightly elevated. The success rate in trial occlusion of PDA in this subset of patient might be related to device patient mismatch. The short term outcome for the patient who underwent PDA device closure is outstanding in this study. Majority of the patients have no significant problem. Selection of patients to undergo a successful PDA device occlusion is of utmost important. Hemodynamic data from the cardiac cath, 2D Echo result, ECG, Chest x-ray, O2 saturation (upper and lower limbs) must be set carefully before the study.

This is a retrospective study with limited number of patients included in the study. A prospective study in patients with large PDA is in order to increase the significance of this study.

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Patent ductus arteriosus is seen in 1:2000 full term infants with varied clinical presentations ranging from clinically silent in small ductus arteriosus to those with signs of volume overloading of left ventricle needing interventions, either medical or closure. One of the complications seen in large nonrestrictive or minimally restrictive ductus arteriosus is the development of irreversible pulmonary vascular disease that requires a definitive therapy in the form of closure of patent ductus arteriosus. Surgical closure in the form of PDA ligation was successfully done by Robert Edward Gross in 1939. Techniques of closure have evolved since 1939 with the advent of devices: conical Ivalon plug in 1967, umbrella type device in 1979, Gianturco coils used to occlude small to moderate patent ductus, and Nit-Occlud coil. Subsequently, newer devices were developed; amplatzer duct occluder for patients with large shunt type B ductus. Serious complications were rare in these devices.

Although surgical therapy is effective and safe, increasing number of PDA patients undergo transcatheter closure and has become the standard of care in patients with LV volume overload due to ductus. In patients with moderate or severe pulmonary hypertension due to PDA, transcatheter trial occlusion is performed prior to release of occluder permanently. The criteria followed are (a) decrease in pulmonary artery pressure or no elevation, (b) no decrease in aortic pressure and (c) no worsening of signs and symptoms which are signs of reversible pulmonary hypertension. In a study by Duan-Zhen Zhang et al on the usefulness of trial occlusion for predicting post procedural pulmonary hypertension in adolescents and adults with elevated pulmonary artery pressures, 13% of patients with a mean PAP >_45 mmHg and Rp/Rs <0.7 who underwent transcatheter closure of PDA, had post-procedural pulmonary hypertension, although they showed a baseline QpQs ratio >1.5 and a significantly decreased PAP after PDA closure. A post-procedural Pp/Ps ratio>0.5 suggests inevitable post procedural pulmonary hypertension.

The authors of this paper presented a retrospective study of the outcomes of transcatheter trial occlusion of PDA with pulmonary hypertension among pediatric patients 0 - 18 years old. Among the 27 patients included, 66% (18) had a successful PDA occlusion while33% had procedures aborted. One of the parameters used in the decision to deploy or abort the procedure was pulmonary arterial pressure before and during trial occlusion as well as PDA sizes. A 20% decrease in pulmonary pressure was seen in those with successful PDA occlusion. Majority of the patients improved (15/18) except one patient who

had device migration to right pulmonary artery that required surgical closure of PDA and retrieval of device. This patient had an increase of >20% in pulmonary pressure after trial occlusion.

Among the 9 (33%) patients whose closure were aborted, PDA sizes ranged from 0 .6- 1 .1cm and ages over 10 years old. Three patients had pulmonary hypertensive crisis. Pulmonary arterial pressure prior to occlusion were obtained, however , Pp/Ps were not computed during the procedure. Types and sizes of device to occlude PDA were not mentioned in the study. Previous studies on transcatheter closure of hypertensive PDA emphasized thorough knowledge about different devices including retrieval techniques is vital before attempting percutaneous closure in high risk patients. A comprehensive evaluation of borderline cases before device closure of hypertensive ductus is inevitable for a successful closure outcomes.

Two patients with aborted transcatheter PDA closure were placed on pulmonary vasodilator and underwent a successful transcatheter closure of ductus arteriosus after 2 - 3 months. Following the pediatric pulmonary hypertension modified algorithm from the AHA /ATS guidelines for operability, patients with negative AVT can be placed on targeted pulmonary hypertension therapy and repeat catheterization with acute vasodilation testing to determine if the patient is high risk or inoperable or considered for device closure.

This paper is a retrospective review of hypertensive PDA cases. The measurements of pulmonary pressures on echo were variable and the pulmonary vascular resistance index was not measured. Overall results of the study are encouraging. It will provide a baseline data for future studies.

Disclosure: none

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Transcatheter Closure of Atrial Septal Defect With and Without Fluoroscopy: a Comparison of Outcome

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Background --- Fluoroscopy has emerged as the standard imaging tool used in device closure of Atrial Septal Defect (ASD) and Transesophageal Echocardiography (TEE) serves as an adjunct guide to it. With advancing skills and excellent views of echocardiographer, TEE now plays a bigger role in sizing of defects and choosing appropriate devices. Techniques have been developed to do ASD device closure under TEE guidance alone without fluoroscopy. To assess the efficiency of this procedure, we compared our initial results with those for the conventional procedure.

Methods --- All patients who underwent ASD device closure under TEE with fluoroscopy from January 2015 to December 2018 in a tertiary cardiovascular center were included in the retrospective cohort. All patients who underwent ASD device closure without fluoroscopy from March 2019 to March 2020 were included in the prospective cohort. Baseline characteristics and procedural outcomes were reviewed.

Results --- Fourteen patients underwent ASD device closure without fluoroscopy and outcomes were compared with that of the 34 subjects who had ASD device closure with TEE and fluoroscopy guidance. Baseline characteristics, ASD size and PA pressure were similar between the groups. Twelve (86%) had successful device closure of ASD without fluoroscopy. There was difficulty in manipulating the catheters and the device in the other two patients and so fluoroscopy was used. We did not identify any significant difference in the outcomes between the two groups in terms of procedural time (p=0.14), having residual shunts (p=0.67), device embolization (p=0.65), and length of hospital stay (p=0.72).

Conclusion --- ASD device closure can be safely performed under TEE guidance without fluoroscopy with similar outcomes with that of the conventional practice of using both TEE and fluoroscopy. ***Phil Heart Center J 2020;22(2):32-36.***

Key Words: Atrial septal defect ■ ASD device closure ■ zero fluoroscopy ■ transesophageal echocardiography ■

Atrial septal defect (ASD) is a common congenital anomaly that accounts for 6-10% of all congenital heart defects[1] and is one of the most common CHD in adults[2]. The outcome of surgical closure of ASD is generally good but it is associated with patient anxiety, morbidity, and scar.[3] Transcatheter closure of secundum type of ASD has become a well established and effective alternative to surgery.[4]

Interventional closure of ASD requires a good echocardiographic assessment and guidance to make the procedure as safe as possible.[5] The procedure requires a margin of more than 5 mm in all of the rims of the defect to be considered adequate for ASD device closure.[6]

Through the years, TEE has been an adjunct imaging procedure during ASD device closure in addition to conventional fluoroscopy. However, ASD device closure use of fluoroscopy is now being done. In the study of Ewert and coworkers, transcatheter closure of ASD without fluoros-

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Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

copy was successful in 19 out of 22 patients and they concluded that the procedure can be safely done under echocardiographic guidance alone[7]. A larger study was done in 2016[8] wherein pediatric patients with ASD underwent transcatheter ASD device closure without fluoroscopy. Out of 114 patients, ASD device closure without fluoroscopy is a safe technique for alternative use in children. This study will compare the outcome of ASD device closure without fluoroscopy versus the conventional practice of a combination of TEE and fluoroscopy. The results of this study may help in reducing the risks of exposure to fluoroscopy like radiation-induced cancers later in life. This will also be beneficial for patients needing ASD device closure but with relative or absolute contraindication to fluoroscopy like during pregnancy.

METHODS

This study was conducted in strict compliance with the ethical principles presented in the Declaration of Helsinki. Prior to the conduction of the study, the protocol was reviewed and approved by the Philippine Heart Center Institutional Ethics Review Board (PHC-IERB). The investigator requested that acquiring of informed consent be waived for the retrospective cohort since it is difficult to obtain individual authorization from all the study subjects in this group. An informed consent was obtained from the guardians of all the patients included in the prospective cohort. Written or verbal assents were likewise obtained from all the patients enrolled in the prospective cohort. The risk to the privacy of the subjects was minimal. No sensitive information was obtained. The anonymity of the subjects was ensured by the investigator.

Study Design. This is an ambispective cohort study done at the Philippine Heart Center.

Recruitment:
- March 2019 to March 2020 for the prospective cohort.
- Procedure done from January 2015 to December 2018 for the retrospective cohort

Observation: March 2019 to March 2020.

Included in the study were all pediatric patients less than 19 years of age weighing ≥ 25 kg with secundum type ASD measuring ≤ 2.5 cm with adequate rim sizes (at least 0.5 cm in the posterior, mitral, superior and inferior vena caval rims). Exluded were all patients with ASD but with other associated intracardiac lesions like patent ductus arteriosus, ventricular septal defect, and pulmonary stenosis that required fluoroscopy during intervention.

Sample Size. A total of 46 patients are required for this study to be divided into two groups, those undergoing ASD device closure under TEE guidance with fluoroscopy and another group without fluoroscopy. This is based on assumed large effect size of patients in terms of either duration of procedure, length of hospital stay, and cost of hospitalization. This computation also accounts for 5% level of significance and 90% power (7).

Identification of Study Variables:
- Duration of procedure – time from establishing the vascular access until release of ASD device
- Residual shunts – echocardiographic evaluation of presence or absence of residual shunts
- Embolization – rate of device embolization of device as documented through post-procedure radiograph and echocardiography
- Length of hospital stay – total number of hospital days from admission until discharge

Study Maneuver. For the TEE with fluoroscopy group (retrospective cohort), a list of patients with ASD who underwent ASD device closure from January 2015 to December 2018 was obtained from the database. The charts of all the patients were retrieved for review. Only patients weighing ≥ 25 kg with an ASD size measuring ≤ 2.5 cm were included to minimize the differences between the TEE alone and the TEE with fluoroscopy groups.

The duration of procedure from establishing the vascular access until release of ASD device was noted from the intraprocedure anesthesia record. Post-procedure 2D echocardiography was reviewed to determine the presence of residual shunts and device emboli-

zation. The length of hospital stay from admission until discharge was noted. For the TEE alone group (prospective cohort), all patients weighing ≥ 25 kg with secundum type of ASD underwent preprocedure TEE to evaluate adequacy of rim sizes. All patients with adequate rim margins and ASD measuring ≤ 2.5 cm who underwent diagnostic catheterization, sizing and transcatheter closure of the defect without fluoroscopy were included in the study. The interventional procedures took place in the catheterization laboratory so that fluoroscopy would have been available at any time should it be needed. There were no restrictions on the operator from switching to fluoroscopic guidance at any time during the procedure. The duration of the procedure was noted. Post-procedure 2D echocardiography was done to identify if the device embolized or if there were any residual shunts. The length of hospital stay was noted.

Statistical Analysis. Descriptive statistics was used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, median and interquartile range for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. Independent Sample *T*-test, Mann-Whitney U test and Fisher's Exact/Chi-square test were used to determine the difference of mean, rank and frequency, respectively, between patients with and without fluoroscopy. All statistical tests were two tailed test. Shapiro-Wilk was used to test the normality of the continuous variables. Missing variables were neither replaced nor estimated. Null hypothesis was rejected at 0.05α-level of significance. STATA 13.1 was used for data analysis.

RESULTS

A total of 48 patients who underwent ASD device closure with or without fluoroscopy were included in the study. For the retrospective cohort, 37 patients underwent ASD device closure with TEE guidance and fluoroscopy from January 2015 to December 2018. Only 34 subjects were included in the study. The other three patients were excluded due to incomplete data record. For the prospective cohort, 14 patients underwent ASD device closure under TEE guidance without fluoroscopy. All were included in the study.

Overall, the study population included 14 (29%) males and 34 (71%) females. Baseline characteristics of subjects for the two groups are detailed in Table 1. There were no statistically significant pre-procedure differences between the two cohorts with regard to age (p=0.42), sex (p=0.73), weight (p=0.43), size of ASD (p=0.51) and echocardiographic assessment of pulmonary artery pressure (p=0.48).

In 12 of the 14 patients studied, cardiac catheterization, sizing of interatrial septal defect, and deployment and positioning of the ASD device were done with TEE as the only imaging tool as guide. Fluoroscopy was used in two subjects. In the first patient, the operator had difficulty in positioning and maneuvering the device into the septal defect. Upon using fluoroscopy, it was found out that the device was defective and had to be replaced. In the second subject, there was difficulty in manipulating and maintaining the catheter in the left atrium (LA) and pulmonary vein. On fluoroscopy, the catheter was found to have looped from the right atrium (RA) to the LA and back into the RA and right ventricle (RV). Although fluoroscopy was used in these two subjects, a statistically significant difference in the total fluoroscopy time was still evident between the two groups (p=0) as shown in Table 2.

One patient included in the prospective cohort (ASD closure without fluoroscopy) had device embolization into the RV and had to undergo surgery for device retrieval and ASD patch closure. However, the incidence of device embolization between the study groups showed no statistically significant difference (p=0.65).

In terms of duration of procedure, having residual shunts, and length of hospital stay, the two study groups did not show any statistically significant difference as shown in Table 2. There were no complications noted among the patients in the study group during and immediately after the procedure.

Table 1. Demographic profile of patients who underwent ASD device closure under TEE guidance with and without fluoroscopy

	With Fluoroscopy	Without Fluoroscopy	P-value
	Frequency (%); Mean +- SD; Median (IQR)		
Age	13.6+-3.8	12.3 +- 3.5	0.42
Sex			
Male	9 (26.5)	5 (35.7)	0.73
Female	25 (73.5)	9 (64.3)	
Body weight. kg	40.1 +- 11.6	43.6 +- 17.9	0.43
Defect Size. mm	17.5 +- 6.0	16.3 +- 5.9	0.51
PA Pressure, mmHg	25.2 +- 11.9	28 +- 14.3	0.48

Table 2. Comparison of outcome among patients who underwent ASD device closure under TEE guidance with and without fluoroscopy

	With Fluoroscopy	Without Fluoroscopy	P-value
	Frequency (%); Mean +- SD; Median (IQR)		
Duration of procedure, mins	41.2 +- 20.2	69.5 +- 106.2	0.14
Fluoroscopy time, mins	8.3 +- 4.8	0.48 +- 1.3	0
Residual shunts			
With leak	3 (8.8)	1 (7.1)	0.67
Without leak	31 (92.9)	13 (92.9)	
Embolization			
Embolized	2 (5.9)	1 (7.1)	0.65
Did not embolize	32 (94.1)	13 (92.9)	
Length of hospital stay	3.6 +- 2.1	3.4 +- 3.4	0.72

DISCUSSION

This study is an ambispective review that compared the outcomes in patients who underwent ASD device closure with and without fluoroscopy. We found out that the outcomes were comparable between the two groups in terms of duration of procedure, occurrence of residual shunts, device embolization, and length of hospital stay.

ASD device closure without fluoroscopy and under TEE guidance alone has become achievable but requires high operator skills of both the interventionalist and the echocardiographer. The successful closure of 12 of 14 patients with ASD without fluoroscopy suggests that the procedure is attainable under TEE guidance alone in many patients and the outcomes were equivalent to those observed in patients undergoing ASD closure with fluoroscopy.

In the two patients in whom the operator decided to use fluoroscopy to manipulate the catheters and to position the device, the reasons were only minor and with further practice and experience, these situations can be handled under echocardiographic guidance as well.

Our results support the findings of Ewert and co-workers in 2000 (7) wherein they were able to close ASD of 19 out of 22 patients without fluoroscopy. They found out that there was no statistically significant difference in the duration of procedure but the group where fluoroscopy was not utilized received significantly higher doses of propofol for sedation owing to extended TEE use.

This study is limited to some extent because of low number of patients with ASD closed without fluoroscopy and because the study population was limited to include patients with ASD to less than 25 mm only. Whether this procedure is suitable for larger defects remains to be determined.

CONCLUSION

ASD device closure under TEE guidance without fluoroscopy is a safe and efficient method that has equivalent outcome with the conventional way of using both TEE and fluoroscopy during the procedure. Whether this approach should be refined and applied in different centers has to be discussed. However, excellent TEE views and the availability of easy-to-manipulate devices validate closure of ASD without the routine use of fluoroscopy.

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Editorial Review

The high success rate of 86% by nonfluoroscopy transcatheter ASD closure is comparable to the fluoroscopy-guided procedure. But the untoward incident of 1 case of catheter and/or delivery system looping at the RA,LA, then RV highlights the basic limitation of the non-fluoroscopy approach. There should have been a risk-benefit comparative analysis between the two approaches in this study, considering that the end-point for this study and further applicative and validative studies in the future is safety for specific sub-set of patients, eg pregnant patients. Furthermore, there is also a need to establish the actuarial rate of risk of radiation-induced problems for this subset of patients against the benefit of radiation protection vis-à-vis fluoroscopy use. But overall, the comparative results showing similar procedural time, hospital stay, and complications in the two groups are commendable.

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This article depicts the new procedural approach in the management of Atrial Septal Defect (ASD), ostium secundum by interventional cardiac catherization. In the 1960s surgical closure of ASD was the norm. By the middle of the 1990s, medical therapy (device closure of Atrial Septal Defect) and surgery were compared with practically the same good outcome. The disadvantage in surgical treatment was the presence of apprehension, anxiety, morbidity, postoperative scar and length of hospital stay.

The norm in device closure of Atrial Septal Defect was through fluoroscopy and transesophageal echocardiography (TEE) as an adjunct to access the feasibility of deploying the device during cardiac catheterization.

This study consists of a total of 48 patients who underwent ASD device closure under TEE with or without fluoroscopy. The subjects were divided into two cohorts; those with fluoroscopy consist of 34/37 patients who underwent ASD closure for a period of 3 years and was based on the retrospective analysis of their chart. Some of them underwent balloon sizing of the defect together with TEE analyzing whether it is receptive for device implantation. What was not mentioned in this study was what type of device was used, and whether this would influence the presence of residual and or complications. The 3 patients were not analyzed because of deficient records.

In the other cohort 12/14 patients underwent device closure of ASD utilizing TEE as the only mode of imaging. But 2 had to undergo fluoroscopy because of complications.

Demographic profiles of patients in the 2 cohorts were almost comparable in terms of age, sex (female over male ratio 2:1), body weight, defect size (2.5 cm) and PA pressure. The comparable outcome in the 2 cohorts was mired with the residual shunts; embolization but was not statistically significant. The length of hospital stay was almost the same in the 2 cohorts.

The result of this study showed that device closure utilizing TEE without fluoroscopy is an acceptable procedure and had been proven in various journal reports. This therefore would be a new procedural approach in ASD closure as it has been found to be safe and efficient method. Though the sample of patients studied was limited this approach is feasible and acceptable. It would however require a seasoned, expert, and skilled interventionist as well as echocardiographer to perform this procedure. Further studies would require whether this mode of device closure can be utilized for larger ASD.

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Predictors of Outcome of Pediatric Patients Undergoing Transcatheter Closure of Atrial Septal Defect at Philippine Heart Center from Year 2011 -2016

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Background --- Ostium secundum atrial septal defect (ASD) is a common congenital heart defect. The adverse prognosis of untreated ASD is well studied and percutaneous device closure of these ASDs has evolved to become the standard of care in pediatric populations.
Objectives --- The aim of this study was to determine predictors of outcome of pediatric patients undergoing transcatheter device closure of ASD at the Philippine Heart Center.
Methods --- This is a retrospective cohort study of all pediatric patients (<18 years of age) who underwent transcatheter device closure of ASD. From January 2011 to December 2016, there are 36 of 42 patients percutaneously treated at our institution. Among the above patients, 12 patients had complication.
Results --- In this study, procedural success rate was 92% (33/36) and complication rates was 33%. The age ranged from 4 to 18 years and weights ranged from 15 to 89.9 kgs. The mean ASD diameter, measured with transesophageal echocardiography was 21.9+ 6.8mm which were significantly associated with complications with p value of 0.032. Hospital stay, number and duration of vasodilators used are also significantly associated with p-values below 0.05. Post-procedure complications included valvular dysfunction in 7 patients; device embolization in 3 patients which were surgically removed; supraventricular tachycardia in 1 patient, successfully terminated with medication; and residual shunt in 1 patient with complete closure on further follow-up.
Conclusion --- Transcatheter occlusion of ASD is an effective and safe procedure with minimal complication rate and short hospital stay. Large ASD (>24mm) is significantly related to complications. Given the low rate of complications and virtual lack of mortality, isolated secundum ASDs should be considered for percutaneous device closure. ***Phil Heart Center J 2020;22(2):38-50.***

Key Words: Trancatheter closure ■ Atrial septal defect ■ pediatrics ■

Atrial septal defect (ASD) is one of the most common congenital cardiac anomalies; constitutes 8 to 10% in children.[1] ASD are classified and named according to their embryonic origin. The most common ASD is a secundum defect versus defects located in the septum primum, sinus venosus defects, or unroofed coronary sinus. ASD, although recognized as a relatively benign form of cardiac disease, if left untreated can eventually contribute to significant morbidity and mortality, as borne out by the natural history studies.[2] These defects may result in right-sided heart failure, arrhythmia, and pulmonary hypertension.

Up to the present time, the primary method of therapy for closure of the atrial septal defect has been surgical repair. As with all forms of cardiac surgery there is a small but definite risk of surgical morbidity (5%) and mortality (<1%). Although surgical closure of ASDs is safe, effective, and time-tested, it still requires open-heart surgery and hospitalization.[3,4] Surgical repair of an ASD is widely accepted procedure,[6] however, it is associated with discomfort, and a thoracotomy scar.

Currently, among the various types of ASDs only the secundum defect is amenable to device

  ISSN 0018-9034

closure; whereas all 4 types can be surgically closed. Over the years, routine closure of ASD in child hood has been justified due to the accessibility of low-risk, curative surgical, and transcatheter options.[2]

Now more than a decade old, transcatheter device procedure in many cardiac catheterization laboratories. It has replaced surgery as the method of choice for ASD closure in most patients.[5] It is also a well-accepted alternative to surgical therapy and has been regarded as generally safe and effective.[2]

Reported complications are rare but they range from 0 to 11.5% and there is a wide variety owing to operator learning curve and also to the combination of large device and young patient.[6]

Transcatheter device closure of atrial septal defect (ASD) is yet an evolving technology in pediatric cardiac interventional procedure. Previous local and international studies have included predominantly adult subjects.[7-9] There are no published reports concerning series of patients less than 18 years of age. No studies, locally, have comprehensively analyzed risk factors and post-procedure complications in pediatric patients. And so, this study was designed to identify risk factors for post-procedure complications and to determine predictors of morbidity and mortality.

