Large patent ductus arteriosus: To close or not to close

Jaganmohan Tharakan, Subramanian Venkateshwaran
Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India

Non-surgical closure of patent ductus arteriosus (PDA) with coils and devices has largely replaced the surgical option for small and medium sized PDA, especially beyond infancy.[1,2] There are few limiting factors for non-surgical closure in this subset due to availability of an array of devices to suit every conceivable anatomy of the PDA. However, large PDA requires clinical judgment in selecting a medical, interventional or surgical approach as brought out in the present study.

In the setting of a large PDA, three important issues determine the management strategy.

1. Pulmonary hypertension- whether reversible or irreversible.
2. Mismatch between size of the PDA device and patient, resulting in compromise of the aortic and/or pulmonary artery lumen.
3. Hardware required to deliver the large device through available vascular access in a neonate or infant and the technical problems encountered in this patient group.

PULMONARY HYPERTENSION AND PULMONARY VASCULAR DISEASE (PVD) IN PDA

Outcome after closure of a large PDA is determined primarily by age at the time of repair and pre-operative PVD.[3] Age is an important predictor of PVD. It is generally agreed upon that children under 1 year of age are unlikely to have irreversible PAH and most agree that irreversibility starts as early as 1 to 2 years of age. This generalization has some limitations as the pathogenesis of irreversible PAH and its progression is multifactorial and unpredictable. Blount and associates' indicated that a PDA may have more marked effect on the pulmonary circulation than a ventricular septal defect and that irreversible pulmonary vascular changes may occur under two years of age.[4] This is probably the result of the high-pressure pulsatile flow transmitted from the aorta to PA throughout the cardiac cycle in PDA. With progression of PVD, PA impedance increases and when it increases beyond the impedance of the systemic vascular bed, the shunt is reversed and results in Eisenmenger syndrome. There is general agreement that patients with Eisenmenger syndrome should not have the defect closed and in fact the defect can be beneficial because the defect acts as an outlet for the RV to pump into the systemic circulation and maintain cardiac output at the cost of arterial desaturation. However, patients with elevated PVR and small left to right or bi-directional shunt need further evaluation to assess if there is a component of reversible or reactive pulmonary vascular resistance that contributes to total PVR and can be expected to regress after PDA closure. The early stages of PVD like muscular hypertrophy are reversible but the more advanced changes like intimal proliferative and fibrotic changes are not entirely reversible, resulting in elevated and fixed pulmonary resistance and this can be described as irreversible PVD. The pulmonary vascular changes even when reversible, take time to normalize and PVR and PA pressures can remain elevated for some time after the PDA is closed.

Clinical examination, X-ray chest, ECG, arterial saturation (upper and lower limbs) and echocardiography are conclusive in assessing operability in the majority of patients with PDA and PAH. However, decision to intervene is difficult if they are equivocal. Hemodynamic data from cardiac catheterization is vital in such cases and include the assessment of reactive pulmonary bed by using pulmonary vasodilators.[5] Reactive PVR can result in minimal or no left to right shunt in the basal state and hemodynamic study using modes to reverse it with 100% oxygen administration and selective pulmonary vasodilators is necessary before labeling the patient as having irreversible PVR. However, there are some limitations for calculating PVR in PDA as pulmonary arterial saturation are different in right and left pulmonary arteries in patients with left to right shunt, as well as ascending and descending aortic saturations are different in patients with right to left shunts making the calculations of systemic blood flow impossible.[5]

Recommendations solely based on pulmonary vascular resistance values may not be correct as several other factors such as age, individual variability, location of defect, etc. may influence the operability status. Despite all this, an indexed pulmonary vascular resistance of <6-8 Woods units may be considered in the operable

Address for correspondence: Prof. Jaganmohan Tharakan, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum- 695 011, India.
E-mail: jaganmohan.tharakan@gmail.com

range. A multicentre study by Balzar *et al*, concluded that use of vasodilators, including inhaled nitric oxide has limited utility in deciding operability.[6] Contrary to the popular belief, a recent study showed that pre-operative hemodynamic information does not correlate with post-operative outcome for various reasons.[7]