OBJECTIVES

The purpose of the study to determine predictors of outcome of pediatric patients undergoing transcatheter device closure of ASD at the Philippine Heart Center.

Specific Objectives:

1. To determine the incidence of post ASD device closure complications.
   - i. Death
   - ii. Device embolization / malposition
   - iii. Cardiac perforations / Erosion
   - iv. Thromboembolic complications
   - v. Residual shunt
   - vi. Device allergy
   - vii. Pericardial Effusion
   - viii. Valvular dysfunction
   - ix. Arrhythmia
2. To determine the pre-procedure risk factors of patients who underwent ASD Device closure.
   - i. Clinical Characteristics
     - a. Physical Examination
       - 1) Age
       - 2) Gender
       - 3) Weight / Wasting / Stunting
       - 4) Character of second heart sound (P2)
     - b. Functional class
   - ii. Laboratory data
     - a. Hematologic data
       - 1) White blood cell count
       - 2) Percentage of segmenters
     - b. Radiographic data
     - c. Electrocardiographic data
   - iii. Echocardiographic data
     - a. ASD size
     - b. Presence and Severity of Pulmonary Regurgitation
     - c. Presence and Severity of Tricuspid Regurgitation
     - d. Presence of RV dysfunction
     - e. Pulmonary artery pressure
     - f. Qp:Qs Ratio
3. To determine the intra-procedure risk factors of patients who underwent ASD device closure.
   - i. Transesophageal Echocardiographic data
     - a. ASD size
     - b. ASD rims
   - ii. ASD device used
     - a. Type
     - b. Size
   - iii. Angiographic data
     - a. Fluoroscopy time
     - b. Procedure time
     - c. Mean aortic pressure
     - d. Mean pulmonary artery pressure
4. To determine the post-procedure risk factors of patients who underwent ASD device closure.
   - i. Hospital Stay
   - ii. Length of intubation
   - iii. Drugs
     - a. Inotropes
     - b. Vasolidator
     - c. Antibiotics
5. To determine the association of the above factors with the development of complications.

METHODS

This is a retrospective cohort study conducted at the Philippine Heart Center from January 2011 to December 2016. This study was approved by the Philippine Heart Center Institutional Ethics Review Board. Request for the waiver of informed consent was likewise approved.

This study included all patients aged <18 years old + 364 days who underwent transcatheter device closure of ASD; patients who got their pre and post-procedure Transthoracic Echocardiography done at Philippine Heart Center; patients who got their pre and post-procedure chest radiography and 15 Lead ECG done at Philippine Heart Center.

Meanwhile, excluded from this study are patients with ASD secundum that is associated with other complex congenital cardiac malformations (partial or total pulmonary venous malformation, interrupted aortic arch, cotriatriatum, double-chambered ventricle, severe mitral valve stenosis); patent foramen ovale with no signs of right ventricular volume overload.

Sample Size. All pediatric patients who underwent transcatheter device closure of ASD at the Philippine Heart Center on January 2011 to December 2016.

Study Maneuver. A retrospective review of the charts of all pediatric patients who underwent transcatheter device closure of ASD from January 2011 to December 2016 was done. Data were extracted from Medical Records of the hospital; and patients were identified by discharge diagnosis from the CV laboratory databases.

An evaluation form containing preoperative risk factors such as demographic data (as to age, gender, age at diagnosis, nutritional status), functional class, arrhythmia, extra-cardiac anomalies/co-morbidities, or other genetic syndrome was filled-up.

Identification of sudy variables with definition of each variable

a. *Independent or Exposure Variables*
- i. Pre-Procedure Diagnostics:
  1. WBC
  2. Chest X-ray
  3. ECG 15 Lead
  4. Pre-procedure 2D echocardiogram
     - a. ASD size
     - b. RAE and RVH
     - c. Pulmonary Regurgitation
     - d. RVEF
     - e. Qp/QS
     - f. Pulmonary artery pressure (mmHg)
       - i. Pulmonary hypertension was graded as mild (40–49 mm Hg), moderate (50–59 mm Hg) or severe (≥60 mm Hg) based on right ventricular systolic pressure (RVSP), estimated from tricuspid regurgitation jet velocity.
  5. Transesophageal Echocardiogram
     - a. Rims
     - b. ASD size
- ii. Device used
  1. Type of the device
  2. Size of the device
- iii. Fluoroscopy time
- iv. Procedure time
- v. Mean aortic pressure (mmHg)
- vi. Mean pulmonary artery pressure (mmHg)

b. *Dependent or Outcome Variables*
- i. Hospital Stay
- ii. Complications:
  1. Death
  2. Device embolization / malposition
  3. Cardiac perforations / Erosion
  4. Thromboembolic complications
  5. Residual Shunt
  6. Device allergy
  7. Pericardial Effusion
  8. Valvular dysfunction
  9. Arrhythmia

c. *Confounding variables*
- i. Age of the patient
- ii. Gender
- iii. Weight
- iv. Wasting
- v. Stunting
- vi. Modified Ross Classification*
  1. Reviewed charts with specified or written Functional class on the history was included in this section and was addressed during data analysis
- vii. Character of second heart sound (P2)

*Modified Ross Heart Failure Classification in Children	
I	- Asymptomatic
II	- Mild tachypnea or diaphoresis with feeding in infants - Dyspnea on exertion in older children
III	- Marked tachypnea or diaphoresis with feeding in infants - Marked dyspnea on exertion Prolonged feeding times with growth failure
IV	- Symptoms such as tachypnea, retractions, grunting, or diaphoresis at rest.

Statistical analysis. Data analysis was done using Stata SE Version 13. Quantitative variables were summarized and presented as mean and standard deviation, while qualitative variables were tabulated and presented as frequency and percentage. Association between risk factors and outcomes were tested using logistic regression analysis. The level of significance was set at 0.05.

RESULTS

A total of 42 patients were enrolled for device closure. Six patients were considered unsuitable on TEE and were excluded. In these patients, the defect was either too large for the age and weight of the patient, more than two rims were deficient. Transcatheter ASD occlusion was done in 36 patients and 12 of them have complication.

The age ranged from 4 to 18 years (median age 11 years). There were 24 females and 12 males (M:F=1:2). The body weight of the patients ranged from 15 kg to 89.9 kg (median 35 kg). Age, Gender, Weight, Wasting, Stunting, Modified Ross Classification and Character P2 are not significant to complications with p-values above 0.05 (*Table 1*). Insignificant results on Wasting and Stunting are due to absence of such cases among those with and without complications.

WBC, segmenters, chest x-ray, arrhythmia, presence of pulmonary regurgitation, presence of right ventricular (RV) dysfunction, PA pressure (based on 2D echo), and Qp:Qs are not significant to complications with p-values above 0.05 as shown on Table 2.

ASD secundum size is significant to complications with p-value of 0.032 (*Table 2*). Those with complications have higher prevalence of large ASD secundum while percentage of moderate ASD secundum is higher among those without complications (*Figure 1*).

Fluoroscopy time, procedure time, ASD Rims, ASD device used; mean aortic pressure and pulmonary artery pressure are not significant to complications with p-values above 0.05 (*Table 3*).

This shows that the observations among those without complications on fluoroscopy time, procedure time, ASD Rims, ASD device used; mean aortic pressure and pulmonary artery pressure are statistically similar among those with complications. Three different ASD devices were used to close a secundum: 1) Cera-flex in 9 patients, 2) Cocoon in 3 patients, and; 3) Lifetech™ in 24 patients. As observed in the pre-procedural ASD size using transesophageal echocardiogram, intra-procedure large ASD size more than 24mm was also clinically significant complication.

Length of intubation, number and duration of inotropes used; and of antibiotics used are not significant to complications with p-values above 0.05. On the other hand, hospital stay, number and duration of vasodilators used are significant with p-values below 0.05 (*Table 4)*. The duration of hospital stay among those with complications is longer than those without complications (*Figure 2*). Four or 33% of the 12 patients with complication stayed more than 7 days in the hospital. Three of them were due to embolization, hence were sent to surgery and prolonging the hospital stay. One patient had supraventricular tachycardia (SVT) 24 hours post-procedure and stayed at the institution for 10 days due to recurrence of SVT episodes.

There was no noted use of vasodilators among patients without complications. However, 4 patients with complication used vasodilator. Thirty three percent (33%) of those with complications have 1 vasodilator and the duration ranges from <24 hours to >72 hours where 1 patient used vasodilators for <24 hours, 1 patient used vasodilators for 24-72 hours while 2 patients used vasodilators for more than 72 hours (*Figure 3*).

One of the four patients was started with nitroglycerin post ASD device closure by anesthesia service due to episode of hypertension but after 6 hours was discontinued and no recurrence of hypertension was noted during the entire hospitalization. Three of these patients underwent surgical intervention due to embolization hence vasodilator was started. One patient used nitroglycerin for 28 hours and two other patients who had mild pulmonary hypertension assessed intra-operatively were started with milrinone; and later shifted to sildenafil.

Among 12 patients recorded with complication post transcathether device closure (*Table 5*); 58.33% or 7 patients had valvular dysfunction, 3 patients had device embolization or malposition (25%), 1 patient had residual shunt (8.335) and another one with arrhythmia (8.33%).

Valvular dysfunction occurred in seven patients. In five patients, which had transthoracic echocardiogram done 6-12 months post procedure showed that the device was protruding to left ventricular inflow causing mitral regurgitation mild to moderate in severity. One patient, the device is protruding to aortic valve hence producing aortic regurgitation described in transthoracic echocardiogram done 6 months post procedure. One patient had pulmonary regurgitation 1 year after device closure. All 7 patients are in follow-up and never had been symptomatic except for one patient with moderate mitral regurgitation; and maintained on an afterloader and a diuretic.

Malposition or embolization of the device occurred in three patients. In two patients device embolized 24 hours after deployment; and in one patient device embolized 12 hours after deployment. Atrial septal defects were of large size in both patients that embolized 24 hours relative to the size of device used. The other patient had an inferior vena cava rim of 4.5mm. In all patients underwent surgical removal of the device and ASD closure. All patients were assessed for a residual defect at the time of discharge. By the time of discharge, 24 hours after ASD closure, one patient (8.3%) had residual shunt measuring 0.3mm. During further follow-up examinations, the complete closure rate was achieved in 100% (n=33/33).

ECG abnormalities associated with transcatheter closure i.e. supraventricular tachycardia (SVT) occurred in 1 case (8.33%) 24 hours after the procedure which settled with adenosine. She was referred to arrhythmia service and maintained on beta-blocker and is in follow-up for last 2 years but never had been symptomatic; and a holter monitoring done 2 days post-procedure showed a non-sustained SVT, sinus tachycardia and some isolated non-conducted beat. She was due for another 24-hour holter monitoring and latest ECG done last January 2017 showed normal result.

Table 1. Clinical Characteristics of Pediatric Patients with and without Post-Transcatheter Complications Who Underwent ASD Device Closure at Philippine Heart Center from January 2011 to December 2016

Clinical Profile	No complications	With Complications	p-value
	N = 24	N = 12	
Age	11.25 ± 4.00	11.24. ± 3.73	0.920
3 - 8 years (early childhood)	5 (21%)	4 (33%)	
9 - 11 years (middle childhood)	9 (28%)	3 (25%)	
12 - 14 years (early adolescence)	3 (13%)	2 (17%)	
15 - 16 years (middle adolescence)	4 (17%)	2 (17%)	
17 - 18 years (late adolescence)	3 (13%)	1 (8%)	
Gender			0.708
Male	9 (28%)	3 (25%)	
Female	15 (63%)	9 (75%)	
Weight	37.70 ± 18.03	33.85 ± 14.76	0.925
10 - 20kg	4 (17%)	2 (17%)	
21 - 30 kg	4 (17%)	3 (25%)	
31 - 40kg	8 (33%)	4 (44%)	
> 40 kg	8 (33%)	3 (25%)	
Wasting			1.000
None to mildly wasted (z = 0 to -1)	24 (100%)	12 (100%)	
Moderately wasted (z = -2)	0 (0%)	0 (0%)	
Severely wasted (z = -3 and below)	0 (0%)	0 (0%)	
Stunting			1.000
None to mildly stunted (z = 0 to -1)	24 (100%)	12 (100%)	
Moderately stunted (z = -2)	0 (0%)	0 (0%)	
Severely stunted (z = -3 and below)	0 (0%)	0 (0%)	
Modified Ross Classification			0.260
I	18 (75%)	6 (50%)	
II	-	-	
III	-	-	
IV	-	-	
Blank	6 (25%)	6 (50%)	
Character of P2			0.718
normal	24 (100%)	11 (92%)	
loud	0 (0%)	1 (8%)	

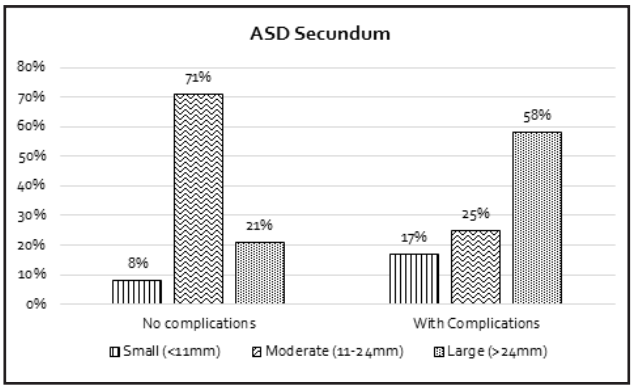

Figure 1. Percentage of ASD secundum based on size with and without Post-Transcatheter Complications after ASD Device

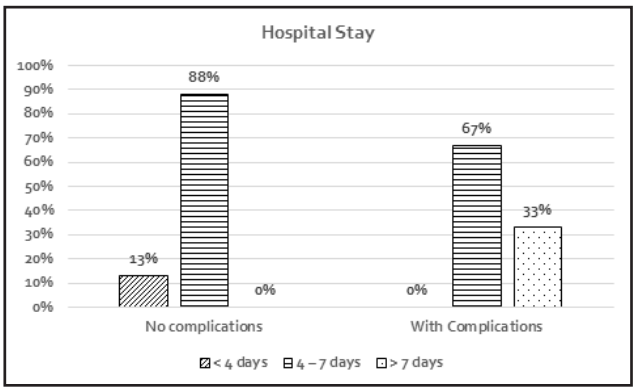

Figure 2. Percentage of the Duration of Hospital stay of patients with and without Post-Transcatheter Complications after ASD Device Closure

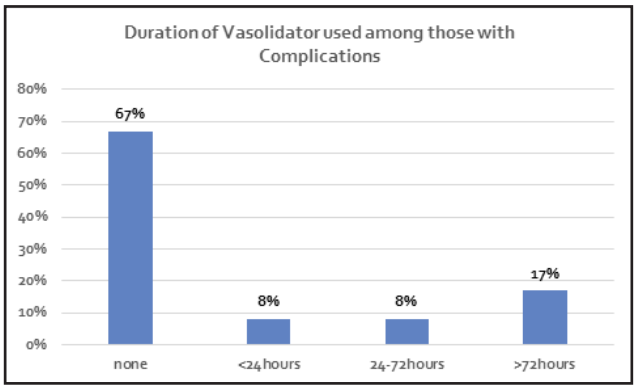

Figure 3. Percentage of the duration of the vasodilator used among those with Post-Transcatheter Complications after ASD Device Closure.

Table 2. Pre-procedure Diagnostic Parameters of Pediatric Patients With and Without Post-Transcatheter Complications after ASD Device Closure, Philippine Heart Center, January 2011 - December 2016

Diagnostics	No complications	With Complications	p-value
	N = 24	N = 12	
WBC	9.36 ± 2.49	10.02 ± 2.85	0.970
<5	0 (0%)	0 (0%)	
5-10	15 (63%)	8 (67%)	
>10	9 (38%)	4 (33%)	
Segmenters			0.863
<65%	21 (88%)	10 (83%)	
->65%	3 (13%)	9 (75%)	
Chest X-ray			0.284
normal	7 (29%)	2 (17%)	
hypervascular pulmonary congestion / edema	17 (71%)	9 (75%)	
MPA Prominent Right ventricular enlargement and Atrial enlargement	0 (0%)	1 (8%)	
Arrhythmia			0.775
None	24 (100%)	11 (92%)	
Atrial	0 (0%)	0 (0%)	
Ventricular	0 (0%)	1 (8%)	
ASD Secundum Size			***0.032****
Small (<11mm)	2 (8%)	2 (17%)	
Moderate (11-24mm)	17 (71%)	3 (25%)	
Large (>24mm)	5 (21%)	7 (58%)	
Presence of Pulmonary Regurgitation			0.863
Present	4 (17%)	1 (8%)	
Severity of Pulmonary Regurgitation			0.876
Mild	3 (13%)	1 (8%)	
Moderate	1 (4%)	0 (0%)	
Severe	0 (0%)	0 (0%)	
Presence of Tricuspid Regurgitation			0.718
Present	10 (42%)	5 (42%)	
Severity of Tricuspid Regurgitation			0.343
Mild	10 (42%)	4 (33%)	
Moderate	0 (0%)	1 (8%)	
Severe	0 (0%)	0 (0%)	
RV Function			1.000
normal (>35%)	24 (100%)	12 (100%)	
mild to moderate (20-34%)	0 (0%)	0 (0%)	
severe (<20%)	0 (0%)	0 (0%)	
PA pressure (based on 2D echo)			0.099
normal (<25mmHg)	14 (58%)	7 (58%)	
mild PAH (25-40mmHg)	10 (42%)	3 (25%)	
moderate PAH (41-55mmHg)	0 (0%)	2 (17%)	
severe PAH (>55mmHg)	0 (0%)	0 (0%)	
Qp:Qs			0.150
<1.5 (small shunt)	11 (46%)	2 (17%)	
>1.5-2 (moderate shunt)	10 (42%)	6 (50%)	

Table 3. Intra-procedure Parameters of Pediatric Patients with and without Post-Transcatheter Complications after ASD Device Closure. Philippine Heart Center, January 2011 – December 2016

Variables	No complications	With complications	p-value
	N = 24	N = 12	
Fluoroscopy time (mins) *mean +- SD*	25.75 +- 6.95	29.67 +- 7.45	0.129
Procedure time (mins) *mean +- SD*	68.25 +- 17.47	80.25 +- 23.76	0.094
ASD size, actual (mm) TTE			0.032
Small (<11mm)	2 (8%)	2 (17%)	
Moderate (11-24mm)	17 (71%)	3 (25%)	
Large (>24mm)	5 (21%)	7 (33%)	
ASD Rims			0.271
<5mm	0 (0%)	1 (8%)	
5-7mm	12 (50%)	7 (58%)	
>7mm	12 (50%)	4 (33%)	
ASD Device used			
Type			0.290
Ceraflex	4 (17%)	5 (42%)	
Cocoon	3 (13%)	0 (0%)	
Lifetech	17 (70%)	7 (58%)	
Size	26.33 ± 5.81	30.17 ± 6.46	0.081
Mean aortic pressure (mmHg)	69.38 ± 11.89	68.5 ± 10.68	0.830

DISCUSSION

Transcatheter device closure of secundum ASDs has significantly altered the management of ASDs. In majority of patients with secundum ASD, it is widely practiced and has replaced surgical ASD closure. It has definite advantages as cosmetic benefits, short procedure time, reduced hospital stay and less painful. However, technical complications cannot be avoided with occasional deaths have been reported. Several modifications in devices as well as delivery systems have been made overtime to improve the success rate of device closure and cover range of ages.

In this study, demographic characteristic of patients that include: the age, gender, weight, wasting, stunting, functional class (measured by Modified Ross Classification) and presence of pulmonary hypertension (character of second heart sound P2) are not significant to complications. In a clinical study of Kim et al. concluded that transcatheter closure of ASD is feasible and safe regardless of the patient's age (range

Table 4. Post-operative Parameters of Pediatric Patients with and without Post-Operative Complications after VSD Repair, Philippine Heart Center, January 2009 – December 2014

Variables	No complications	With complications	p-value
Hospital Stay (days)			
< 4 days	3 (13%)	0 (0%)	**0.007**
4-7 days	21 (88%)	8 (67%)	
> 7 days	0 (0%)	4 (33%)	
Length of intubation			
<12 days	24 (100%)	9 (75%)	0.055
12-24 hours	0 (0%)	3 (25%)	
>24 hours	0 (0%)	0 (0%)	
Number of inotropes used			
no inotropes	24 (100%)	9 (75%)	0.055
1 inotrope	0 (0%)	3 (25%)	
≥ 2 inotropes	0 (0%)	0 (0%)	
Durations of inotropes used			
none	24 (100%)	9 (75%)	0.055
< 24 hours	0 (0%)	0 (0%)	
24-72 hours	0 (0%)	3 (25%)	
> 72 hours	0 (0%)	0 (0%)	
Number of vasolidators used			
no vasolidators	24 (100%)	8 (67%)	0.055
1 vasolidator	0 (0%)	4 (33%)	
2 >- vasolidators	0 (0%)	0 (0%)	
Duration of vasolidators used			
none	24 (100%)	8 (67%)	**0.015**
< 24 hours	0 (0%)	1 (8%)	
24-72 hours	0 (0%)	1 (8%)	
> 72 hours	0 (0%)	2 (17%)	
Number of antibiotics used			
no antibiotics	23 (96%)	9 (75%)	0.172
1 antibiotic	1 (4%)	3 (25%)	
2 antibiotics	0 (0%)	0 (0%)	

Table 5. Frequency and Percentage of Post-transcatheter Complications in Pediatric Patients who Underwent ASD Device Closure. Philippine Heart Center, January 2011 – December 2016

Complications	N-12	%
Death	0	0%
Device Embolization/malposition	3	25%
Cardiac perforations/erosions	0	0%
Thromboembolic complication	0	0%
Residual shunt	1	8.33%
Device Allergy	0	0%
Pericardial Effusion	0	0%
Arrhythmia	1	8.33%
Valvular Dysfunction	7	58.33%

1.2 to 80.6 years).[12] This was also reported earlier in year 2003 by Butera et al. that percutaneous ASD closure can be performed safely and successfully in selected young and very young children (range 8 months to 5 years).[13] The youngest patient in our study is a 4 year old and the lightest was 15 kilogram. Since the catheter closure of pediatric or very young with ASD population has attracted research interest over the past two decades, study of Bartakian, et al. which patients age were 3 months to 4.92 years and weighed <15 kg concluded that transcatheter ASD closure is highly successful but with an increase in complication rates and still strongly recommended that in small asymptomatic patients, deferral of closure until the 4 to 5 years of age.[14] Most of the patients in this study were normal to mildly wasted and stunted, had normal to mild elevation on pulmonary pressure; and asymptomatic hence gave an insignificant result. In a review of Akagi, et al. reported that majority of pediatric patients are asymptomatic and diagnosed by school physical examination, heart murmur detected by primary care pediatrician, and cardiac echocardiographic screening in the newborn period.[15] On the contrary, adult patients with ASD are usually symptomatic.

On the pre-procedural diagnostics and intra-procedure parameters included in this study, only the ASD size showed a significant risk for complication. ASD secundum sized more than 24mm is higher among those with complications. In contrary, a recent study of Guo J, et al. on outcomes of device closure of very large ASD (minimal defect diameter of >30mm) via transcatheter closure or intraoperative closure approach concluded that it is technically feasible and associated with excellent long-term safety and efficacy.[16] Regarding the key points of larger ASD sizes at risk for complications as criticized by other studies, these will be discussed in detail with each complication.

Among the post-procedural parameters, the hospital stay, number and duration of vasodilators used are significant. Patients with complication verge to have longer hospital stay (more than 7 days).

Most of the patients in this study who stayed longer underwent surgical closure due to device embolization. A multicenter non-randomized trial of comparing transcatheter and surgical closure on ASD was done by Hijazi Z, et al. and concluded that the complication rate was lower and length of hospital stay was shorter for device closure than surgical repair.[17] The number and duration of vasodilators in this study were used due to different clinical implications but majority is due to mild pulmonary hypertension assessed intraoperatively. Although most pediatric patients with ASD have significantly lower incidence of pulmonary artery hypertension than of adult populations; expansion of therapeutic indications is considered under the combination of new pulmonary hypertension specific medical treatment, such as prostanoids, endothelin receptor antagonists, and phosphodiesterase-5 inhibitors.[15]

While device closure has proven to be technically safe and feasible and have the obvious advantage of being nonsurgical technique, it is not free of complications. These complications include: death, device embolization or malposition, cardiac perforation or erosions, thromboembolic complication, residual shunt, device allergy, pericardial effusion, arrhythmia and valvular dysfunction.

In this study, procedural success rate 92% (33/36) and complication rates 33% are comparable to studies with young children by Voget, et al. which discussed 25% of 12 young children underwent ASD device closure 3 had complication (2 embolization and 1 thromboembolic complications).[18]

Malposition or embolization is the most common reason for surgical intervention. Out of 36 patients who underwent percutaneous closure of ASD, three (8.3%) patients needed surgical intervention because of embolization in the right ventricle. Chessa, et al. reported upon 417 patients, ten cases of malposition or embolization that needed surgical intervention.[7] The reported sites of embolization include right ventricle, pulmonary artery, left ventricle, arch of aorta and peripheral vessels. Levi DS, et al. reported 0.55% (21 embolizations in 3824 ASD device placements) with a range of patient demographics, atrial septal defect sizes, and device sizes.[19] Most embolizations occurred because of inadequate rim or undersized devices; which were also the cases in this study. As Amin Z, et al. reported device embolization occur mostly in the cardiac catheterization laboratory

and during the first 24 hours after device placement.[20] A rare case of embolization was reported on a follow-up patient after months of ASD device closure.[7] Amin Z, et al. also discussed that the two most common cause of device embolization were rim absence or significant deficiency, and physician error. ASDs with a diminished or absent IVC rim are particularly prone to embolization, and interrogation of the IVC rim is important in all patients but crucial in patients with large ASDs. The latter type of embolization occurs in the catheterization laboratory, as both discs were either in the left or the right atrium at the time of release.[20]

Accurate measurement of ASD is required since percutaneous closure of ASDs has become the first option with fewer complications than surgery. In this study, only the ASD size had clinically significant with post-procedure complications. Large ASDs measuring more than 24mm in the pre and intra-procedure were more associated with to complications. According to Mullins et al, there are 2 main considerations for effective closure of secundum ASD: the absolute size of the ASD and the amount of supporting rim of the atrial septum.[21] Hijazi ZM, et al. reported that the best ASD for transcatheter closure is centrally located in the septum with a >5mm rim of septal tissue and is situated >5mm from the atrioventricular valves, the coronary sinus and the pulmonary veins.[17] In a study of pathologic specimens, to test the feasibility of ASD occlusion using Clamshell device,[22] a mean ASD size of 8x10mm was considered favorable and ASDs of >25mm in diameter with a circumferential rim of <2mm were judged unsuitable for transcatheter closure. As observed in this study, ASD secundum size is significant to complications with p-value of 0.032 (*Table 2*). Those with complications have higher prevalence of large ASD secundum (>24mm) while percentage of moderate ASD secundum (11-24mm) is higher among those without complications. ASD rim was not significant to complication in this study because 35 of 36 cases had rims >5mm except for 1 patient who had embolization with an IVC rim measuring of 4.5mm. In another study of the buttoned ASD device,[21] 3 predictive factors were size, <15mm; identified for successful ASD occlusion: ASD, <15mm; ratio of ASD ratio of ASDand ratio of superior and inferior rim length to ASD diameter >0.75. Of the 3 factors, investigators found the ASD size to be the best predictor of successful occlusion. This was supported by another study done by Rosenfeld and co-authors; they observed that only the ASD diameter predicted effective closure while other factors (atrial rim size and dimension) did not.[23]

Device allergy is due to nickel; and in 2008 a rising incidence of nickel allergy in the United States was reported.[24] Almost all ASD devices are made of nitinol, with approximately 45% nickel and 55% titanium. Nickel allergy is fairly common in humans, especially women. These symptoms include dermatitis, chest discomfort, new-onset or worsening migraine-type headaches with or without aura, and palpitations.[25] Fortunately, these cases are rare, and the symptoms subside in a few months. Steroids were given in some patients to obviate these symptoms. In rare cases, systemic effects of nickel allergy have been described, and removal has been performed. In this study, no device allergy was documented among the 36 patients who underwent ASD device closure.

Conduction abnormalities and arrhythmias may occur in patients following transcatheter device closure. In this study, one patient (2.7%) suffered non-sustained supraventricular tachycardia with isolated nonconducted beat on holter monitoring post-procedure. Hill, et al. had a study done that described early ECG abnormalities associated with transcatheter closure of ASD using Amplatzer septal occluder; which concluded that there is an acute increase in supraventricular ectopy (SVE) and a small risk of AV conduction abnormalities. It reported that supraventricular ectopy in 26 patients (63%) out of 41 post closure and a significant increase in post-closure number of supraventricular premature beats per hour; which 9 patients (23%) with non-sustained SVT, 3 of whom had short runs of SVT prior to closure.[2]

Even though there was no reported case of cardiac perforation; it is the most feared complication described in literature. Cardiac perforations are related to technique and can occur during catheterization or typically before

hospital discharge. Patient can present with haemopericardium, pericardial effusion and cardiovascular collapse. There may be sudden death due to perforation.[27]

In a study of 1000 patients who underwent percutaneous device closure, an incidence report of thrombus formation in 1.2% of ASD patients and 2.5% in patent foramen ovale were one of the important concern.[28] Some significant predictors of thrombus formation were persistent atrial septal aneurysm and post-procedure atrial fibrillation.[28] All patients in our study group were started on Aspirin in antiplatelet dose immediately after the procedure. However, none of our patients developed evidence of thrombus formation in immediately or late follow-up.

In this study, there is one case of residual shunt measuring 0.3mm in transthoracic echocardiogram done 24 hours post procedure. The ASD size of the said patient was 23mm and the device used was Searcare 30mm. Residual shunts are more frequent with percutaneous closures than with surgical closures. Variable incidence of residual shunts was mainly related to the devices' designs. Rao, et al. reported residual shunts in 45% of patients on colour doppler with buttoned device[29] while Worms et al found residual shunt in 37% patients with Sideris device.[24] The incidence is very low with Amplatzer septal occluder,[30] and this was the case in this study too where only one patient had a small leak immediately post procedure which resolved on long term follow-up.

Despite of the concerns regarding large sizes of the device in young children undergoing device closure of ASD, one study reported that it flattened nicely and assumed a fairly slim configuration at serial follow up in all cases. In this study, one patient suffers aortic regurgitation due to protruding device to aortic valve. Kazmi, et al. reported two patients (1%) developed aortic regurgitation on long-term follow-up (9–12 months). In both patients, the regurgitation jet emerged in the centre of the aortic valve and was mild. Balloon stretch diameter technique was significantly associated with possible over sizing resulting in AR in both these patients. No augmented splaying of the right and left atrial device disc around the aortic root was obvious in patients with AR.[27] In this study, the protuberance of the device on the aortic valve obviously caused the aortic regurgitation. Patient is an 8 year old female weighed 15kgs, ASD size was 20mm, all ASD rims were adequate (>5mm) and device used was Ceraflex 24mm. The issue of device oversizing on this case was defended by a study of Galapatthy, et al. which documented that device closure using transthoracic echocardiogram and device upsizing of 4-6mm instead of invasive imaging and a sizing formula, and of balloon sizing is feasible, safe and reduces fluoroscopy and procedure times.[25] In another study of Takaya, et al. reported about the fate of mitral regurgitation after transcatheter closure of atrial septal defect in adults.[31] The volume overload of pulmonary circulation improves post atrial septal defect closure; but the increasing left ventricular preload may contribute to mitral regurgitation deterioration. One-month post ASD device closure, Takaya et al assessed 288 ASD patients with MR; and the MR ameliorated in 3 patients and unchanged in whereas MR deteriorated in 32. However, a median follow-up of 24 months, patients with MR deterioration had no cardiovascular events, and the event-free survival rate was not different between patients with MR deterioration and those with MR amelioration or no-change (p=0.355) 31. Wilson, et al. also reported that after a year follow up shows no progression of mitral regurgitation in 227 patients.[32] On the other hand, new-onset mitral regurgitation (MR) may result from atrioventricular valve rim deficiency hence the edge of the device may sit on the anterior mitral valve leaflet.[15] In this study, all five patients have a new onset MR. Four of which have a mild severity from the device protruding to LV inflow; they are asymptomatic and have a normal LV geometry by echocardiogram. In another study done by Nishimura S, et al., the mechanism of aggravated MR was poor coaptation associated with annular dilatation, thickened anterior mitral leaflet, and shortened posterior mitral leaflet hence careful follow-up is needed.[33] Although these mechanisms were not observed in our patients; careful interrogation of mitral valve will be of benefit for future preferences. One of the five patients had MR mild that progressed to moderate 6 months post procedure due to left atrial disc at the tip of the anterior

mitral valve leaflet that require medication. This said patient aged 14 year old female and weighed 35 kgs with ASD size of 32mm occluded with Lifetech septal occluder 38mm. Although MR in this patient was not observed intraprocedure during TEE post ASD device; Amin, et al. advised that if this is noticed in the cardiac catheterization laboratory, the device should be removed and replaced with a smaller device if the size of the defect allows it.[20]

CONCLUSION

Over the past two decades, transcatheter closure of ASD among pediatric patients has attracted research interest and is gaining popularity. However, several potential complications can occur. This procedure is feasible and safe regardless of the patient's age and weight. The data presented in this paper strongly suggest that ASD size is the best predictor of successful occlusion[17,18] and is significantly related to complications. Given the low rate of complications and virtual lack of mortality, isolated secundum ASD should be considered for percutaneous device closure.

RECOMMENDATION

Transcatheter closure of ASD using currently available devices has been established as safe and effective alternative treatment for most patients with ASD secundum. Although some specific anatomical features are not suitable for this procedure, the remaining patients are probably treatable by cardiac surgery. On the other side, complications due to this procedure, especially embolization and valvular dysfunction, are still observed in a certain number patients. The mechanism of valvular dysfunction has not been clarified completely, some occurred even in the long-term after the procedure. Thus, longitudinal follow-up after this procedure is essential. Other important concerns, such as device-induced late arrhythmias, residual shunts, cardiac erosion and reaction of myocardial tissue should be checked in the future.

LIMITATION

Our study was a retrospective report and information of the subject was limited to what is seen in the chart.

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Editorial Review

Reporting the Institution's experience on transcatheter device closure of Atrial Septal Defect is a necessary undertaking. Analyzing the predictors of outcome of pediatric patients undergoing such procedure is valuable and informative. This will provide insights for further improvement of patient's selection and outcome. Atrial Septal Defect is one of the common congenital heart lesions with a birth prevalence of 1 to 2/1,000 livebirths. Secundum Atrial Septal Defect accounts for 70% of Atrial Septal Defects. Hence, a large number of patients benefit from this non-surgical procedure.

Transcatheter device closure is generally accepted as the treatment of choice for this type of ASD. It has similar efficacy and hemodynamic results with surgical closure. But has advantages such as reduced complication rates, shortened hospital stay, cosmetic benefit and reduced need for blood products/medications.

In this retrospective study, all of the patients were stable with their clinical profile and diagnostic parameters within the accepted criteria for device closure. However, complications were noted in 12 patients (12/36) which is about 33 percent. Among the 12 patients with complications, only 4 were considered significant and/or serious, 3 patients with embolization requiring surgery, longer hospital stay and need for more blood products/medications while another patient with moderate mitral regurgitation requiring medical management and more frequent monitoring. Therefore, the rate of complication was about (4/36) about 1 percent, which is fairly satisfactory, and at par with other advanced centers. Complications such as arrhythmia was managed and resolved. The small residual shunt completely closed on follow up. The other 6 patients had mild valvular dysfunction and did not need medical treatment.

Device embolization as well as valvular dysfunction were attributed to underestimation or overestimation of the size of the defect, respectively as well as the adequacy and stability of the rim of tissues. The result would be an undersized or oversized occluder device. Measurements were done by transesophageal echocardiography and balloon stretch diameter technique. Accuracy of these modalities had been well established and noted to be reliable.

One patient with embolization of the device had a 4.5 mm IVC rim which is a little shorter than the required 5 mm. However, other institution would consider 4 to 5 mm as suitable for device closure. Hence, the problem may be ascribed to the integrity of the IVC rim.

As extensively discussed in the paper, transcatheter device closure of secundum ASD is associated with complications. This is also true with surgical repair. Therefore, one should exercise prudence in the selection of patients as well as adherence to the appropriateness criteria for the procedure. It should be done on patients with significant left to right shunts with evidence of volume overload, acceptable pulmonary vascular resistance and if paradoxical embolism is suspected. Some patients in the study had hemodynamically insignificant shunts. Likewise, one should aim for an accurate assessment of the size, shape and location of the ASD as well as the adequacy and characteristic of the rims surrounding the ASD, which can be augmented by using 3D, TTE and/or 3D TEE. The limitation of this study is the small patient population. Therefore, some important parameter cannot be evaluated as significant to complications.

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Transcatheter occlusion of ostium secundum Atrial Septal Defect has been comprehensively studied in the adult population. Though it is still an evolving cardiac interventional procedure in Pediatrics, this study is promising as there is no previously published article or data on predictors of outcome collected in patients less than 18 years old.

This is a retrospective study limited to chart review which showed good predictor of successful occlusion in small and moderate-sized ASD regardless of age and weght. This offers better alternative, rather than performing open heart surgery, and it carries small but definite risk of morbidity. In this study, the author reported complications that occur in 12 patients. Of the twelve, 7 had valvular dysfunction but what is more relevant was there was no reported mortality. However, 3 of the 12 patients had device embolization/malposition after 12 and 24 hours after deployment, which is attributable to the large size of ASD in these patients. The question arises therefore whether large size ASDs are worth closing by this procedure or could there be definite modifications for this subset of patients. It is worth mentioning also that the success and complication rate were comparable to published data in the literature.

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Transcatheter Closure of Fenestrated ASD Device Using a Multifunctional Occluder (A Device within a Device)

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Background --- Atrial septal defect (ASD) associated with pulmonary hypertension (PH) is observed in 8% to 10% of all ASD cases.[1] Percutaneous closure of atrial septal defect (ASD) secundum type is a widely accepted procedure of care and is indicated in any patient with signs of right ventricular volume overload. In the setting of pulmonary hypertension (PH) treatment is challenging and percutaneous closure may be performed under specific conditions.

Objectives --- To report a case of ASD associated with PH previously closed percutaneously with an ASD fenestrated device. Another aim is to present a staged medical and interventional management strategy for patients with ASD and PH.

Case --- This is a case study of a 21-year-old female weighing 60 kg who presented with exertional dyspnea and easy fatigability at the age of 16 years. 2D ECHO showed an ASD defect measuring 1.2 – 2.6 cm with a QP: QS of 4:1, and pulmonary artery pressure was 52 mmHg by PAT and 58 mmHg by TR jet. On hemodynamic study, pulmonary vascular resistance was computed at 13.6 Wu/m^2. She underwent transcatheter closure using an ASD device (Lifetech CERA JFO Fenestrated ASD occluder device 36mm) with an 8 mm fenestration. For 1 year and 9 months, she was maintained on sildenafil at 50mg/day and aspirin at 300mg/day. Repeat hemodynamic study showed significant decreased of PVR to 4.8 Wu/m^2. Then, a complete closure of the residual shunt was successfully performed using a Multifunctional occluder device (Lifetech MFO) size 10/8mm.

Conclusion --- Patients with ASD with PH may in fact tolerate device closure after a staged interventional procedure (fenestrated closure) and aggressive treatment of pulmonary hypertension. The case describes technical challenges and various options regarding ASD with pulmonary hypertension. ***Phil Heart Center J 2020;22(2):52-59.***

Key Words: Atrial septal defect, secundum ■ Pulmonary hypertension ■ ASD device closure ■ fenestrated closure of ASD

Atrial septal defect (ASD) is a common congenital heart defect (CHD) with a worldwide incidence of 100 per 100,000 live-births and 75% of which are of ASD secundum type.[2] Development of pulmonary hypertension (PH) is observed in 8-10% of all ASD patients. There is no known linear relationship between ASD secundum and pulmonary hypertension in comparison to other intracardiac shunt defects. Several evidences showed that ASD associated with PH is usually independent of the degree, duration of shunting, and the defect size. Due to the potential risk of increase in pulmonary vascular resistance (PVR) even after complete closure of the defect, fenestrated closure of ASD was introduced. Hence, in the event of PH crisis or a critical increase in PVR, it provides adequate cardiac output with a mechanism of right heart decompression.[1] Fenestrated device also allows a controlled residual shunt and may further prevent the progression to advanced pulmonary vascular obstructive disease.

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Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

There are limited cases or evidences regarding complete closure of the fenestrated ASD residual shunt with PH. We reported a case of ASD secundum in presence of moderate to severe pulmonary hypertension that was successfully closed with fenestrated ASD device and given a PH therapy for almost 2 years. With evidence of decrease pulmonary artery pressure on 2D echo and catheterization data, she underwent complete closure of the residual shunt successfully. We also wanted to present a staged interventional approach and medical management strategy for patients with ASD secundum and PH.

Case:

This is a case of a 21-year-old female who presented with exertional dyspnea and easy fatigability with an incidental finding of a murmur during a routine physical examination prior to school enrollment. Patient was apparently well until 16 years of age, the patient started to have easy fatigability and exertional dyspnea. No consult was done until at 18 years of age, an incidental finding of murmur on routine medical clearance was noted and persistence of the above symptoms; hence was referred to a pediatric cardiologist for further evaluation and management. Physical examination showed NYHA Functional Class II, vital signs are within normal for age and a normal peripheral oxygen saturation of 98% on all extremities. Cardiac examination revealed adynamic precordium, apex at the 5th left intercostal space midclavicular line, no heaves/thrills, normal rate, regular rhythm, S1 normal, wide fixed splitting of the second heart sound with accentuation of the P2 component and a grade 3/6 systolic ejection murmur over the left upper sternal border.

Chest x-ray (*Figure 1*) revealed slight increased pulmonary vascularity, prominent MPA, rounding of the apex and retrosternal fullness indicating right ventricular hypertrophy. electrocardiogram (*Figure 2*) revealed sinus rhythm, right axis deviation and right ventricular hypertrophy. Transthoracic echocardiography (*Figure 3*) showed a moderately large secundum-type ASD measuring 1.6 – 2.6 cm with left to right shunting and a QP: QS of 4:1. The rims around the defect were adequate. In addition, the right chambers and pulmonary artery were dilated, both right and left ventricular functions were normal. Tricuspid regurgitation and pulmonic regurgitation were moderate. Systolic pulmonary artery pressure was 72 mmHg by PAT and 68 mmHg by TR jet with a mean pulmonary pressure of 46 mmHg by PR jet.