When pulmonary blood flow cannot be reliably estimated by Ficks principle, the next method to assess the impact of PDA flow on pulmonary pressure and pulmonary vascular resistance is occluding the PDA with a balloon or the device and measuring the PA pressure and the cardiac output to calculate the PVR. A practical approach is to see if PA systolic pressure falls by 20% from the basal state, with systemic pressure remaining constant indicating significant left to right shunt across the PDA.[8] Yan *et al*, reported 29 adults with PDA and PAH. In this study, trial occlusion with the device was performed for 30 minutes, without unscrewing the device. The criteria they followed were: (a) a fall in the pulmonary artery pressure or no elevation; (b) no decrease in the aortic pressure; and (c) no worsening of signs and symptoms. If all the criteria were satisfied, pulmonary arterial hypertension was considered to be reversible and device released. Otherwise, it was considered to be irreversible pulmonary arterial hypertension, and occlusion was abandoned. 20 of the 29 patients had successful occlusion. 7 patients failed trial occlusion due to worsening symptoms or increase in PA pressures. 2 failed due to lack of appropriate device.[9] This method appears a pragmatic attempt to identify the patients who might worsen with the closure acutely, however, long term follow up data of patients treated on the premise of balloon occlusion are not available. Velocity-encoded cine MRI imaging for estimation of left-to-right shunting may have additional clinical utility.[10] Open lung biopsy presently has a very limited role in the management of patients with PDA and PAH.

Each technique individually has limitations in assessment of operability in a borderline case, and hence a comprehensive evaluation is necessary.

By convention, patients with a pulmonary vascular resistance of >6 to 8 units when breathing 100% oxygen are considered unsuitable candidates for PDA closure as they are at high risk of sustained pulmonary hypertension, right heart failure, and hypertensive crises immediately after surgery.[11,12] It can be fatal either in the immediate post-operative period or on long-term follow up.[13-17] In the early years, Rudolph and Nadas described a case of PDA with irreversible pulmonary vascular changes who was operated on at one year of age and died a year later of right-sided cardiac failure.[13] Similarly, Ellis *et al,* reviewed 30 cases of PDA complicated by pulmonary hypertension (the pulmonary artery pressure exceeded 60 mm. Hg in all). The over-all mortality rate was 18 per cent, but where shunt reversal had occurred the mortality rate reached the forbidding figure of 56 per cent.[14] Natural history of such patients is considerably worse than those with Eisenmenger syndrome. Not only is there the risk of peri-operative mortality, the likelihood of right heart failure from progressive increase in PVR despite repair of the defects exists.[18] In practice, the quality of life of such patients is far worse than that of patients with Eisenmenger syndrome and PDA followed up medically. Therefore it is important to be certain of operability before referring such patients for surgery.

Successful transcatheter closure of large PDA with severe PAH has been reported.[9,19,20] All these have adopted various methods to assess reversibility of PAH. They have excluded patients with irreversible PAH. Although results of these studies are encouraging, it is prudent to appropriately select patients with reversible PAH, who are likely to benefit from PDA closure. Vasodilators prior to closure have been reported to favorably influence the outcome in borderline cases.[21]

The present study in this issue of the annals, 76 patients with large PDA referred for device closure is a heterogeneous group with a wide age range from neonate to late adulthood.[22] Nine patients were assessed to have Eisenmenger syndrome by various non- invasive methods. Of the remaining 69, 4 were assessed as having irreversible PAH at hemodynamic study including PDA occlusion and measuring drop in PA systolic pressure. The remaining 65 patients had device closure and the short and intermediate term outcome was reported as satisfactory. Being a retrospective study a uniform approach to evaluation of every patient may not have been possible. Six patients were assessed as Eisenmenger syndrome based on clinical and echo Doppler study alone. In the present study, the hemodynamic study was not done administering of 100% oxygen or other vasodilators. In this study, only 2 patients were found to have no drop in PA pressure on balloon occlusion. The decision to have balloon occlusion in patients with PA systolic pressure >90% of systemic pressure without taking into account the left to right shunt is not routinely recommended and one should take into consideration the quantum of left to right shunt on 100% oxygen administration and pulmonary vasodilators because a patient with PA systolic pressure less than 90% systemic pressure and small left to right shunt is equally likely to have unfavorable outcome after PDA closure.

NEONATES AND INFANTS WITH LARGE PDA

In a neonate or small underweight infant, the large PDA poses problem of device size to patient mismatch. In this age group, a large PDA is almost always associated with flow related PAH (hyperkinetic PAH) and PVR is only

mildly elevated. However, the aortic retention rim often cannot be accommodated in the ampulla of the duct because of its small size and can remain in the descending thoracic aorta (covering the aortic rim of the duct) and compromise the aortic flow. Similarly, if the proximal end of the device has been pulled into the PA, it may cause LPA stenosis. Often an inflated balloon placed in the aorta opposite the PDA when deploying the device, ensures the retention rim stays snugly on the aortic rim of the PDA. It is prudent, that a device obstructs the descending thoracic aorta or the LPA be captured before deployment and alternative management strategy including surgery is considered. Availability of better braided- sheaths allow use of standard guide wires and the procedure can be completed without serious hypotension and bradycardia.