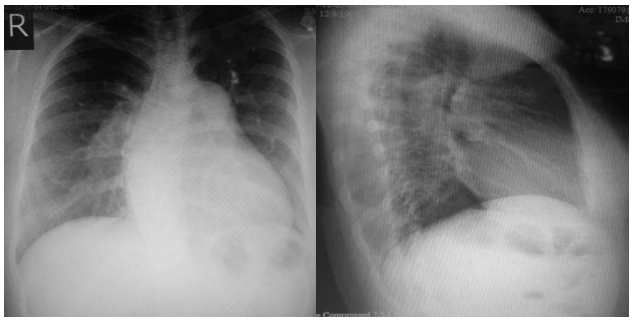


Figure 1. Chest X-ray a. PA view b. lateral view showing slight increased pulmonary vascularity, prominent main pulmonary artery, rounding of the apex and retrosternal fullness and rigth ward deviation of the thoracic spine

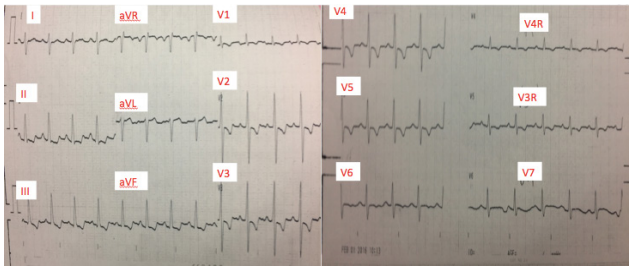


Figure 2. 15 Lead Electrocardiogram showing heart rate of 88bpm; Axis: 105 Intervals: PR 0.16 QRS 0.08 QT 0.38 QTC 0.36 with noted pure R in V4r, T wave inversion in V1, V4R and V3R and was interpreted asSinus rhythm Right axis deviation; right ventricular hypertrophy

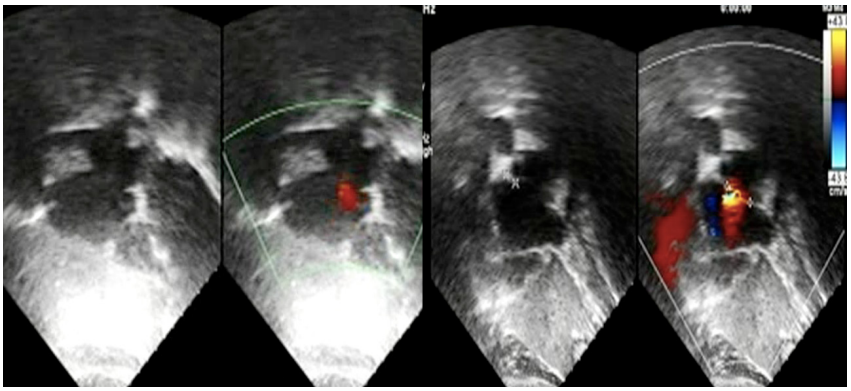
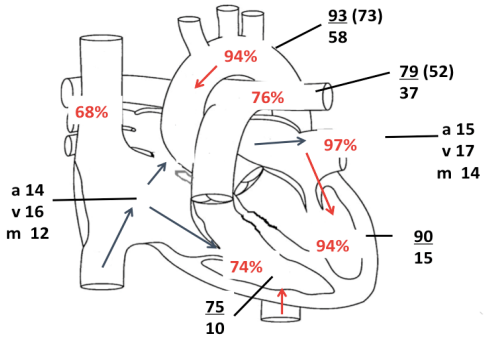


Figure 3. 2D echo with color Subcostal view: a. 4-chamber view, b. Long axis view showed interartrial drop out, measuring 1.6- 2.6 cm with adequate mitral and posterior rims, all 4 pulmonary veins seems to be draining into the left atrium



FLOWS	Patient
Qp	2.9/min/m2
Qs	2.1/min/m2
Qp:QS	1.4:1

	Patient
PVR	13 Wu/m2
SVR	29 Wu/m2
	0.4

Figure 4. Hemodynamic Study Data (Pre-closure)

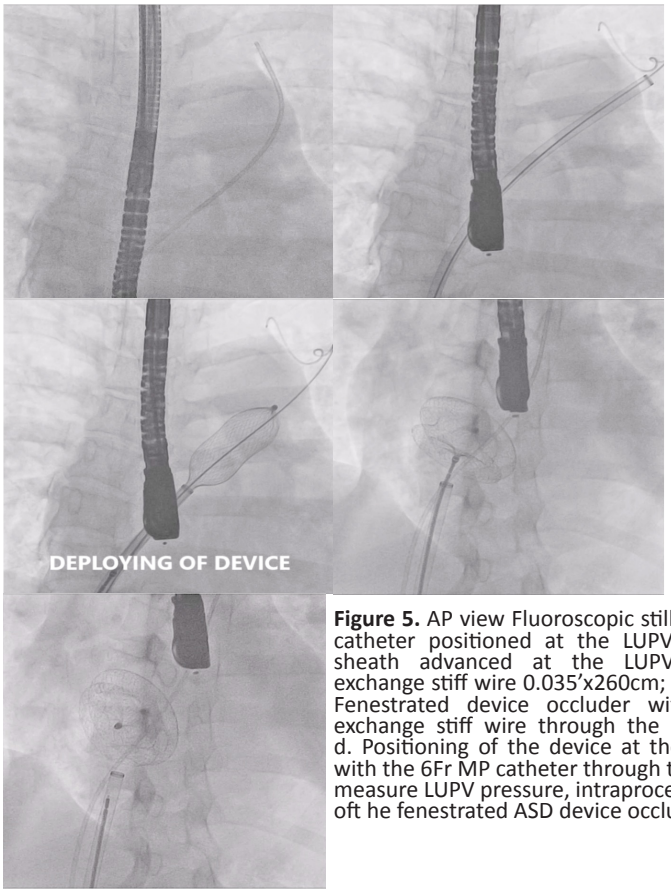
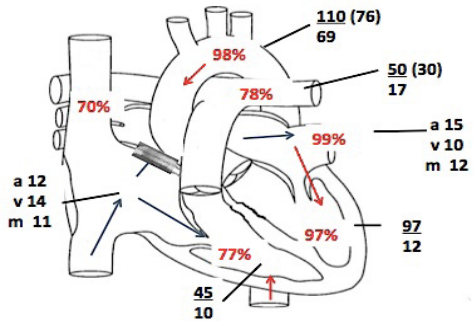


Figure 5. AP view Fluoroscopic still images: a. 6Fr MP catheter positioned at the LUPV; b. 14Fr delivery sheath advanced at the LUPV with Amplatzer exchange stiff wire 0.035'x260cm; c. Deploying of the Fenestrated device occluder with the Amplatzer exchange stiff wire through the 8mm fenestration; d. Positioning of the device at the interatrial defect with the 6Fr MP catheter through the fenestration to measure LUPV pressure, intraprocedural; e. Releasing oft he fenestrated ASD device occluder.

Management:

A. Partial defect closure of ASD with fenestrated ASD Device

ASD device On hemodynamic study (*Figure 4*): Aortic pressure was 93/58 mmHg MAP 73 mmHg, LV end diastolic pressure of 15mmHg and Pulmonary arterial pressure was 73/41 mmHg MAP 52 mmHg. Pulmonary vascular resistance at FiO2 of 100% was computed at 13.6 Wu/m^2. The patient provided written consent; and then underwent sufficient preoperative preparation, including the administration of Milrinone for reducing the pulmonary arterial pressure and oxygen inhalation (24 hours preprocedure). From right femoral vein (*Figure 5*), 6Fr Multipurpose (MP) Catheter was manipulated with 0.035 x 260cm Terumo Straightwire to IVC, RA to LA thru interatrial defect and to left upper pulmonary vein (LUPV). Straightwire was replaced with Amplatzer exchange stiff wire 35'x260cm then a 14Fr delivery sheath was advanced to the proximal LUPV. She then underwent transcatheter closure using an ASD device (Lifetech CERA JFO Fenestrated ASD occluder device 36mm) with a 8 mm fenestration under general anesthesia and the guidance of intraoperative transesophageal echocardiography. Post procedure TEE revealed device in place with decreased in size of interatrial shunt. Post-closure hemodynamic study (*Figure 6)* showed aortic pressure was 110/69 mmHg MAP 76 mmHg, LV end diastolic pressure decreased to 12mmHg and



FLOWS	Patient
Qp	2.9/min/m2
Qs	2.2/min/m2
Qp:QS	1:1.3

	Patient
PVR	6 Wu/m2
SVR	30 Wu/m2

Figure 6. Hemodynamic Study Data (Post-closure)

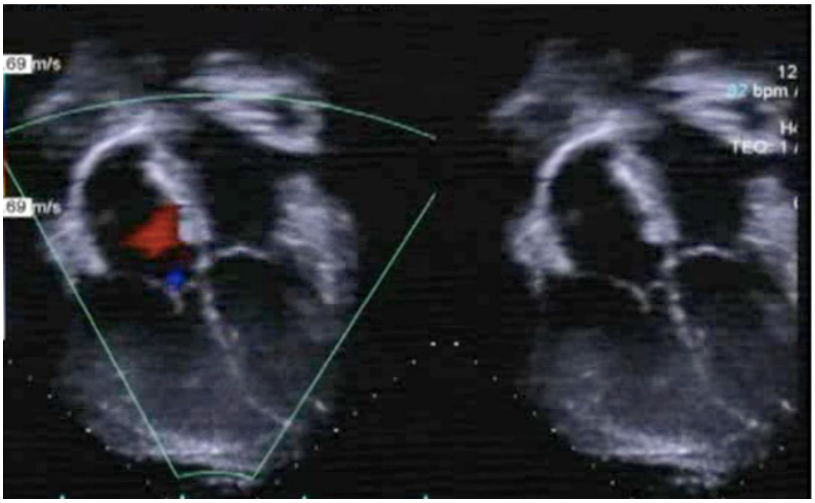


Figure 7. Transthoracic 2d echo with color (1 year and 9 months post closure), 4 chamber view showing the device in place at the interatrial defect with left to right shunt at the fenestration

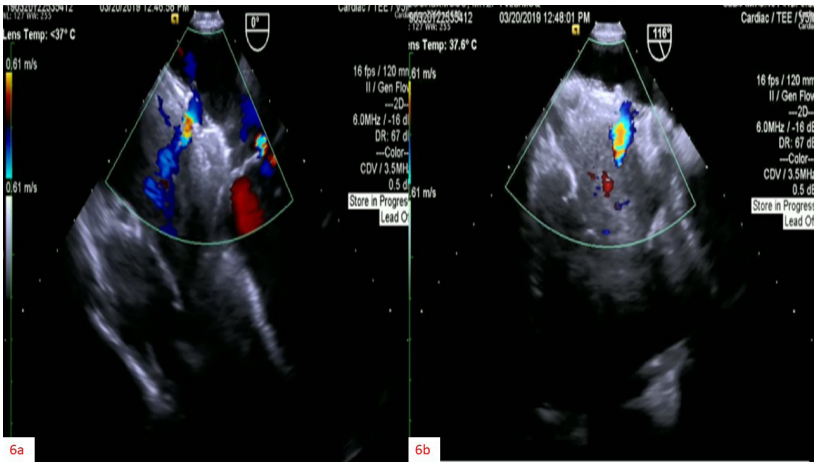
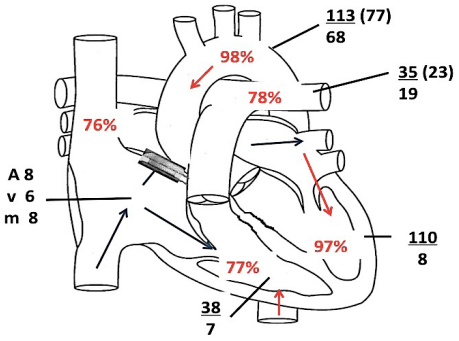


Figure 8. Transesophageal echocargiogram (TTE) pre-device closure, a. 4 chamber view and b. Bicaval view showing the fenestrated ASD device in place with left to right shunt

Pulmonary arterial pressure was significantly decreased at 50/17 mmHg MAP 30 mmHg. Significant decreased of PVR at FiO2 of 100% was computed at 6 Wu/m^2 and increase in systemic vascular resistance (SVR) at 30 Wu/m^2. Course in the ward was unremarkable and the patient was then sent home with Aspirin (300mg/day) and Sildenafil (50mg/day). Post Fenestrated ASD device occlusion, the patient's symptoms improved significantly on follow up. Serial transthoracic echocardiogram (TTE) evaluation (*Figure 7*) revealed in place ASD device with left to right shunting at the fenestrated area, normal pulmonary artery pressure and normal chamber sizes.

B. Closure of fenestrated ASD with multifunctional (MFO) occluder

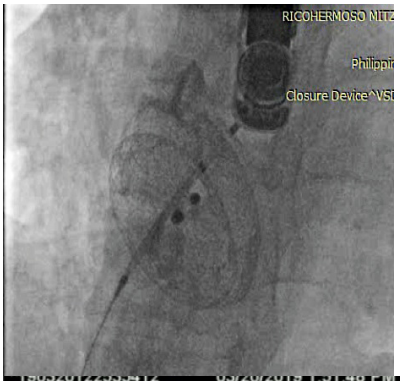
After 1 year and 9 months, complete closure of the residual interatrial shunt was performed under general anesthesia and intraprocedural transesophageal echocardiography with estimated diameter of fenestration in the device is 0.42 to 0.6 cm (*Figure 8*). On hemodynamic study (*Figure 9*): Aortic pressure was 113/68 mmHg MAP 77 mmHg, LV end diastolic pressure of 8mmHg and pulmonary arte rial pressure was 35/19 mmHg MAP 23 mmHg. Pulmonary vascular resistance was computed at 4Wu/m^2. The fenestration on the ASD device was accessed and placed antegradely at the LUPV using 4Fr Berenstein catheter and 0.032x 260cm Terumo Straight Hydrophilic wire. After 4Fr



FLOWS	Patient
Qp	3.1/min/m2
Qs	2.9/min/m2
Qp:QS	1:1

	Patient
PVR	4 Wu/m2
SVR	24 Wu/m2

Figure 9. Hemodynamic Study Data (Pre-closure of the residual shunt)



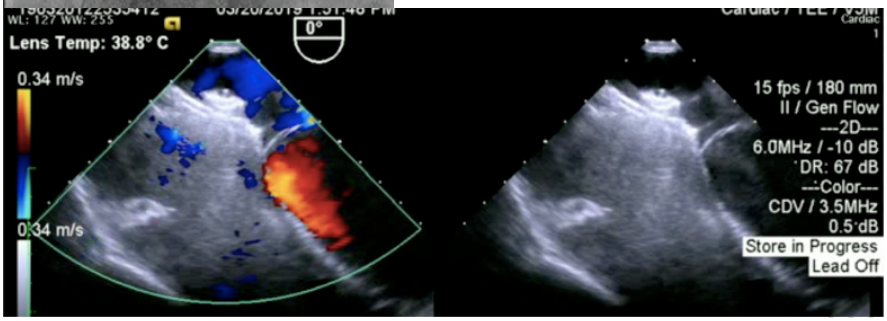


Figure 10. Intraprocedural closure of the residual shunt a. Flouroscopic still image at AP view showing the deployment of the MFO device occluder within the Fenestrated ASD device; b. TEE with color at 4 chamber view showing the MFO device in place with no shunting.

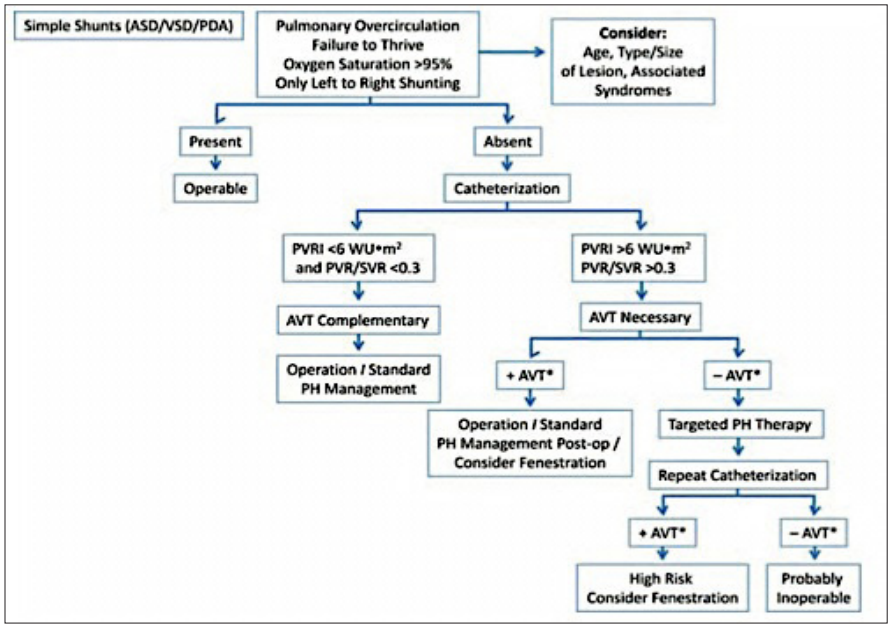


Figure 11. Algorithm for Management of Simple Shunts (ASD) in Pediatric Patients with PH. Reprinted from Abman SH, Hansmann G. Archer SL, et al. Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic Society. Circulation. 2015;132(21): 2037- 2099.

Figure 12. The Lifetech Cera JFO Fenestrated ASD device

Table 1. Recommendations for Closure of Simple Shunt Defects in Adults with PH

Recommendation for Closure of ASD	ESC/ERS 2015[13]	ACC 2018[14]
YES	PVRi 4 WU m	Systolic PA Pressure < one-half systemic PVR / SVR <0.3
INDIVIDUALIZE	PVRi 4 to 8 WU m	Systolic PA pressure one-half to two-thirds systemic PVR / SVR 0.3 to 0.66
NO	PVRi >8 WU m	Systolic PAP >two-thirds systemic PVR / SVR >0.66 and Qp/Qs <1.0

Berenstein catheter was removed, 6Fr delivery sheath was advanced and multifunctional occluder (Lifetech MFO) size 10/8mm was successfully deployed (*Figure 10a*). Post device TEE (*Figure 10b*) revealed MFO device in place with no residual shunting. Patient was then sent home with Aspirin at 300mg/day for another 6 months and Sildenafil was decreased to 25mg/day.

DISCUSSION

In most intracardiac shunts, pulmonary hypertension often develops as a result of prolonged left-to-right shunting and associated with a fixed increase in PVR that may lead to inoperability. Congenital heart disease other than ASD; the timing and severity of the development of pulmonary hypertension is directly related to the size and severity of the defect, and is influence by both pressure and volume overload in the pulmonary arteries.[3] However, the development of PH with volume overload alone in ASD is not well elucidated by this mechanism. In a study done by Kaley et al. stated that there was no direct correlation between the size of the ASD and the development of PH as well as the duration of the shunting. This study suggests that the development of PH in some patients with ASD is multifactorial cause with a likely role for unknown genetic factors especially with female preponderance.[1,4] In relation to our patient developing a PH may be contributed by many factors as have mentioned: with a large ASD measuring a 1.6 – 2.6 cm, chronic volume overload (19 years) and a female.

ASD closure in children and adult with PH were extensively discussed by each subspecialty and with different guidelines and algorithm. In pediatric congenital heart disease, the younger age of repair is an important predictor of operative or interventional an important predictor of operative or interventional survival and freedom from long-term PH. A pediatric PH modified algorithm from the AHA/American Thoracic

Society (ATS) provides guidance for operability (*Figure 11*).[12] In comparison with the adult population, the European consensus guidelines generated by the Joint Task Force for the diagnosis and Treatment of Pulmonary Hypertension of the European Respiratory Society (ERS),[13] and American College of Cardiology Guidelines[14] are summarized in Table 1.

The medical treatment alone of ASD with pulmonary vasodilators is controversial as this treatment for pulmonary hypertension may lower PVR resulting in increased pulmonary blood flow which itself can lead to development of fixed PVR. Due to the potential risk of pulmonary vascular disease with an increase PVR and right heart failure without the positive effect of right-to-left shunting, complete closure of ASDs with PH via transcatheter or surgery is debatable.[6]

In attempt to solve this crisis, there are multiple improvisations in surgical treatment such as the use of flap valves for ASD patients with PH.[7] In the study of Cho YH, et al. showed a satisfactory surgical outcome but had been associated also with significant morbidity and mortality. They also concluded that patients had poorer prognosis if they developed PH immediately or several months or years after ASD closure.[8]

In modern times, transcatheter closure of ASD secundum in patients with normal pulmonary artery pressure or mild to moderate PH is widely accepted and a good alternative to surgical closure in many centers. But for ASD patients with moderate to severe PH, partial defect closure is the only interventional treatment option, hence, the birth of the artificially created fenestration using the sheath dilators, bare metal stents and balloon stretching in standard Amplatzer devices. However, these modifications can be risky because large fenestration can lead to excessive shunting, desaturation and death whereas small-sized fenestrations are at risk for spontaneous occlusion.[9,10] The crisis of creating and maintaining a stable fenestrated size gives way to the development of Fenestrated ASD devices (*Figure 12*). This new device limits the left-to-right shunt and allows a controlled residual shunt (right-to-left shunt) as a decompression mechanism during episode of transient rise in PVR while maintaining an adequate cardiac output. Gonzalez-Barlatay, et al. previously reported successful use of fenestrated ASD device in children with ASD associated with PH.[10]

With the discussion of algorithm for the management of the ASD with PH on both patient and adult populations, our case who presented and detected the cardiac lesion early in adulthood was not a good candidate for complete closure. With the application of the adult algorithm, our patient with systolic pulmonary pressure greater than two-thirds of the systemic pressure, PVRi > 8WU m ASD closure is contraindicated. Same recommendation is followed if we use the pediatric guideline or algorithm; it is not to perform closure but rather to give a targeted PH therapy and repeat catheterization after 3-6 months with possibility of closure with fenestrated ASD device. As have been mentioned, with PH medical therapy without closure of ASD is controversial as if may lead to lowering of PVR resulting in increased pulmonary blood flow which itself can lead to development of fixed PVR. Hence, we decided to adopt a staged interventional management and an aggressive medical treatment.

The team decided to have a partial defect closure using a fenestrated device occluder (Lifetech CERA JFO Fenestrated ASD occluder device 36mm) and a targeted PH therapy using sildenafil. Post-closure hemodynamic study with significant decreased in PVR 6Wu/m^2, PVR: SVR ratio of 0.2 and systolic PA pressure at 50mmHg; despite the lack of solid data these can be considered to indicate a favorable outcome after a partial defect closure.

After almost 2 years, with taking into consideration the clinical, radiological, electrocardiographic and echocardiographic parameters with the cardiac catheterization data we decided to completely close the residual shunt using a multifunctional occluder device (Lifetech MFO) size 10/8mm. According to AHA 2011 recommendation, transcatheter secundum ASD closure is indicated in patients with hemodynamically significant ASD with suitable anatomic features. It is also said that it is reasonable to

perform transcatheter secundum ASD closure in patients with transient right-to-left shunting at the atrial level who are symptomatic because of cyanosis and who do not require such a communication to maintain adequate cardiac output. The closure of the residual shunt was also indicated considering the possibility of paradoxical embolism and patient's desire to be employed (social significance). Pre-closure of residual shunt hemodynamic study showed a PVR of 4 Wu/m^2 and mean PA pressure of 23 mmHg with LVed pressure of 8 mmHg together with echocardiographic data of normal PA pressure prompted the team to consider the complete closure and its high yield of good outcome.

CONCLUSION

Closure of ASD secundum with moderate to severe PH is still a clinical dilemma. Considering all the data from clinical parameters as well as from multiple modalities such as radiological, electrocardiographical, echocardiographical and catheterization can aid a physician in making a reasonably accurate decision to close the ASD.[15] The case reported here suggests transcatheter closure using fenestrated ASD device (Lifetech CERA JFO Fenestrated ASD occluder device) early in patients with associated moderate to severe pulmonary hypertension is clinically feasible in young adult population and thus preventing progression to advanced pulmonary vascular obstructive disease. In addition, with continuation of long-term medical treatment using pulmonary vasodilators and complete closure of the fenestration further decrease of pulmonary pressure is expected.

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Editorial Review

Pulmonary hypertension is known to be the effect of a long standing left to right shunt Congenital Heart Disease.[1] In the new ESC ERS Guideline of 2020 the definition of pulmonary hypertension is revised as a mean PA pressure of 20 mmHg from the previous guideline of ESC/ERS Guideline of 2015 to PA mean pressure of 25 mmHg. Complete evaluation of the patient is necessary to determine if the patient is still a good candidate or will benefit closing the defect after a significant medical regimen for pulmonary hypertension. Closure of these lesions should be done early in life to prevent this complication.[2] However in our setting, most patients are brought to our attention when they're symptomatic already or at late stages of the disease mainly for financial reasons. Thus it entails more workups and treatments, and worst if it's the "end of the road" for them. This article opens a new hope for our patients with this problem. Newer drugs for the treatment of Pulmonary hypertension cost so much management wise. Medications have to be taken for prolonged period of time and these drugs costs are prohibitive in a "third world country". The development and modifications of devices used to close the defect is a welcome development in the management of these lesion – fenestrated ASD Device as used in this patient. (Lifetech CERA JFO Fenestrated ASD occluder device 36mm) with a 8 mm fenestration The commercially available fenestrated device is already available made to close the defect in patients prepared for the procedure.[3-6] The use of targeted drugs therapy (TDT) is successful in preparing the patients for final closure of the defect. As seen in this patient, ASD was closed after 1year and nine months of Sildenafil. Hemodynamics study revealed PA mean pressure of 19 mmHg which is abit lower than ESC/ERS 2020 Guideline for Pulmonary Hypertension. PVR also dropped to 4 Wood units. The result is very encouraging but long term plan and follow-up should be emphasized. In There are reports that even after closure of these shunts, pulmonary hypertension may re-occur later.[7] Probably a ten-year follow-up is necessary to detect early development or recurrence of pulmonary hypertension.

In the critical review by Balaji, et al. I quote the following "although ''treat and repair'' strategy might have reduced the perioperative mortality of patients with shunt and raised PVRI, the long-term outcome needs to be carefully investigated. The need for continued TDT after operation and its financial implications, especially in the low- and middle -income countries, needs to be taken into account since not ensuring drug supply may in fact be counterproductive. The ''treat and repair'' approach, which could rather be paraphrased as ''treat, repair and treat'', seems to have expanded the window of opportunity in selected patients with moderately raised PVRI

Based on our analysis of the magnitude of PVRI change brought about by TDT, we empirically suggest that patients with pretricuspid shunt with PVRI elevation up to 11 WU.m^2 may be treated with TDT for at least six months and should be reassessed. Systematic and large volume prospective multicentre studies with longer duration follow-up are needed to ascertain the safety of the treat and repair approach. Considering the difficulties in designing such a study, multicentre systematic registry-based database should be initiated. The routine application of the ''treat and repair'' strategy may instead lead to ''repair in haste and regret at leisure'' outcome for many patients."[8]

And finally, family planning should be emphasized as well for a planned pregnancy to have a better outcome for the mother and the baby.[9]

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This case report is about a 21-year old female who was diagnosed as a case of ASD secundum late in her adolescence with complaints of exertional dyspnea and easy fatigue. Physical examination findings confirmed the presence of heart disease, NYHA class II. Echocardiography demonstrated an ASD secundum, 1.6-2.6 cm, severe pulmonary hypertension (68-72 mmHg systolic). Medical management for heart failure was started and subsequently underwent hemodynamic study when she was 18 years old. Findings were consistent with severe PAH, pulmonary vascular resistance at 100% oxygen was 13.6 Wu/m^2. Decision to partially close ASD with an ASD device (Life tech CERA JFO fenestrated occluder with 8 mm fenestration) was performed. Post device hemodynamics PVR at 100% decreased to 6 Wu/m^2. Discharge medications included aspirin and sildenafil with advice to repeat hemodynamics study. After 21 months, she underwent a successful closure of a fenestrated ASD with a Lifetech MFO size 10/8 following a normal pulmonary pressure and PVR of 4 Wu/m^2. Sildenafil dose was decreased and aspirin was continued for 6 months.

Atrial septal defect is a common congenital heart defect with an incidence of 8-10 % among live births. Depending on the size of defect and other associated anomalies, small isolated ASD can spontaneously close, other ASDs that are hemodynamically significant are surgically closed by 2-5 years of age. Significant ASD that were not closed are at risk of developing pulmonary hypertension. This case report adhered to the 2015 guidelines issued by the AHA/American Thoracic Society (ATS) on operability in shunt anomalies including ASD. The decision to partially close the ASD with a fenestrated ASD occluder is backed with several studies that show the advantage of a staged-management of ASD with a PVR >6 Wu/m^2. One of these papers by Jain and Dhalvi studied ASD patients with moderate and severe PAH. If the ASD is not closed, irreversible PAH will ensue which can cost patients lives dearly and affect the quality of life and longevity.

During the hemodynamic study, acute vasoreactivity testing was recommended in cases with baseline PVR index 6-9Wu/$m^{2.}$ A decline of 20% in PVR, decrease of 20% in PVR:SVR ratio, final PVR:SVR ratio of <0.33, final PVR index <6.0 Wu/m^2 were considered favorable outcomes after shunt closure. They concluded that in patients with moderate to severe PAH and in those with significant LV restriction, the decision is to use a fenestrated device or leave the ASD open. In this case, the AVT result did not show a decrease in PVR to <6.0 Wu/m^2, hence a staged approach was considered. ASD was partially closed with a fenestrated ASD occluder with 8mm opening.

Kayley and Dahdah et al. reported their experience on ASD patients with PAH using a fenestrated device. They concluded that the device was beneficial for these patients with PAH and no major device-related complications were encountered. The fenestrated device restricts left to right shunting but allows decompression of the right heart during pulmonary hypertensive crisis. Meticulous care toward patient selection, adequate ASD and device sizing and fenestration size is required for optimal outcomes. Alain Fraisse et al reported on ASD closure indications and contraindications. Parameters considered for ASD transcatheter closure are pulmonary arterial pressure less than 2/3 of systemic arterial pressure, PVR less than 2/3 of systemic resistance and a positive response to pulmonary vasodilator testing. The hemodynamic contraindication for ASD closure was a PVR >8 Wood units. However, a fenestrated device may be considered. In another paper by Faccini and Butera, it is said that TCC is a widespread technique used to treat a secundum ASD. It provides a less invasive approach with quick recovery and reduced physical and psychosocial impact. Limitations that may have a significant impact on the feasibility and success of percutaneous ASD closure are grouped into anatomical, device-related, associated defects and untoward treatment-associated issues, physiological and complications. Subjects with contraindications for complete closure by catheter device may be tried on drugs like diuretics, ACE inhibitors for 3-6 months and re-evaluate hemodynamically during ASD balloon occlusion or undergo partial ASD closure with a fenestrated device.

After 21 months, the fenestrated ASD device was occluded by a single device following a hemodynamic study which showed favorable result, PVR of 4Wu/m^2. The device was a Life tech multifunctional occluder size 10/8. No residual shunting was noted and the patient was discharged on aspirin and sildenafil. In 2012, Roie Tal, Qarawani. Dahud and Abraham Lorber reported a case of a 45 year old who had closure of fenestrated ASD device using a single device (Occlutech Figula Flex ASD occluder). Use of life tech MFO device has been reported by different authors and one post market clinical follow up study to collect patient outcomes and procedural success and performance of Lifetech. KONAR-MF VSD occluder for patients with VSD is estimated to start June 30, 2020. It will only after two years that the medical community will

have informations on its feasibility and safety.

According to its product insert, life tech KONAR MFO is a new soft woven mesh self-expanding device with 2 discs joined by an articulated waist. Each disc has a hub on the external surface, so the device can be either positioned antegradely or retrogradely. It is used to treat cardiac septal defects, patent ductus arteriosus and other selected defects successfully without significant complications but with more options. The low profile in different measures allows closure of large defects even in low weight infants. Since this device is still new in the market, meticulous monitoring of safety in this 21 year old female is recommended.

This case report represents a case of a young adult with severe pulmonary hypertension that was managed successfully with the staged approach: closure of defect with fenestrated Lifetech MFO device while maintained on pulmonary vasodilator and aspirin. After 21 months, complete closure of the fenestration was successfully performed.

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Outcome of Percutaneous Transcatheter Device Closure of Ventricular Septal Defect in Children Weighing Less than 10 Kilograms

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Background --- Ventricular Septat Defect is the most common congenital heart disease in children. Infants weighing less than 10 kilograms with hemodynamically significant shunts may benefit from early transcather closure of VSD.
Methods --- Patients who underwent percutaneous transcather closure of VSD from December 1, 2019 to April 30, 2020 were included in this study. All charts and records of the study group including demographic data, echocardiographic studies, angiographic data and procedural details were reviewed and analyzed.
Results --- All patients in the study group underwent successful percutaneous transcatheter VSD device closure. Mean age of the subjects is 16.7±8.56 months with mean weight of 7.38±1.87 kilograms. Angiography revealed mean VSD size of 0.43±0.09 cm and all were occluded using the Lifetech Konar Multifunctional Occluder with device size ranging from 6/4 to 10/8 and mean delivery sheath size of 5.2±0.91. There was significant improvement on follow -up after 1 month in terms of weight gain (mean weight gain of 1.22 kilograms), decrease in left ventricular end diastolic dimension (7.37% decrease from baseline) and pulmonary arterial pressure (33.16% decrease from baseline) with t-value of 0.008 9, 0.0202 and 0.0455 respectively. Minor complications noted were blood loss requiring transfusion in 60% of subjects and the presence of residual shunt in 10% of the subjects with mean hospital stay of 3.6 ± 0.69 days.
Conclusion --- Early percutaneous transcatheter closure of hemodynamically significant ventricular septal defect in patients weighing less than 10 kilograms using the low profile Lifetech Konar Multifunctional Occluder is feasible and effective. ***Phil Heart Center J 2020;22(2):63-76.***

Key Words: transcatheter device closure ■ ventricular septal defect ■ multifunctional occluder ■

Ventricular septal defect (VSD) is the most common congenital heart disease identified in children.[1] Surgical and transcatheter closure of VSD are both well established modes of treatment. Both procedures carry some risks but are generally well tolerated. Percutaneous closure of VSD in patients less than 10 kilograms is rarely done and the usual practice is to wait for the natural closure of small shunts in children. However, patients with hemodynamically significant large shunts may benefit from early closure.

In Philippine Heart Center, percutaneous transcatheter closure of shunts in pediatric patients have been done successfully. PDA and ASD device closure procedures were started in the early 2000 and percutaneous closure of VSD followed after a few years. Several studies on early transcatheter closure of patent ductus arteriosus and atrial septal defects but there are limited literature available on percutaneous VSD device closure in children weighing less than 10 kilograms, or even in children less than 2 years of age. Reports on device closure in small infants

are done via perventricular access and complications of this approach includes wire perforation of cardiac chambers, esophageal perforation, pericardial effusion and mediastinitis.[2]

Thakkar, et al. reported a single center experience of muscular VSD device closure in infants in India. The study was done between 2008 to 2010 and it included 24 infants 2-12 months of age and weighing 2.7-4.9 kilograms. The perventricular access is used to accommodate the 6Fr -8Fr device loaders. They included symptomatic children with hemodynamically left to right shunt. The device was deployed under the guidance of transesophageal echocardiography using 6Fr to 8Fr delivery sheaths and the procedure was successful in 21 out of the 24 infants. The remaining three infants who underwent perventricular device closure had immediate surgery for the following reasons: perforation of the left ventricle, difficult access of the VSD and a large residual shunt after release of device. There were 4 major complications reported - death in 2 infants due aspiration and severe pneumonia, 1 infant with esophageal tear, and 1 infant with complete heart block and left ventricular outflow obstruction.[2]

In the study by Thakkar, et al. perventricular apporoach to device closure of VSD in small infants is preferred to percutaneous access due to the large delivery sheaths needed to deploy the device. However, with the availability of the newer Lifetech Konar Multifunctional Occluder (MFO), with the availability of the newer Lifetech Konar Multifunctional Occluder (MFO), which can close shunt susing 4Fr to 7Fr delivery sheath, percutaneous transcatheter VSD closure in smaller infants is possible. This study aims to determine the outcome of percutaneous transcatheter device closure of hemodynamically significant VSD in children weighing less than 10 kilograms.

The objective of the study is to describe the outcomes of transcatheter device closure of a hemodynamically significant ventricular septal defect in children less than 10 kilograms; specifically it aims to determine the prevalence of percutaneous transcatheter VSD closure in children with hemodynamically significant VSD weighing less than 10 kilograms and describe the demographic profile and characteristics of children weighing less than 10 kilograms undergoing transcatheter VSD device closure (age, sex, actual weight, Z value of weight for age, comorbidities and associated cardiac lesions) to describe the pre-procedural echocardiographic parameters and indications for transcatheter VSD device closure of children less than 10 kilograms (type of ventricular septal defect, size of the defect (cm), Qp:Qs ratio, left ventricular end-diastolic dimension and corresponding z value, pulmonary artery pressure); to describe the intraprocedural characteristics of VSD transcatheter device closure on patients less than 10 kilograms (type of occluder used, size of occluder used, size of the VSD on angiogram, size of delivery sheath used, flouroscopy dose (Cumulative Air Kerma in mGy); to describe the outcomes of transcatheter VSD device closure on patients less than 10 kilograms and to describe the post-procedural echocardiographic parameters 1 month after transcatheter VSD device closure in children less than 10 kilograms:

- presence of residual shunts
- left ventricular end-diastolic dimension and corresponding z-value
- pulmonary artery pressure

METHODS

This is cross-sectional descriptive study. Included in the study were pediatric patients ages 0 to 5 years old weighing less than 10 kilograms who underwent transcatheter VSD device closure from December 1, 2019 to April 30, 2020 while those excluded were patients with complex congenital heart disease or cardiac lesions other than an atrial septal defect or a patent ductus arteriosus, with other interventional procedure done other than hemodynamic studies and transcatheter device closure, and those with no informed consent granted by their parents or legal guardians.

This study was approved by the Philippine Heart Center Institutional Ethics Review Board and informed consent was obtained from the legally authorized representative of the patient included in the study.

Operational Definitions:

Hemodynamically significant VSD

the presence of a ventricular septal defect in a patient with signs and symptoms of heart failure secondary to the shunt anomaly, has a QP:QS ratio of 1.5:1 or greater, LV enlargement on chest x-ray and echocardiography

VSD device closure

patients who were qualified for VSD device closure are those with hemodynamically significant VSD and underwent percutaneous closure of the defect. The patients were screened at least a week before the procedure with routine pre-catheterization work-up done such as chest x-ray, electrocardiogram, creatinine, complete blood count, prothrombin time and partial thromboplastin time. The qualified patients were admitted a day prior to the procedure and are reevaluated and referred to Anesthesia Department for sedation. Patients less than 10 kilograms, were intubated and were given general anesthesia for the procedure.

Weight for age

The patient's weight was plotted in the WHO growth charts to get the z-score for the weight for age. The Z-scores were reported as follows:

- Z-score of less than -2: underweight
- Z-score of -2 to +2: normal weight for age
- Z-score above +2: overweight

Echocardiographic Studies

All echocardiographic studies were done within 1 month before and a month after the transcatheter device closure. The echocardiogram was done by a non-invasive clinical research fellow and was counterchecked by a level III pediatric echocardiographer. All echocardiographic studies were reviewed by the interventionalist prior to the procedure. The result of the echocardiogram was relayed to the attending physician. The following echocardiographic findings were described and reported in the study as follows:

Type of VSD

The VSD was described according to the location as seen in at least 2 echocardiographic views (parasternal long axis, parasternal short axis, 5chamber view and subcostal view):

a. Perimembranous
b. Subaortic
c. Subpulmonic
d. Doubly committed
e. Muscular

Size of the defect

a. The VSD measurement was taken in at least 2 echocardiographic views (parasternal long axis, parasternal short axis, 5-chamber view and subcostal view)

QP:QS

a. The QP:QS ratio was measured echocardiographically using the formula:

$$\frac{\text{RVOT diameter x Pulmonic Valve VTI}}{\text{LVOT diameter x Aortic Valve VTI}}$$

Left ventricular end-diastolic dimension (LVEDd)

The LVEDd was measured in the m-mode of the short axis view. Normal values are based on LVEDd z-score for weight and are used to describe the LVEDd dimension as follows:

a. less than the normal for weight (z-score less than -2): Small LV cavity
b. Within the normal limits for weight (z-score less than -2): normal LV dimensions for age
c. Above the normal limits for weight (z-score above +2): LV dilatation

Pulmonary artery pressure (PAP)

The pulmonary artery pressure measurements were derived from the following:

a. Pulmonary acceleration time – measured in the color doppler pulse wave of the pulmonic valve

b. VSD gradient – measured in at least 2 views. The pulmonary artery pressure was measured by subtracting the systemic blood pressure of the patient from the measured

Study Maneuver

All patients ages 0 to 5 years old and weighing less than 10 kilograms who underwent VSD device closure from December 1, 2019 to April 30, 2020 were included in the study. Consent were obtained from the parents. The following data were also obtained:

1. Demographic profile and characteristics
   a. Age
   b. Sex
   c. Actual weight
   d. Z value of weight for age and corresponding z-value
   e. Comorbidities and associated cardiac lesions
2. Pre-procedural echocardiographic parameters and indications for transcatheter VSD device closure
   a. Type of ventricular septal defect
   b. Size of the defect (cm)
   c. Qp:Qs ratio
   d. Left ventricular end-diastolic dimension and corresponding z-value
   e. Pulmonary artery pressure
3. Intraprocedural characteristics
   a. Occluder used as to:
   - type of occluder
   - size of occluder
   b. Size of delivery sheath
   c. Size of the VSD on angiogram the VSD measurement will be taken by the interventionalist on either the left anterior or true lateral view or both
   d. Fluoroscopy dose as cumulative air in kerma in milligray (mGy)
4. Procedural Outcomes
   a. **Procedural success or failure**

Device implanted and released – the device is successfully deployed and released. Cineangiographic imaging post deployment shows proper placement of the device with no heart block upon deployment of device.

Device implanted but not released – the device is implanted but cineangiographic imaging post-deployment shows device placement that is not amenable for release (ex: the presence of a significant leak, the presence of a significant aortic regurgitation secondary to the device, etc.) or note of complete heart block upon deployment of device.

Device embolization – the device was deployed and released but embolized after release.

Procedure aborted – The procedure is aborted prior to deployment of the device for whatever reason.

b. Complications will be described as either having no complications, minor complications and major complications
   i. None
   ii. Minor complications
   a. Device embolization requiring percutaneous removal
   b. Hematoma in the groin or puncture site
   c. Blood loss requiring transfusion - patients with significant blood loss during the procedure that would require blood transfusion during or after the procedure (within the same hospitalization).
   d. Residual shunt – leak or residual shunt after the transcatheter closure seen on post-procedure angiogram and follow-up echocardiogram
   e. New onset or increased regurgitation
   f. Arrythmia other than complete heart block not requiring pacemaker insertion

g. Prolonged hospital stay - patients less that 10 kilograms who underwent VSD device closure were expected to be admitted for 5 days or less. Patients who were admitted for more than 5 days were considered as having prolonged hospital stay

h. Hospital acquired infection - Patients who developed fever and clinical sepsis were referred to the pediatric infectious disease specialist for evaluation. Work-up for infection was done such as CRP, procalcitonin, CBC and blood culture. Those patients who were require additional antiobiotics for hospital acquired infection as assessed by the pediatric infectious disease specialist were described as having hospital acquired infection as a complication.

iii. Major complications

a. Thromboembolism - patients with signs and symptoms of arterial or vascular thrombosis (*Table 1*) after the procedure was referred to vascular service for assessment and underwent doppler studies for documentation;

b. Device embolization requiring surgical removal;

c. Complete heart block - patients who had successful transcatheter VSD device closure but developed complete heart block after release requiring pacemaker insertion;

d. New onset or increased regurgitation requiring surgery;

e. Death occurring within 1 month from the procedure regardless of cause

Table 1. Clinical presentation of venous thrombosis and arterial thrombosis based on symptomatology

Venous Thrombosis	Arterial Thrombosis
Bluish discoloration	Pallor
Engorgement of the veins	Mottling
Weight	Cold and clammy extremities
Edema	Decrease in the pulse

5. Post-procedural echocardiographic parameters

The echocardiogram was done 1 month after the procedure. The following parameters were described:

i. Presence of residual shunts including the size and gradient across the residual shunt if present

ii. Qp:Qs if a residual shunt is present

iii. Left ventricular end-diastolic dimension and corresponding z-value

iv. Pulmonary artery pressure

Statistical analysis

Data were tabulated for organization and was analyzed using statistical tool STATA 13.1. Descriptive statistics was used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion was used for categorical variables, median and inter quartile range for non-normally distributed continuous variables, and mean for normally distributed continuous variables. Ttest was used to compare the echocardiographic parameters before and after transcatheter VSD closure.

RESULT

The study included 10 subjects (n=10) weighing less than 10 kilograms and who underwent transcatheter closure of VSD from December 1, 2019 to April 30, 2020. All medical records underwent a thorough medical chart review. Demographic data preprocedural and post-procedural echocardiographic parameters, and intraprocedural characterstics and outcomes were recorded and analysed.

Table 2 shows the demographic profile of the studied group. The results indicate that majority of the subjects were aged 13-23 months (60%) while the minority were 24-36 months old comprising 10% of the total population. In terms gender, it shows that majority were female which is 60% of the population. For the actual weight in kilograms, 70% weigh more than 6 kilograms with weight range of 4.9 to 10 kg in all patients in this study group. Majority of them were classi-

fied as severely underweight (50%) in terms of weight-forage with a z-value of less than -3. No other comorbidities were reported among the patients. However, 3 out of 10 patients had other shunt lesions reported as follows – patent foramen ovale, patent ductus arteriosus and atrial septal defect.

Pre-procedural echocardiographic parameters of the studied group are presented in Table 3. Based on the results, all patients (n=10) had perimembranous type of VSD. Mean size of VSD defect in centimeters was 0.47 cm (range 0.3-0.7), mean Qp:Qs was 2.33 (range 1.5-6.0), left ventricular end diastolic dimension was 3.16 cm (range 2.4-3.5) and the mean left ventricular enddiastolic dimension based on z-value was 2.1 (range 0-5). In terms of pulmonary artery pressure, 30% had normal PAP, 30% had mild pulmonary arterial hypertension, 20% had moderate pulmonary arterial hypertension and 20% had severe pulmonary arterial hypertension.

Table 4 shows the intra-procedural characteristics of the studied group based on the angiographic findings, type of occluder and delivery sheath used, technique used as well as the total fluoroscopy dose. Based on the results, majority of patients had a perimembranous (90%) type of VSD. However, one patient had a subpulmonic type of VSD on angiogram. For all the patients in this study, a Lifetech Multifunctional Occluder was used (100%) and the device size used were 6/4 to 10/8, using delivery sheaths ranging from 4Fr to 7Fr. The frequently used technique for the procedure was retrograde (70%) versus antegrade approach (30%). The mean size of VSD defect seen on angiogram was 0.43 cm (range 0.33 to 0.6cm). The mean fluoroscopy dose expressed as cumulative Air Kerma in mGy was 218.94 (range 88.3 – 320.69).

Table 5 shows the clinical outcome of transcatheter VSD device closure among the studied group. Results show 100% procedural success with no reported cases of embolized device or aborted procedure. Conversely, 60% of the total population reported intraprocedural blood loss requiring transfusion of blood components particularly packed red blood cell. Patients had a mean hospital stay of 3.6 days (range 3-5 days).

Post-procedural echocardiographic parameters are seen in Table 6. From the above results, it shows that one month postprocedure, 90% of the studied patients had no residual shunts or leaks noted. On the other hand, one of the patients who was seen to have a large perimembranous VSD had residual shunt measuring 0.3 cm. New onset valvular regurgitation was also noted in one patient wherein the echocardiogram on follow-up reported trivial tricuspid regurgitation. Furthermore, the left ventricular end-diastolic diameter shows improvement with a mean of 2.93 cm (range 2.6 – 3.5) from its initial mean of 3.16 cm (range 2.4-3.5). Likewise, the pulmonary artery pressure also improved wherein 7 out of 10 patients have normal (70%) pulmonary pressure, 2 patients (20%) have mild PAH and 1 patient (10%) has moderate PAH.

Table 7 shows the comparison of the three parameters before and after transcatheter closure of the VSD. Paired T-test was done to test and determine if the mean difference between two groups is statistically significant. It was observed that weight, pulmonary artery pressure measured by echocardiogram, and left ventricular end diastolic dimension showed significant difference from the prepocedural to post-procedural results with t-value of 0.0089, 0.0202 and 0.0455, respectively. This table also shows that there was a 16.53% increase in the weight of the patients after 1 month and 33.16% and 7.37% decrease in the pulmonary artery pressure and LVEDd respectively on their follow-up echocardiogram.

All adverse events after transcatheter VSD closure seen in this study group are listed in Table 8. Similar to the study of Yang, et al. the complications are categorized as minor or major adverse events. No major events were noted in all patients and minor event noted were blood loss requiring transfusion, presence of a residual shunt on follow-up echocardiogram and new onset regurgitation.

Listed in Table 9 is the summary of the pre-, intra- and post-catheterization parameters as to the subjects' weight, left ventricular end diastolic dimension, QP:QS ratio, VSD size by angiography, associated cardiac lesion, occluder and delivery sheath size, technique used by the operator, length of hospital stay

and the complications noted during the entire hospital course up to the follow-up at 1 month post-procedure.

Table 2. Demographic Profile

Parameters	Frequency/ Mean ± SD
Age in months	
0 - 12 months	3
13 - 23 months	6
24 - 36 months	1
Mean ± SD	16.7 ± 8.56
Sex	
Male	4
Female	6
Actual Weight (kg)	
<3 kg	0
3-6 kg	3
>6 kg	7
Mean ± SD	7.38 ± 1.87
Weight-for-age Z-value	
Overweight (>2)	0
Normal (0 to 2)	2
Underweight (-2 to 0)	3
Severely underweight (< - 3)	5
Comorbidities	
With Comorbidities	0
Without Comorbidities	10
Other Cardiac Lesions	
PFO	1
PDA	1
ASD	1

PFO - patent foramen ovale, PDA - patent ductus arteriosus, ASD – arterial septal defect

Table 3. Pre-procedural Echocardiographic Parameters

Parameters	Frequency/ Mean ± SD
Type of Ventricular Septal Defect	
Perimembranous	10
Subaortic	-
Subpulmonic	-
Muscular	-
Mixed	
Size of VSD Defect (cm)	
Qp:Qs ratio	
	0.47 ± 0.10
	2.33 ± 1.33
	3.16 ± 0.55
	2.1 ± 1.91
Left ventricular end-diastolic dimension (cm)	
Left ventricular end-diastolic dimension (z-value)	
Pulmonary artery pressure	
Normal	3
Mild (25-40)	3
Moderate (40-60)	2
Severe (>60)	2

PFO - patent foramen ovale, PDA - patent ductus arteriosus, ASD – arterial septal defect

DISCUSSION

Percutaneous transcatheter VSD closure is already a well-accepted treatment for patients with VSD. From the time it was first performed in the 1980s,[4] numerous device occluders, delivery systems, deployment techniques and approaches have been developed. Nevertheless, transcatheter device closure procedures in small infants are not yet prevalent due to the possible risks and complications that the procedure may incur. Device closure of VSD was initially done via the perventricular approach which eliminates the risk of having acute limb ischemia but otherwise still carries major risks such as ventricular perforation and ventricular pseudoaneurysm.[2] Percutaneous closure of VSD in small infants have been done by many centers but are described to be more challenging compared to transcatheter procedures in older and bigger patients because of the more difficult catheter manipulation as well as the limited available calibers of the delivery systems suitable for small patients. According to Xing, et al. a number of published studies even suggested that small

Table 4. Intra-procedural Characteristics

Parameters	Frequency/ Mean ± SD
Type of Ventricular Septal Defect based angiogram	
Perimembranous	9
Subaortic	-
Subpulmonic	1
Muscular	-
Mixed	
Type of occluder used	
Multi-functional Occluder (MFO)	10
Muscular VSD Occluder	0
Membranous VSD Occluder	0
Size of occluder used	
6/4	2
7/5	3
8/6	3
9/7	2
10/8	2
Size of delivery sheath used	5.2 ± 0.91 (range 4Fr-7Fr)
Technique	
Retrograde	7
Antegrade	3
Size of VSD Defect (cm)	0.43 ± 0.09
Flouroscopy dose (cumulative Air Kerma in mGy)	218.94 ± 81.23

infants weighing less that 10 kilograms are not suitable for percutaneous transcatheter VSD closure.[5]

In this study, 10 patients with mean weight of 7.38 ± 1.87 kilograms and mean age of 16.7 ± 8.56 months underwent successful transcatheter VSD closure. This result is similar to the study of Xing, et al. who reported successful transcatheter VSD closure of infants with mean weight of 6.8 ± 2.8 kilograms but with a younger study group whose mean age is 7.2 ± 4.7 months. The older age group of our patients may be attributed to the later timing of intervention in our setting. Fifty percent of the patients in this study are malnourished with z-value of their weight forage noted to be less than -3. On follow up, all patients were noted to have increase in their weight with average weight gain of 1.22 kg and mean weight of 8.6 ± 2.7 kg for all patients after a month from discharge.

Table 5. Outcome of VSD Transcatheter Device Closure

Parameters	Frequency/ Mean ± SD
Procedural success	
Device implanted and released	10
Device implanted but not released	-
Device embolization	-
Procedure aborted	-
Complications noted during hospitalization	
Vascular thrombosis	-
Bleeding requiring transfusion	6
Prolonged hospital stay	-
Hospital acquired infection	-
Death	-
None	-
Hospital stay (days)	3.6±0.69

Table 6. Post-procedural Echocardiographic Parameters

Parameters	Frequency/ Mean ± SD
Presence of residual shunts	10
Yes	-
No	-
	-
New valvular regurgitation/ obstruction	-
None	6
Trivial	-
Mild	-
Moderate	-
Severe	-
Left Ventricular end-diastolic dimension (cm)	2.93 ± 0.34
Left Ventricular end-diastolic dimension (z-value)	1.39 ± 0.8
Pulmonary artery pressure	
Normal	7
Mild (25-40 mmHg)	2
Moderate (40-60 mmHg)	1
Severe (>60 mmHg)	0

Table 7. Comparison of weight, pulmonary artery pressure and left ventricular end diastolic dimension before and after transcatheter device closure

Parameters	Pre-Procedure	Post-Procedure	Percent Change	Paired T-Test p value
Weight	7.38 ± 0.59	8.60 ± 0.86	16.53% increase	0.0089
Pulmonary Artery Pressure (mmHg)	38.60 ± 6.11	25.80 ± 3.03	33.16% decrease	0.0202
Left Ventricular End Diastolic Dimension (cm)	3.16 ± 0.17	2.93 ± 0.11	7.37% decrease	0.0455

Table 8. Minor and major adverse events after transcatheter VSD closure

Complications	Total
Minor	
• Device embolization requiring percutaneous removal	-
• Hematoma in the groin or puncture site	-
• Blood loss requiring transfusion	6
• Residual shunt on follow up echocardiogram	1
• New onset or increased regurgitation	1
• Arrhythmia other than complete heart block not requiring pacemaker insertion	-
• Prolonged hospital stay	-
• Hospital acquired infection	
Major	
• Device embolization requiring surgical removal	-
• Complete heart block	-
• New onset or increased regurgitation requiring surgery	-
• Death	-

All patients in this study underwent transthoracic echocardiogram prior to the procedure and all patients included had a perimembranous type of VSD with mean VSD size 0.47 ± 0.10 cm. Angiographic findings were were different in 20% of the patients wherein 1 patient had a subpulmonic type of VSD on angiogram while another patient had a mixed type of VSD with a perimembranous and subpulmonic component. These findings were also confirmed in the intra-procedural as well as the post-procedural transthoracic echocardiogram done. A subpulmonic and a subaortic VSD is more challenging to close percutaneously the distance of the defect from the semilunar valves will help the operator decide if device closure can be done. In both patients with the subpulmonic defect, the occluder was successfully implanted and completely occluded the subpulmonic defect. For the patient with both perimembranous and subpulmonic defects, the subpulmonic VSD was successfully occluded but there was still egress of contrast material noted through the perimembranous exit on angiogram.

Comparing other echocardiographic parameters before and after VSD closure showed significant improvement as well. The mean left

Table 9. Summary of pre-, intra- and post-catheterization parameters

Patient #	Age (mo)	Weight (kg)		LVED (cm)		QP;QS ratio	VSD size (cm)	VSD type	Associated lesion	Device size	Delivery sheath (Fr)	Approach	Hospital Stay	Remarks
		Pre	Post	Pre	Post									
1	11	6.5	7	2.5	2.6	2.6	0.33	SP	none	8/6	5	retrograde	4	Blood Transfusion
2	14	4.9	5	2.4	2.8	6	0.45	SP	PDA	8/6	5	retrograde	5	Blood Transfusion (+) residual shunt
3	13	5.9	6	3.2	2.7	2	0.5	PM	PFO	9/7	7	antegrade	4	Blood Transfusion
4	36	10	14	3	2.9	1.5	0.4	PM	none	6/4	4	retrograde	3	None
5	13	9	10	3.3	2.7	1.6	0.6	PM	none	10/8	6	antegrade	3	Blood Transfusion (+) TR trivial
6	22	8	9.5	3.4	3	2	0.4	PM	none	7/5	5	retrograde	3	None
7	17	7	8	4	3.5	2.1	0.5	PM	none	7/5	5	retrograde	3	None
8	24	10	11.5	3.5	3.2	1.5	0.33	PM	ASD	7/5	5	retrograde	4	Blood Transfusion
9	10	7.5	8	2.53	2.5	2	0.3	PM	none	6/4	4	retrograde	3	Blood Transfusion
10	7	5	7	3.8	3.4	2	0.5	PM	none	10/8	6	retrograde	4	

LV ED left ventricular end diastolic dimension, SP – subpulmonic VSD, TR - tricuspid regurgitatio n

ventricular end diastolic dimension of the study group is 3.16 ± 0.55. On follow up, the mean LVEDd of the study group is 2.93 ± 0.34. Using the Z-value for LVEDd, the difference of the pre-procedure mean Z-value of 2.1 to the post-procedure mean Z-value of 1.3 is significantly lower. Considering that the follow-up echocardiogram of the patients in this study was done a month after the procedure, this is comparable to the report of Yang, et al. in 2014 wherein they reported improvement in the LVEDd Z-value from 1.7 to 0.7 after 2 years. Pulmonary arterial pressure measurement preand post-procedure show that all patients with moderate to severe pulmonary arterial hypertension had significant decrease in the PA pressure. Two patients from the study group had severe pulmonary arterial hypertension prior to the device closure and both of them had more than 30% fall in the PA pressure decreasing their PA pressures to 39 mmHg and 45 mmHg from the baseline of 66 mmHg and 68 mmHg respectively.

In all patients in this study group, Lifetech™ Konar Multi-Functional Occluders (MFO) (*Figure 1*) were used with occluder sizes ranging from 6/4mm to 10/8 mm. The MFO is made from nitinol mesh with 144 wires of nitinol cables.[6] It is designed as a combination of two discs wherein 1 disc serves as a high-pressure disc (left disc) attached to a truncated cone and the other serves as a low-pressure disc (right disc) and is attached to the waist arm.[7]

The high-pressure disc is usually placed in the left ventricular (LV) side and the low pressure is placed in the right ventricular (RV) side. Conversely, the delivery system can be attached to either disc can be deployed either from the arterial access (retrograde technique) or from the venous access (antegrade technique). In one of the patients with a subpulmonic defect (*Figure 2*), the technique used was retrograde technique but the LV disc was placed in the right ventricle and the RV disc was placed in the left ventricle. There was a mild obstruction to the right ventricular outflow tract (RVOT), immediately post occlussion but nogradient was noted on the follow-up echocardiogram.

The Konar MFO device is suitable for small infants because of the smaller caliber delivery sheaths available. The delivery system (*Figure 3 & 4*) is low profile with a 3Fr delivery cable and 4Fr to 7Fr delivery sheath7. Majority of the patients in this study group with a VSD size of 0.3 – 0.4 cm used a 4Fr to 5Fr delivery sheath while the patients with VSD size of 0.5 to 0.6 cm and used device size of 9/7 to 10/8 used a 6Fr to 7Fr delivery sheath.

Two patients in this study had other significant shunt anomalies. One patient had a Patent Ductus Arteriosus (PDA) and was occluded using also a Konar-MFO 7/5 device and the other patient (*Figure 5*) had a secundum Atrial Septal Defect (ASD) which was closed using a 10mm Ceraflex ASD device.

There were no reported major complications in all the patients in this study group with a mean hospital stay of 3.6 ± 0.69 days (range of 3-5 days). This is comparable to the study done by Yang, et al. in 2010 where they reported a mean hospital stay of 3.3 days.[8] In our institution, all patients less than 10 kilograms undergoing catheterization procedure are intubated and are weaned and extubated in the intensive care unit. All patients in this study were discharged in 35 days and were only reported to have minor complications. Yang reported that major adverse events in patients undergoing transcatheter VSD closure are thromboembolism, heart block requiring pacemaker insertion, device embolization and new-onset regurgitation requiring surgery while minor adverse events are hematoma, blood transfusion due to blood loss, embolization with transcatheter removal, hemolysis, arrhythmia, new or increased valvular regurgitation and fever.[8]

Minor complications noted in the patients postprocedure in this study are blood loss requiring transfusion in 60% of the patients, presence of residual shunt in one patient and trivial tricuspid regurgitation in one patient seen on follow up echocardiogram.

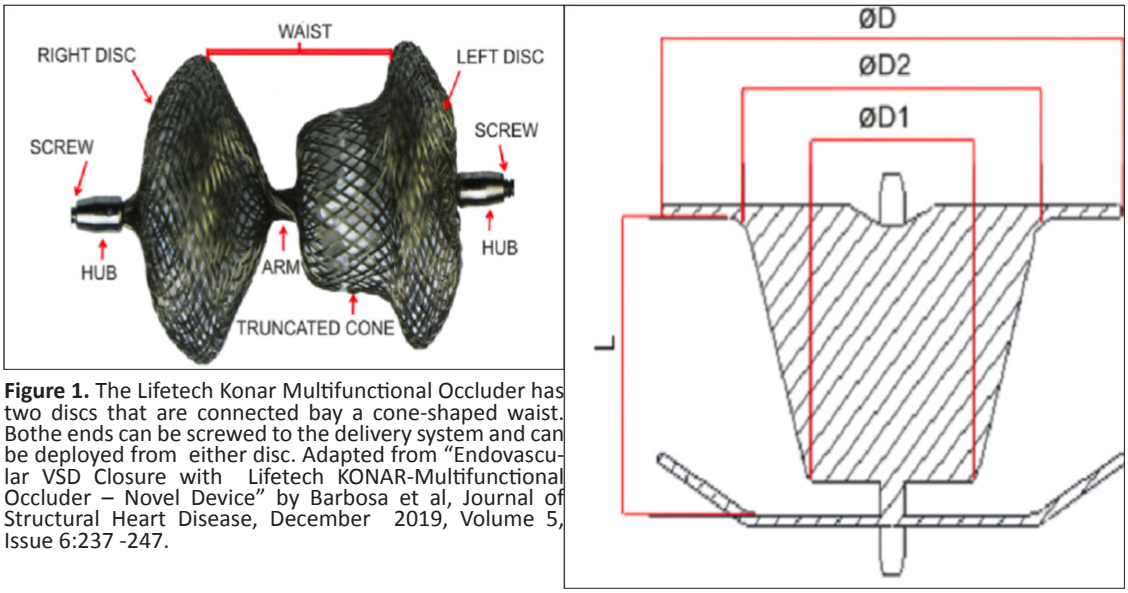

Figure 1. The Lifetech Konar Multifunctional Occluder has two discs that are connected bay a cone-shaped waist. Bothe ends can be screwed to the delivery system and can be deployed from either disc. Adapted from "Endovascular VSD Closure with Lifetech KONAR-Multifunctional Occluder – Novel Device" by Barbosa et al, Journal of Structural Heart Disease, December 2019, Volume 5, Issue 6:237 -247.

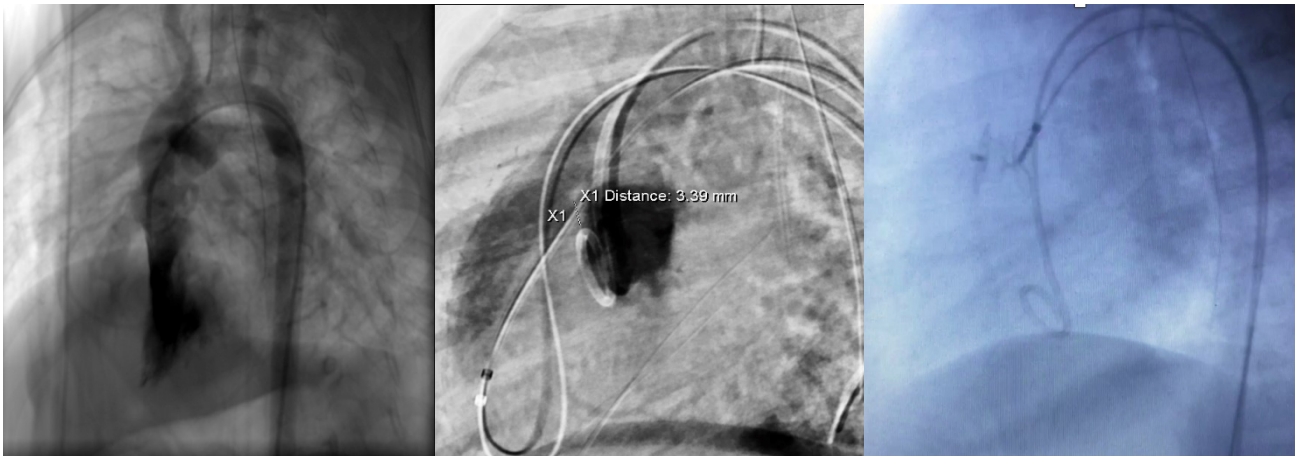

Figure 2. Patient PA, 11 months old weighing 6.5 kilograms with a subpulmonic VSD. A: LV angiogram taken at left anterior oblique view showing the defect. B: The defect was measured at 0.33cm. C: A Lifetech Konar- MFO device deployed from the arterial access (retrograde technique) but with the MFO device inverted (LV disc placed in the RV and the RV disc placed in the LV).

Catalog Number		D Disc Diameter (mm)	D2 Waist Diameter LV Side (mm)	D1 Waist Diameter RV Side (mm)	L Waist Length (mm)	Recommended Delivery Sheath (Fr)
	LT-MFO-5-3	10	5	3	4	4F-5F
	LT-MFO-6-4	10	6	4	4	
	LT-MFO-7-5	12	7	5	4	
	LT-MFO-8-6	12	8	6	4	
 with membrane	LT-MFO-9-7	14	9	7	4	6F
	LT-MFO-10-8	14	10	8	4	
	LT-MFO-12-10	16	12	10	4	7F
	LT-MFO-14-12	18	14	12	4	

Figure 3. Different sizes of MFO and their corresponding recommended delivery sheaths. Sizes 5/3 to 8/6 have no membrane and uses a 4Fr to 5Fr delivery sheath while 9/7 to 4/12 devices have a PTFE membrane within the disc and uses 6Fr to 7Fr delivery sheath adapted from "Endovascular VSD Closure with Lifetech KONAR-Multifunctional Occluder – Novel Device" by by Barbosa et al, Journal of Structural Heart Disease, December 2019, Volume 5, Issue 6:237 -247.

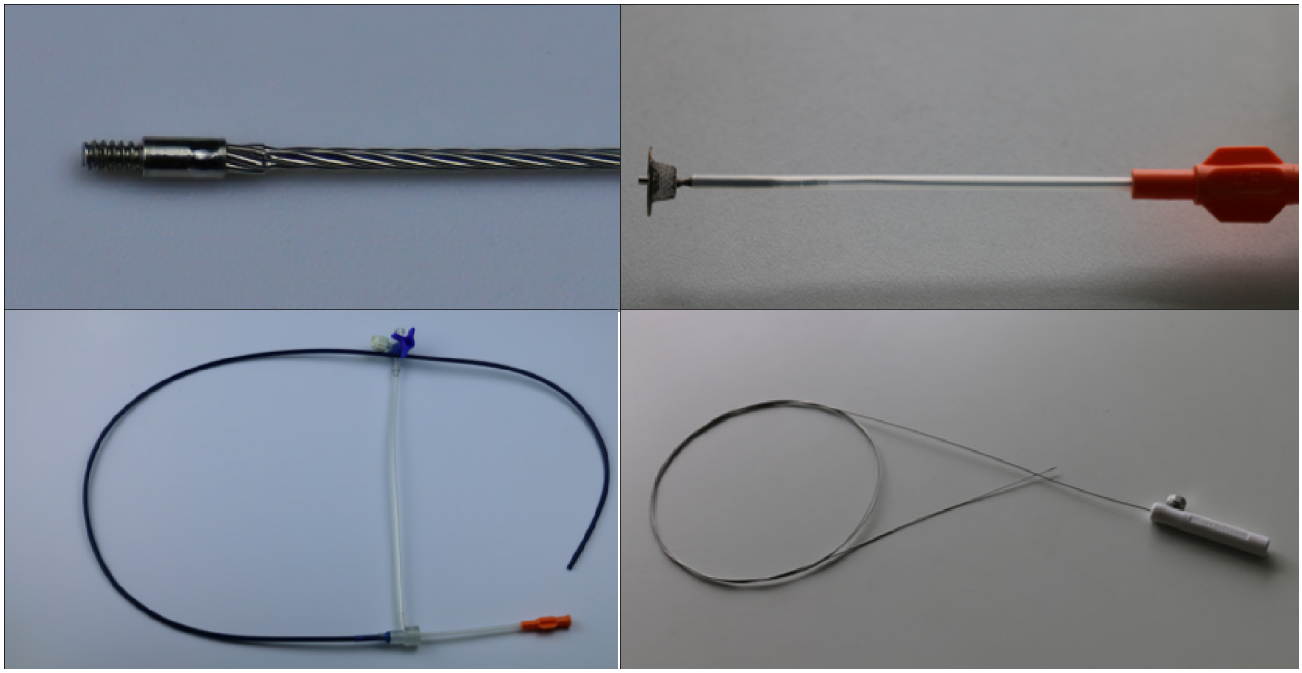

Figure 4. The Konar-MFO delivery system is low profile which makes it easier to manipulate. A: Screw at the end of the delivery cable which can attach to either disc of the device. B: The loader with the delivery cable and device through it. C: The delivery sheath. D: The delivery cable with a screw for the device on one end and the handle on the other. Adapted from "Endovascular VSD Closure with Lifetech KONAR-Multifunctional Occluder – Novel Device" by by Barbosa et al, Journal of Structural Heart Disease, December 2019, Volume 5, Issue 6:237.

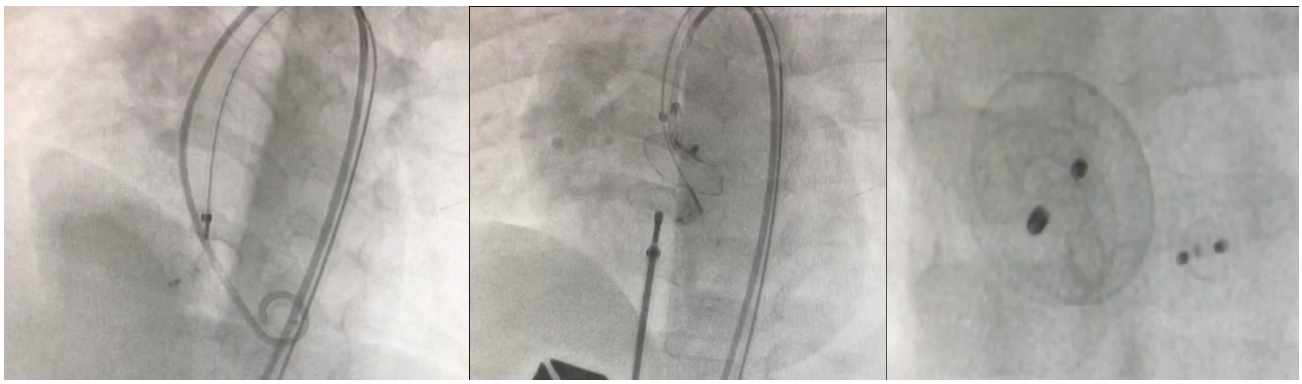

Figure 5. Patient VP, a 2 year old patient with a 0.8cm secundum ASD and a 0.3cm perimembranous VSD. A: Retrograde technique of VSD device closure using Konar-MFO device 7/5. B: ASD device and MFO device (VSD) in their places attached to their respective cables. C: Both devices were released.

CONCLUSION

Transcatheter closure of ventricular septal defect was done successfully in 10 patients weighing less than 10 kilograms using the Lifetech Konar Multifunctional Occluder. Minor complications noted were blood loss requiring transfusion and the presence of residual shunt. On follow-up after 1 month, there was noted clinical improvement in terms of weight gain and decrease in the pulmonary arterial pressure and left ventricular end diastolic dimension.

RECOMMENDATION

We recommend a larger, multicenter, and prospective controlled study to further evaluate the feasibility and long-term results of percutaneous transcatheter closure of ventricula septal defects in infants. A continuous follow-up among subjects is also necessary to evaluate the long term complications.

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Editorial Review

"Transcatheter closure of perimembranous ventricular septal defect (Pm VSD) is not new. The eccentric device was introduced in 2006 had changed the scenario in the world.[1] But soon after the early results, the device was withdrawn due to unacceptably high incidence of complete heart block. The novel KONAR-MF TM device is unique in nature by several folds and appears promising for Pm VSD closure.[2] The device has low-pressure disc and high-pressure disc with a major hemodynamic advantage due to incremental diameters of the central connecting cone shaped structure. This advantage allows the operator to position the device easily in the defect. The medium profile design can be easily negotiated through 5-6fr delivery sheaths. The clamping force and shear stress by the device is negligible due to its profile and design. The added advantage of retention screws on either side is useful to deploy from either side of the device.

"The authors of the study "Outcome of percutaneous transcatheter device closure of ventricular septal defect in children weighing less than 10 kilograms" are very much appreciated for producing good clinical outcome. All the patients of the study were under 10 kilograms and underwent successful closure of Pm VSD using KONAR-MF. There were no major complications. The delivery sheath was < 6fr. This study clearly shows the device can be effectively used in the young. All patients in the study were having shunt >2:1. The men left ventricular end diastolic dimension was > 3.16 ± 55 suggests that all patients were having hemodynamically significant Pm VSD. There were 7 children had mild to severe pulmonary hypertension in the study group became normal after the device closure. The operators chose to deploy the device using retrograde method in 70% of cases.[3] This is possible with KONAR-MF due to retention of screws on either side. The high-pressure disc is positioned in the arterial side in case of retrograde deployment. Authors chose this method probably due to the device can be easily deployed using smaller size sheath even in the young patients.

The follow-up echocardiographic results are very much encouraging in the present study. The left ventricular end diastolic dimension ('z') decreased significantly to 1.39 ± 0.8. All patients gained the weight during follow-up by 16.5% (p=0.008). Overall the results of the study is very much encouraging. The study power is somewhat less due to a smaller number of patients. This is due to smaller number of patients suitable for the device closure. The case suitability and indications for the device closure are usually less in this subset of population. Therefore, the present study shows that usage of KONAR-MF in young children under 10 kilograms is feasible with negligible complications. Retrograde method is useful even in smaller children to close the Pm VSD effectively."

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Pediatric Invasive Cardiology

Percutaneous Mitral Valvuloplasty in Children Using Arteriovenous or Venoarterial Loop Technique with TMP-PED Balloon

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Background --- Percutaneous Mitral Valvuloplasty (PMV) is a well accepted management for mitral stenosis. PMV using the standard approach has been done successfully in children but difficulties may arise in the most crucial part of the procedure, which is the transseptal puncture and crossing of the balloon into the mitral valve. ***Case*** --- We reviewed four pediatric patients with mitral stenosis secondary to rheumatic heart disease who underwent successful PMV using the arteriovenous or venoarterial loop technique with the TMP-PED balloon. ***Conclusion*** ---The use of TMP-PED balloon with the arteriovenous or the venoarterial loop technique in performing percutaneousmitral valvuloplasty in children is a novel yet effective innovation that can successfully reduce the obstruction across the mitral valve in patients with mitral stenosis. ***Phil Heart Center J 2020;22(2):78-84.***

Key Words: Mitral Stenosis ■ Percutaneous Mitral Valvuloplasty ■ Arteriovenous loop ■ Venoatrial loop ■ TMP-PED balloon

Rheumatic Heart Disease is the most common cause of Mitral Stenosis (MS). It is a dreaded complication that usually occurs 15-40 years after the initial episode of Rheumatic Fever. It may, however, occur earlier in patients from developing countries like the Philippines wherein symptoms attributed to mitral stenosis manifest as early as the second decade of life.[1]

In mitral stenosis, the main problem is the presence of a mechanical obstruction and the only definitive treatment is to relieve the obstruction. This may be addressed by open mitral valve repair, mitral valve replacement, or percutaneous mitral valvuloplasty (PMV).[2]

The usual procedure when doing PMV is through the antegrade approach using an Inoue Balloon Catheter. This balloon is a 12F poly-vinylchloride tube with coaxial lumina. Right heart catheterization is performed by inserting a 9F femoral sheath in the venous access. Once at the right atrium (RA), transeptal catheterization is then performed via a standard.

Brockenbrough procedure is done wherein the Brockenbrough needle is advanced beyond the interatrial septum. A coiled-tip wire is then placed in the left atrium (LA) through the Brockenbrough sheath. The Inoue balloon catheter is advanced through the coiled-tip wire and eventually advanced further until the tip of the catheter has crossed the mitral valve into the left ventricle. The distal part of the balloon is inflated partially and the catheter is withdrawn slightly until a resistance is felt. The balloon is inflated further while monitoring the transmitral gradient through the tip of the Inoue catheter in the left atrium and a pigtail catheter in the left ventricle (LV) from the arterial access.[3]

PMV using the standard approach has been

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Available at **http://www.phc.gov.ph/journal/publication** ISSN 0018-9034

done successfullt in children but difficulties may arise in the most crucial part of the procedure that is the transeptal puncture and crossing of the balloon into the mitral valve. The presence of hemodynamic instability, difficult anatomy and operator experience are just some of the variables that may dictate procedural success or failure. Crossing the Inoue Balloon across the mitral valve is one of the challenges that were encountered when doing PMV in children. Several reasons for the difficulty of the Inoue Balloon to cross the mitral valve include the following: a very dilated left atrium, a low or anterior transseptal puncture, altered inflow across the mitral valve, a severely stenotic mitral valve and the presence of a subvalvular stenosis.[4] Different techniques have been done by adult interventionalists in performing PMV. Case reports in adult patients undergoing PMV have described various ways in doing the procedure such as the veno-arterial loop technique,[2] rapid snare technique,[4] and over the wire technique.[5] However, there are very limited reports in the different techniques in performing PMV in children since most centers still use the Inoue balloon via the standard approach. One novel technique that has been tried in the Philippine Heart Center is the use of TMP-PED balloon and the arteriovenous (AV) or venoarterial (VA) loop.

TMP-PED™ balloon is from Tokai Medical
Products and its main purpose is for congenital valvular stenosis for both pulmonic stenosis and aortic stenosis in children as well as balloon static dilatation of patent foramen ovale in neonates with critical congenital heart diseases. In the Philippine Heart Center, the TMP-PED balloon is being used only for this indication since it was introduced in 2016 until it was utilized lately in performing PMV in children using the arteriovenous and venoarterial loop technique. This balloon is made of polyamide elastomer that allows the balloon to engage in native tissues without slippage.[6]

This case series reviews four pediatric patients with mitral stenosis secondary to rheumatic heart disease who underwent PMV using the arteriovenous or venoarterial loop technique with the TMP-PED balloon.

Procedural Details

In this case series, all patients were referred to cardiovascular anesthesia for intraprocedural sedation. The younger patients were intubated and were given general anesthesia while the the 18-year old patients were only given intravenous sedation with midazolam and nalbuphine. Right heart catheterization was done via a femoral vein percutaneous puncture and a Fr 8 femoral sheath was inserted. Left heart catheterization was done via a femoral artery percutaneous puncture and a Fr 5 femoral sheath was inserted in the arterial access. A Fr 5 pigtail catheter was inserted through the arterial access and manipulated up to the LV. Left ventricle angiography at RAO 30° and lateral projections as well as right atrium angiography at AP and lateral projections were done for guidance in the transseptal puncture. A Mullins sheath was inserted through the venous access and was positioned in the RA adjacent to the atrial septum.

A transeptal puncture was performed using a Brockenbrough needle. After gaining access to the LA, simultaneous pressure measurement at the LA through the Mullins sheath and LV through the pigtail catheter in the arterial access was done. Either an arteriovenous loop or a venoarterial loop was used to allow effective passage and anchorage of the TMP-PED balloon across the mitral valve.

To make an arteriovenous loop, a slightly angled tip 0.035 inch x 260 cm hydrophilic wire was inserted through the arterial access and manipulated into the descending aorta, ascending aorta, LV and LA. A Fr 6 20 mm gooseneck snare catheter was inserted through the venous access and manipulated into the IVC, RA, through the transeptal puncture and then to the LA. The end of the hydrophilic wire in the LA was snared out from the LA and manipulated to exit the femoral vein to complete the arteriovenous loop *(Figure 1)*.

To make a venoarterial arterial loop, the hydrophilic wire is inserted through the Mullins sheath placed across the interatrial septum and the hydrophilic wire was manipulated to the LA, LV and then to the aorta. Using a 20 mm snare

and a Fr 6 snare catheter inserted through the femoral artery access, the end of the hydrophilic wire at the aorta is snared out to exit the femoral artery to complete the venoarterial loop (*Figure 2*).

Once the arteriovenous loop or the veno-arterial loop was secured, a Fr 8 femoral sheath positioned across the mitral valve, balloon dilatation was done by manual inflation using diluted contrast material (1:4 dilution) in a 50 cc Luer-lock syringe. Simultaneous pressure recording in the LA and LV was again done post-PMV.

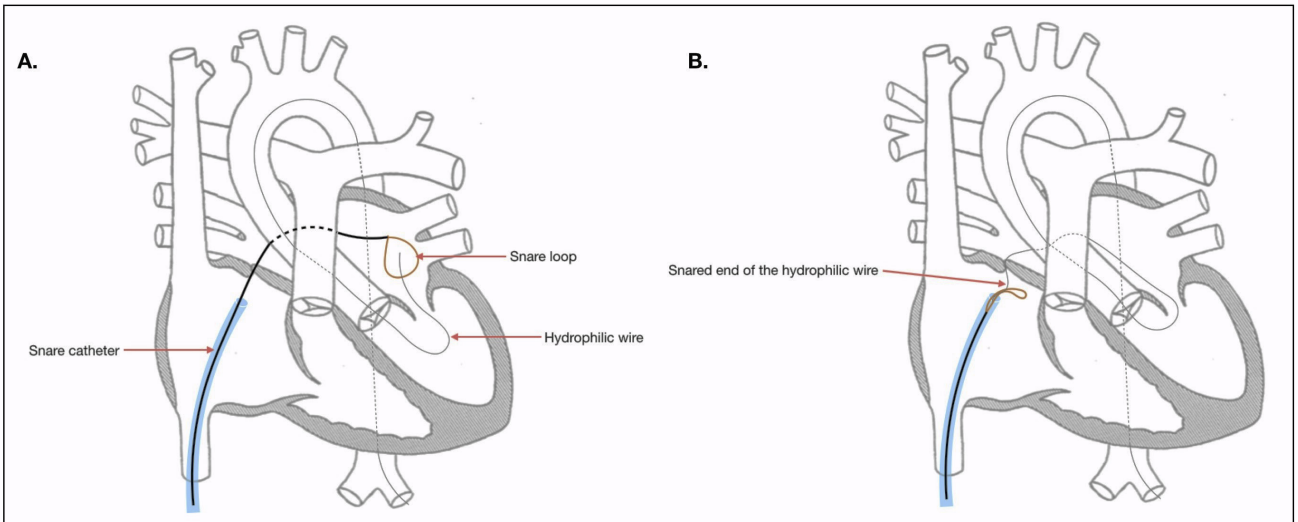

Fig 1. Arteriovenous loop technique. **A:** A hydrophilic wire inserted in the arterial access with its end in the left atrium. **B:** The end of the hydrophilic wire in the LA is snared to the RA and manipulated in the venous access to exit the femoral vein.

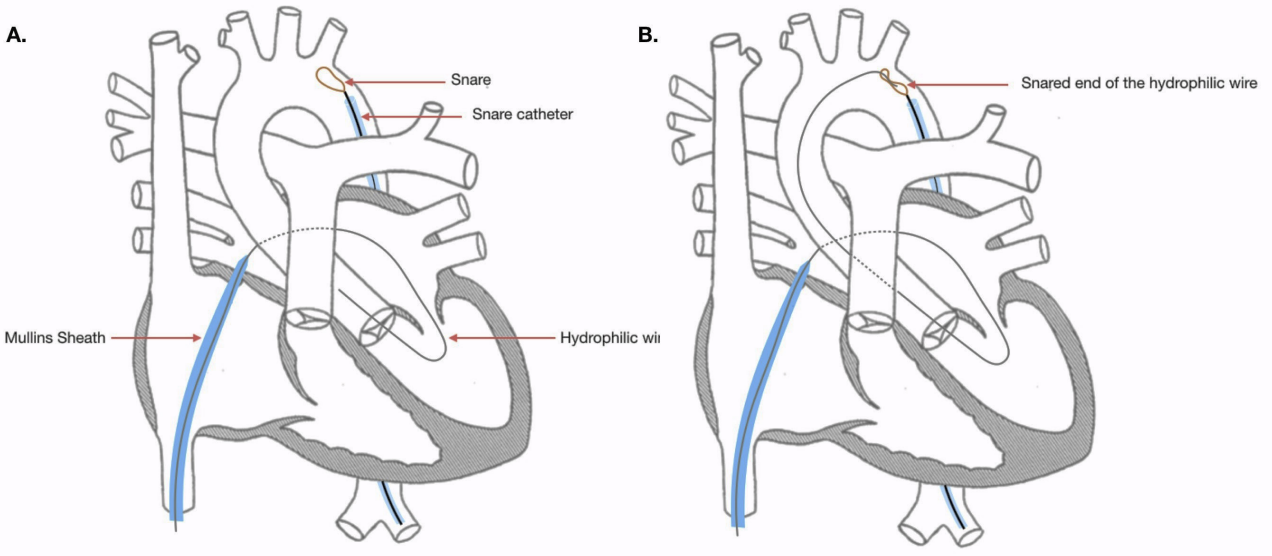

Fig 2. Venoarterial loop technique. **A:** With the Mullins sheath across intertatrial septum, a hydrophilic wire inserted inside the Mullins sheet was manipulated to the LA, LV and then to the aorta. A snare with a snare catheter is also inserted through the arterial access. **B:** The end of the hydrophilic wire was manipulated towards the aorta where it will be snared out of the arterial access to exit the femoral artery.

Table 1. Profile of TMP PED Balloon Used

Balloon diameter	20mm (up to 20.7 mm at RBP)
Balloon length	30mm
Cable length	120cm
Sheath	7Fr
Nominal pressure	2.0atm
Rated burst pressure (RBP)	2.5atm

Case 1

The first case was an 11-year old male who was admitted due to one month history of easy fatigability, difficulty of breathing and edema.

On admission, he presented with signs of severe heart failure such as orthopnea, anasarca, pericardial effusion and hepatomegaly. Echocardiography showed severe mitral stenosis, mild mitral regurgitation, severe tricuspid regurgitation and moderate aortic regurgitation with pericardial effusion. The mitral valve area was measured 0.9 cm^3 by planimetry, 0.6 cm^3 by pressure half time (PHT) and 0.6cm^3 by velocity time integral (VTI), with a mean gradient of 11 mmHg and Wilkins score of 11. The pulmonary arterial pressure by pulmonary acceleration time was also elevated at 42 mmHg. Medical management for heart failure was optimized and after 2 weeks, the patient was referred to Pediatric Invasive Cardiology for PMV. The patient was referred to CV anesthesia and intubation was done prior to PMV. Sedation was done with general anesthesia. Transeptal puncture was achieved via antegrade approach using a mullins sheath and simultaneous pressure measurement of the LA and LV showed a transmitral gradient of 15 mmHg. Placement of the Inoue Balloon across the mitral valve was attempted several times but failed. A 0.035 hydrophilic wire was then inserted in the aorta then to the LV and LA. A 20mm Fr 6 snare catheter was used to snare the end of the hydrophilic wire at the LA through the venous line and finally exiting the femoral vein to complete the arteriovenous loop. A 20 mm TMP-PED balloon balloon (*Figure 3*) was then inserted through the hydrophilic wire in the femoral vein and was positioned across the mitral valve. The TMP-PED balloon was then rapidly inflated to its maximum capacity and then deflated quickly. Dilatation was repeated two times. An indentation and waistline was noted in the mid-portion of the balloon during inflation. Post-PMV, a transmitral gradient of 5mmHg was recorded. Post-procedure, patient stayed at the PICU for 3 days with significant improvement in the heart failure symptoms characterized by resolution of the edema, pericardial effusion and decrease in the degree of hepatomegaly.

Case 2

The second case was an 18-year old female who was diagnosed with rheumatic fever at 11 years old and was eventually diagnosed with rheumatic heart disease and mitral stenosis at 13 years old. She was referred for intervention when she presented with easy fatigability. On echocardiography, the mitral valve area measures 0.9cm^3 by pressure half time, 0.4cm^3 by planimetry, peak gradient of 15 mmHg across the mitral valve and Wilkins score of 8. She was referred to the Pediatric Invasive Cardiology Division for PMV. She was referred to CV anesthesia for IV sedation. Transeptal puncture was done via the standard approach with a mullins sheath and a brokenbrough needle. After transseptal puncture, an 0.035 hydrophilic wire was inserted to the LA and LV and was snared out of the femoral artery to complete a veno-arterial loop. The TMP-PED balloon (*Figure 4*) was inserted through the femoral vein and balloon dilatation was performed. The transmittal gradient improved to 5mmHg from pre-PMV transmittal gradient of 25mmHg.

Case 3

The third patient in this case series was, an 18-year old male who was diagnosed with RHD a year ago. He was initially asymptomatic and missed his follow-up schedule until he presented with shortness of breath, easy fatigability and palpitations; which occurs with less than ordinary activity. Echocardiography shows severe mitral stenosis with mitral valve area of 1.1cm^3 by PHT with a mean gradient of 22 mmHg. Wilkins score was 8. There was also noted moderate to severe tricuspid regurgitation, moderate to severe aortic regurgitation, mild

pulmonic regurgitation and mild pulmonary arterial hypertension measuring 32 mmHg by PAT. PMV was done via the venoarterial loop as previously described and was done under intravenous sedation. The transmitral gradient pre-PMV was 22 mmHg and improved to 10 mmHg post-PMV. Repeat echocardiography post-PMV also showed no mitral regurgitation with residual transmitral gradient of 8 mmHg.

Case 4

The fourth case is a 13 year old who was diagnosed with RHD at 9 years old. Referral to our center was done when the patient developed easy fatigability and shortness of breath. Initial echocardiography showed severe mitral stenosis with mitral valve area of 0.6 cm^3 by planimetry with a mean gradient of 19 mmHg; associated with severe tricuspid regurgitation. The Wilkins score was 8. PMV was done with the patient intubated and under general anesthesia via the venoarterial loop technique using a 20mm TMP-PED balloon. Transmitral gradient improved from 28 mmHg to 8 mmHg. Post-PMV echocardiography showed mild mitral regurgitation and moderate residual mitral stenosis with MVA of 1.0 cm^3 by planimetry.

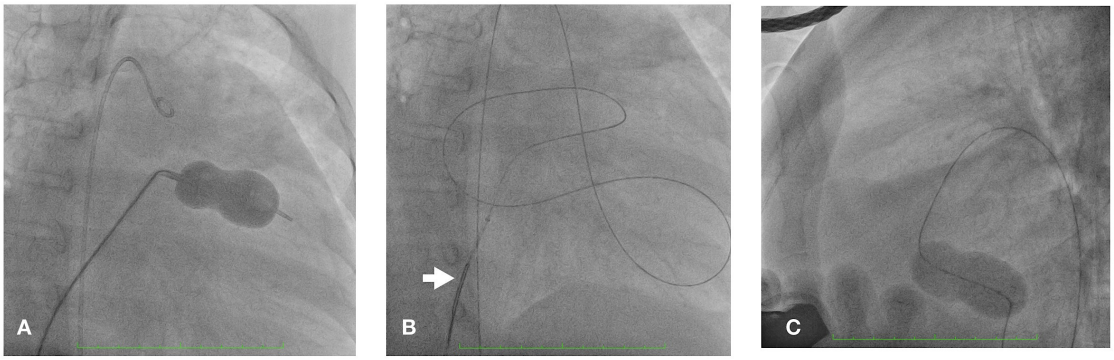

Fig 3. Arteriovenous loop done in the first case (patient RC). **A**: Attempted PTMC with Inoue Balloon. **B:** Arteriovenous loop technique done by snaring the end of the hydrophilic wire in the LA out of the venous line (white arrow). The hydrophilic wire was inserted in the femoral artery, femoral artery and was manipulated to the descending aorta, ascending aorta, LV and LA and was snared out to the RA, IVC and exiting in the femoral vein. **C**: Inflation of the TMP-PED balloon that was positioned across the mitral valve through the arteriovenous loop.

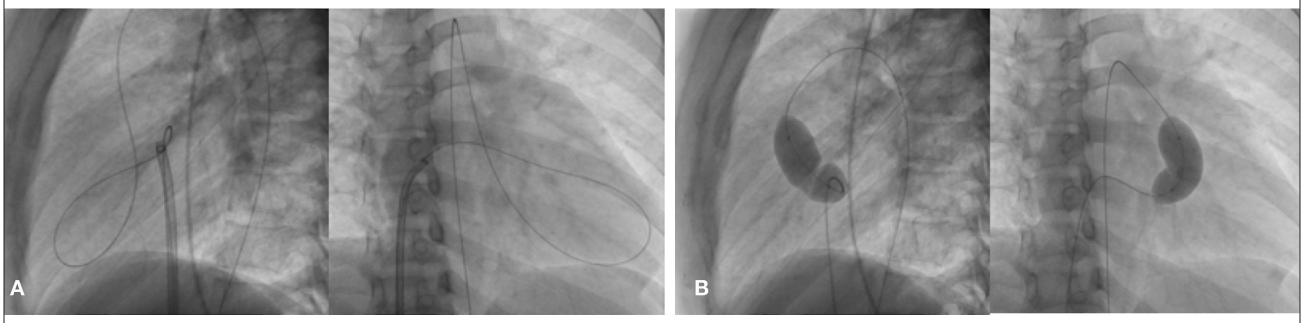

Fig 4.Venoarterial loop done in case 2 (patient MM). **A**: A hydrophilic wire was inserted in the Mullin's sheath through the venous access and was manipulated from the RA to the LA, LV and aorta. A snare catheter was inserted through the arterial access and the end of the hydrophilic wire was in the aorta was snared out of the femoral artery completing a venoarterial loop. **B**: Inflation of the TMP-PED balloon that was positioned across the mitral valve through the venoarterial loop.

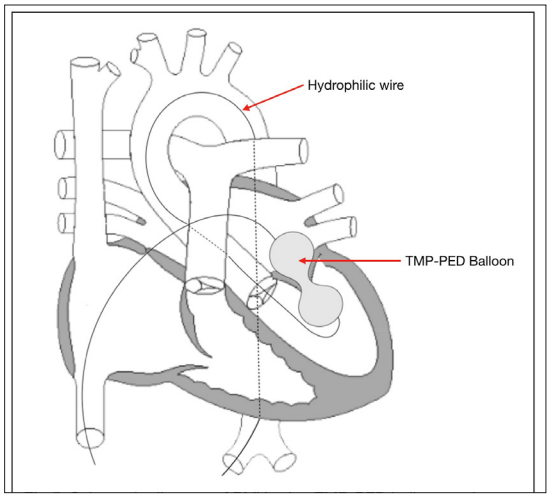

Figure 5. Schematic diagram of PMV using TMP-PED balloon and arteriovenous or venoarterial loop technique

Table 2. Comparison of patients' baseline profile

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	11	18	18	13
Sex	Male	Female	Male	Female
Weight	37 kg	41 kg	50 kg	35 kg
Height	135 cm	152 cm	165 cm	150 cm
NYHA Functional Class	IV	II	III	II

Table 3. Comparison of patients' hemodynamic data

	Patient 1 (RC)	Patient 2 (MM)	Patient 3 (EA)	Patient 4 (VM)
MV area (cm^3) pre-PMV (echo)	0.6	0.9	1.1	0.6
MV area (cm^3) post PMV (echo)	0.7	0.9	1.2	0.8
Transmitral gradient (mmHg) pre-PMV (simultaneous LA and LV pressure recording)	15	25	22	28
Transmitral gradient (mmHg) post-PMV (simultaneous LA and LV pressure recording)	5	5	8	8
Transmitral gradient (mmHg) pre PMV Echo	24	18	25	22
Transmitral gradient (mmHg) post-PMV (echo)	14	9	12	8

Table 2 and 3 lists the patients' baseline profile upon admission prior to the procedure and comparison of their hemodynamic data pre- and post-PMV.

DISCUSSION

PMV is a well-accepted managemement for mitral stenosis. If done properly, this procedure relieves the obstruction, provides hemodynamic improvement and even delays the need for mechanical valve replacement. Proper patient selection, correct echocardiographic diagnosis and appropriate patient preparation are imperative in achieving a good outcome. In this case series, the patients in the 2nd to 4th cases were good candidates for PMV with Wilkins score of 8, 7 and 8 respectively.

Although patients 3 and 4 had other valvular lesions that might need surgical repair eventually, it was deemed reasonable to address the more severe lesion and do the PMV first so as to delay the need for open heart surgery. The first patient had a Wilkins score of 11 and theoretically not a good candidate for PMV. He presented with signs and symptoms of frank heart failure putting him at a higher risk for mortality if he will be subjected to open heart surgery. After PMV, all patients showed significant improvement as seen in the echocardiographic parameters pre- and post- PMV as well as the marked improvement in the transmitral gradient in the simultaneous LA and LV recording.

Certain challenges when doing PMV in children make it difficult for the interventionalist to do the procedure using the standard approach. When faced with these challenges, several techniques or modifications may be done to overcome these difficulties. In the first case in this series, the standard approach was attempted but the problem was encountered in positioning the Inoue Balloon across the mitral valve. The arteriovenous loop done addressed this problem by providing additional tension in both ends of the hydrophilic wire allowing easier balloon passage across the mitral valve and eventually, successful balloon dilatation (*Figure 5*). Another modification done in all the cases was upsizing of the femoral sheath used for easier manipulation. The recommended femoral sheath for a 20mm TMP-PED balloon is only a 7Fr sheath. The use of 8Fr femoral sheath allowed the operator to easily advance or withdraw the balloon through the sheath.

The use of TMP-PED balloon with the arteriovenous or the venoarterial loop technique in performing percutaneousmitral valvuloplasty in children is a novel yet effective innovation that can successfully reduce the obstruction across the mitral valve in patients with mitral stenosis.

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Editorial Review

The use of TMP-Ped balloon for PMV in pediatric patients, outside of its original intended purpose of valvuloplasty in congenital PS and AS is indeed a novel and innovative approach. Although it is born out of necessity for pediatric interventionalists and their smaller patients it has the benefit of negating the inherent technical difficulties and possible complications of PMV in children.

The main limitation of the study however is its design, which is just a case series and limited subjects of four in a novel technique which will be scrutinized under the magnifying glasses of peers that will always question the validity of novel techniques in the field of interventional cardiology. In this light, the acceptability of long-term use of TMP-Ped balloon in PMV for children as a new technique is not established by this paper. Further cohort and comparative studies are needed to validate this novel approach.

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Rheumatic heart disease in children is now rare in countries like Japan, while percutaneous mitral valvuloplasty (PTMC) is still an essential option for childhood rheumatic mitral stenosis in many countries. Inoue balloon is the standard choice for this procedure, however, a large sheath may occasionally limit its usage in children.

TMP-PED balloon is the originally designed for valvuloplasty and static balloon atrial septostomy in neonate and/or small infant. Extremely low non-slip profile balloon, which goes through 3F up to 10mm diameter, and 12mm through 4F, with extra short tip and shoulder design, secures safe and comfortable procedure in such age group. At this time, Tokai medical has extended its specification to 18 and 20 mm in diameter and the length of 30 mm, which goes through 7F sheath. These specifications will extend the use of this balloon to valvuloplasty, such as aortic, pulmonic, and mitral, in adolescents and adults.

Soriano ED and Villareal JA reported PTMC in children using loop technique with this balloon. Arteriovenous or venoarterial loop technique is a novel and effective modification to facilitate advancement of the balloon, while a low profile TMP-PED balloon may be compatible with this technique.

Great care should be paid in making the loop to cross the true orifice, as crossing the interchordal space may cause severe mitral regurgitation."

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Review Article

The Division of Invasive Pediatric Cardiology of the Philippine Heart Center: then and now

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The Philippine Heart Center (PHC) is known to be the premier hospital for the management of cardiovascular diseases in our country. From adult cardiology, to pediatric cardiology and other allied medical subspecialties, PHC has produced hundreds of specialists who continue to bring pride and glory to our institution.

After the PHC was inaugurated on February 14, 1975, countless cardiovascular surgeries and procedures using state-of-the-art facilities have been done annually; aside from offering open and closed heart surgeries, the Division of Pediatric Invasive Cardiology started to undertake their fair share of transcatheter diagnostic and interventional procedures.

It has been said that great things start with small beginnings and Dr. Wilberto L. Lopez, the founding Chairman of the Department of Pediatric Cardiology fondly recalled how their small group practice of specialists trained in Adult and Pediatric Cardiology, Anesthesia and Cardiovascular Surgery managed heart diseases through cardiac surgeries and catheterizations in V. Luna Medical Center (now known as the AFP Medical Center), Veterans Memorial Medical Center, Makati Medical Center and University of Sto. Tomas Hospital prior to the formal operation of the PHC. The first open (and televised) heart surgery was actually done at the V. Luna Medical Center on a case of severe Rheumatic Mitral Stenosis. Its success garnered the interest and enthusiasm of the then First Lady Madam Imelda Romualdez Marcos and paved the way for the planning, construction, and inauguration of the PHC.

In the late 1970s, transcatheter procedures in pediatrics were limited to diagnostic hemodynamic studies. In the latter part of 1975, the first inter ventional catheterization, Balloon Atrial Septostomy was performed by Dr. Wilberto Lopez using the Rashkind Balloon Catheter. Dr. Bienvenido Abesamis, assistant Medical Director of the PHC likewise performed hemodynamic and BAS procedures. During this time echocardiography was not yet available such that the primary diagnostic procedure for patients with congenital heart disease was done invasively. Upon the arrival of the echocardiography machine, the first balloon atrial septostomy procedure was performed under the echocardiographic guidance of Dr. Emerenciana Collado. It was not long before other interventional procedures followed, such as percutaneous pulmonary balloon valvuloplasty and percutaneous transmitral commissurotomy.

In 1984 following the publication of the paper on Balloon Valvuloplasty on Pulmonary Stenosis by Kan and associates (University of Michigan Children's Hospital), a pediatric interventional team led by Dr. Lopez, assisted by the first four cardio fellows in training - Drs. Teofilo Cantre, Della Pelaez, Aurora Meneses and Dr. Maria Clara Faustino - successfully performed its first case using the Cook balloon catheter that was modified for Filipino children. This provided the impetus to venture into balloon angioplasty of aortic coarctation and balloon valvotomy in patients with severe aortic stenosis.

In the area of acquired heart disease, especially that of mitral stenosis, mitral valvuloplasties were initially performed using the Mansfield catheter. Later on, the Inoue balloon catheter introduced by the adult service was subsequently adopted by the Pediatric Department for its severe mitral stenosis cases. Dr. Lopez was then assisted by Dr. Ed Manrique.

When the Philippines hosted the World Congress of Cardiology in the 1990s, the Atrial Septal Defect Starflex Device closure was intro-

duced. In 1998, Dr. Schneider and in 1999, Dr. Philip Moore (CardioSeal, a first generation clamshell ASD Occluder) proctored the ASD Device closure of our PCI Team composed of Dr. Wilberto Lopez, Dr. Ed Manrique, Dr. Aurelia Leus with Dr. Juan Reganion (Present Chief). PDA transcatheter occlusion, which is now considered by most cardiologists as the definitive management of choice for patent ductus arteriosus, also started in the late 1990s.

The division entered the year 2000 still eager for advancement and innovation. As we faced the millennium, more interventional procedures were being mastered by our graduates, noteworthy of which was Dr. Marites Flores. Dr. Flores and Dr. Teofilo Cantre (the center's first interventional fellowship graduate), were proctored on the use of Amplatzer PDA and ASD devices. Under the leadership and tutelage of these dedicated student-teachers and with the support and presence of our chairman emeritus Dr. Wilberto Lopez; Dr. Teofilo Cantre (past Division Chief), the present division chief Dr. John Reganion, and the present training officer Dr. Jean Villareal (who was our Invasive CRF at that time), more and more interventional procedures are being done and mastered such as PDA Closure, coronary fistula closure, ASD Occlusion and PDA and eventually, transcatheter closure of VSD. In 2007, the first PDA stenting was performed on patients with critical pulmonary stenosis, by a team led by Dr. Wilberto Lopez, under the supervision of Dr. James Ho and assisted by Dr. Marites Flores. There was a notable increase in the number of newborns with duct-dependent cardiac lesions being referred for PDA stenting, which according to published studies, is comparable to the surgical placement of a Blalock-Taussig shunt in terms of outcome. Hence, there was a consequent steady shift to non-surgical, interventional device closure of defects and intervention.

Through the years, the Division of Pediatric Invasive Cardiology of the PHC continues to aim for excellence and to meet international standards. Interventionalists from neighboring Asian countries have been sent to our institution to observe and learn from our cases. Our present Division Chief, Dr. Juan Reganion, and the present training officer, Dr. Jean Villareal, have also been requested by our colleagues from other countries to share with the other foreign interventionalists some of our practices and tips on complex procedures.

In 2019 alone, the Division of Pediatric Invasive Cardiology had several workshops and interventional missions with local and foreign pediatric interventionalists. Dr. Hideshi Tomita from Showa University, Northern Yokohama Hospital Japan visited from March 28-29, 2019 for a workshop on stenting of the Coarctation of the Aorta. This was the second part of a Coarctation of the Aorta Stenting Workshop wherein a total of 15 cases were done – 4 cases of redilation (initial stenting done during the first workshop held last October 2018) and 11 cases of coarctation stenting. There were also 2 separate workshops on VSD Device Closure in May and August 2019. Pediatric Interventional Cardiologists Dr. Hsing-Yuan Li from Taipei, Taiwan and Dr. Limheng Sreng from Siem Reap, Cambodia, came to our institution for proctorship on VSD closure. A workshop on VSD and PDA device closure on small infants weighing less than ten kilograms was also held in 2019. In this workshop, the Multifunction Occluder of Lifetech were used in successfully occluding shunts in very small infants. An offshoot of this workshop were the papers written and presented by two of the Division's recent graduates - A Case Series On PDA Device Closure On Preterm Neonates by Dr. Ma. Rosita Quitola-Manangan and a Study On VSD Closure In Infants Weighing Less Than 10 Kilograms by Dr. Elissa Dyann Soriano - which have been presented in local and international online conferences. Another noteworthy activity was the Zero-fluoroscopy ASD closure workshop held last June 2019. Zero-fluoroscopy ASD closure is a novel technique in interventional cardiology. One of our graduates, Dr. Claudio Gayeta, has written a pilot study on Zero-fluoroscopy ASD closure in the Philippines and this initial venture will also lay the foundation for future studies on other zero-fluoroscopy transcatheter procedures.

Aside from workshops with foreign interventionalists held in our institution, we also had

international collaborations held abroad. Our training officer, Dr. Jean Villareal, was sent to Cambodia and Pakistan to proctor interventionalists from those countries on VSD closure. Our Division Head, Dr. Juan Reganion together with Dr. Mae Dagooc and Dr. Elissa Dyann Soriano, went to Japan to meet with the makers of the TMP-PED Balloon to share our experience on percutaneous mitral valvotomy using the arteriovenous or venoarterial loop technique with the TMP-PED balloon. The entire team also went to Guangzhou, China last February 2019 to attend the CSI-Asia Pacific Conference. In this esteemed gathering on Congenital and Structural Interventions, Dr. Babie Catherine Causapin presented her paper on the comparison of clinical outcome of transcatheter closure of ventricular septal defect using antegrade and retrograde approaches. This paper was also presented in other international and local conferences such as the PHC's annual research contest wherein she won 2nd place, as well as in the Philippine Society of Cardiovascular Catheterizations Inc. Annual Convention and the Asia Pacific Society on Cardiology Congress. Dr. Causapin also participated in the CSI Conference held in San Francisco, USA as faculty member where she presented a case on PDA closure in interrupted IVC. Dr. Juan Reganion and Dr. Jean Antonio Villareal had also been invited to share their expertise in several conferences, both locally and internationally.

Aside from learning activities, proctorship and workshops, the Division of Pediatric Invasive Cardiology also partakes in medical and interventional missions all over the country. Started a decade earlier by Dr. Marites Flores, mission days in PHC and mission trips in the different key cities nationwide continues to this day. Dr. Babie Catherine Causapin, Dr. Ma. Rosita Quitola and Dr. Elissa Dyann Soriano went to Vicente Sotto Memorial Medical Center in Cebu where they participated in a 2-week interventional and surgical mission last September 2019 and were joined by Dr. Rudy Amatong and Dr. Naomi Poca, our interventional graduates who are based in Cebu. In June 2019, Dr. Juan Reganion, Dr. Babie Catherine Causapin and Dr. Claudio Gayeta went to Western Visayas Medical Center in Iloilo City, where they were joined by Dr. Mae Dagooc, another pediatric interventionalist and a product of our training program who is currently practicing in Iloilo.

We look back with a sense of fulfillment and pride at our developmental years. We look forward to more fruitful and productive years of learning, training and bringing cardiac interventions where they are most needed. The Division is pursuing great plans for 2021 and beyond. One of these is the i.PIC.PHC 2021, an international congress on pediatric invasive and non-invasive cardiology. Pediatric Cardiologists from different countries have signed up for this event and although it has been postponed because of the pandemic, online options are being explored. Adjustments have to be made but it will not deter the achievement of the Division's mission and vision. Adaptation to the new normal has been made through the various online platforms now available. This enabled us to join international and local scientific conferences by hosting and participating in several online conferences and webinars.

Our international network has widened and has been strengthened through the online i.PIC.PHC *e*-learning series which is being conducted twice a month. It is remarkable to collaborate with pediatricians and pediatric cardiologists from all over the country and globally. Specialists from the Philippines, Japan, Indonesia, Cambodia, Malaysia, Pakistan and other countries would gather together in this *e*-learning series to share each other's cases, procedures and experiences.

A lot has changed from the 1970s to 2020. We have evolved from hemodynamic studies and diagnostic angiographies to complex interventional and hybrid procedures. What was then quite complex has been made simpler by advancements that revolutionized the operations of the Division. We continue to develop and improve with the changing times, keep up with innovations in medicine and adjust to the new normal as we, in the Division of Pediatric Invasive Cardiology strive for excellence in training, research and education while pursuing our highest passion – the compassionate care and treatment of all children with heart disease.

ACKNOWLEDGMENT

We sincerely express our gratitude to Philippine Heart Center PHC) for providing us a comfortable place to work on our articles. We are truly grateful to the Education, Training and Research Services (ETRS), Clinical Research Department, Clinical Trial and Research Division, the Members of Technical Review Committee (TRC); and lastly the Members of the Institutional Ethics and Review Board (IERB).

We want to thank our colleagues Dr. Paulene Ver Serna-Zarate, Kim Martin G. Tolentino, Ma. Karen B. Quin from Asian Hospital and Medical Center for their expertise and for sharing their patients in the study entitled "Transcatheter Closure of PDA in Preterm Neonates Using Konar MFO; Initial Experience."

We also would like to thank our colleagues from Cagayan de Oro Polymedic Medical Plaza; Drs. Maria Rowena C. Sanchez and James Herminio G. Salon for sharing their expertise and patient in the study entitled "Transcatheter Closure of PDA in Preterm Neonates Using Konar MFO; Initial Experience."

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Braunwald E and Rutherford JD. Reversible ischemic left ventricular dysfunction: evidence for the "hibernating myocardium." J Am Coll Cardiol 1986;8:1467-1470.

Dilsizian V, Rocco TP, Freedman NM et al. Enchanted detection of ischemic but viable myocardium by the reinjection of thallium after stress -redistribution imaging. N Engl J Med 1990;323:141-146.

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Dillman WH. The Cardiovascular System in Thyrotoxicosis. In Braverman LE and Utiger RD, eds. The Thyroid - A fundamental and Clinical Text. 6th ed. Philadelphia: JB Lippincott Co; 1991,759-770.

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