The combination of the absent retention ring and the slight taper of the Amplatzer PDA device toward the pulmonary end of the PDA runs a risk of extrusion of the device toward the aorta after its release. If PA pressure is identical to aortic pressure or shoots up as in situations like pulmonary hypertensive crisis or sudden increase in intra thoracic pressure due to cough or straining, the device can embolize to the aorta. A muscular VSD device with retention rims on both ends is an alternative choice for such patients. Amplatzer muscular VSD device occluder (AMVSDO) has been successfully used to close large PDA.[9,23] The Muscular VSD device is more stable and is available up to 24 mm size.

However, a subset of patients may be treated by surgical division of the PDA in view of the small but definite risk of device embolization.

Similarly, the availability of low profile ADO -2 devices can facilitate the closure in small infants. This device [24] can be delivered by venous and arterial routes, is fabric free, has a low profile and requires smaller delivery systems and can treat all morphological variants of PDA from 2.5 mm to 5.5 mm. However, experience with this device is limited.

The results of trans catheter occlusion of PDA have been excellent as reported in the present study. Complete closure rates at follow-up exceed 90% to 95% in most studies. The most common complication is embolization of the device. Other potentially important complications are turbulence to flow in the proximal left pulmonary artery or descending aorta from a protruding device, hemolysis from high-velocity residual shunting,[25] femoral arterial or venous thrombosis related to vascular access, and infection.[26] Stiff wires and sheaths stretching cardiac tissues cause bradycardia and hypotension due to vagal stimulation. It responds promptly to removal of stretch or atropine. At times this bradycardia is accepted or tolerated temporarily to complete the procedure.[27] This problem is less with newer braided sheaths used with standard guide wires.

In conclusion, it is important to note that a small percentage of patients with borderline hemodynamic data with PDA and PAH, can deteriorate after PDA closure due to non regression of pulmonary hypertension and progressive PVD and right heart failure after PDA closure and their natural history is then similar to primary or idiopathic PAH. These patients have a more favorable natural history, if PDA is left untreated. A foolproof investigation to identify who will benefit from PDA closure with long term regression of PAH, and who may worsen with progressive PVD and right heart failure is currently not available. Future research on type and extent of morphological changes in the pulmonary vessels, its individual variability and correlation with genetic and epigenetic factors may give a clue to this vexing issue. Till such time, in clinical practice, an occasional patient who will not benefit from closure of a large PDA may have PDA closure with adverse outcome and vice versa.

REFERENCES

1. Faella HJ, Hijazi ZM. Closure of the patent ductus arteriosus with the amplatzer PDA device: immediate results of the international clinical trial. Catheter Cardiovasc Interv 2000:51:50-4.
2. Pass RH, Hijazi Z, Hsu DT, Lewis V, Hellenbrand WE. Multicenter USA Amplatzer Patent Ductus Arteriosus Occlusion Device Trial: Initial and one year results. J Am Coll Cardiol 2004;44:513-9.
3. Bando K, Turrentine MW, Sharp TG, Sekine Y, Aufiero TX, Sun K, *et al*. Pulmonary hypertension after operation for congenital heart disease: Analysis of risk factors and management. J Thorac Cardiovasc Surg 1996;112:1600- 7; discussion 1607-9.
4. Blount SG, Vogel JH. Pulmonary hypertension. In: Moss AJ, Adams FH, editors. Heart Disease in Infants, Children and Adolescents. Baltimore: Williams and Wilkins; 1968. p. 947.
5. Rudolph A. Functional assessment. Congenital diseases of the heart: clinical-physiological considerations, 3rd ed, Vol. 4. s.l.: Hoboken, New Jersey: Wiley-Blackwell; 2009. p. 75.
6. Balzer DT, Kort HW, Day RW, Corneli HM, Kovalchin JP, Cannon BC, *et al*. Inhaled Nitric Oxide as a Preoperative Test (INOP Test I): the INOP Test Study Group. Circulation 2002;106(12 Suppl 1):I76-81.
7. Kannan BR, Sivasankaran S, Tharakan JA, Titus T, Ajith Kumar VK, Francis B, *et al* . Long term outcome of patients operated for large ventricular septal defects with increased pulmonary vascular resistance. Indian Heart J 2003;55:161-6.
8. Roy A, Juneja R, Saxena A. Use of Amplatzer ductal occluder to close severely hypertensive ducts: utility of transient balloon occlusion. Indian Heart J 2005;57:332-6.
9. Yan C, Zhao S, Jiang S, Xu Z, Huang L, Zheng H, *et al*.

Transcatheter closure of patent ductus arteriosus with severe pulmonary arterial hypertension in adults. Heart 2007;93:514-8.

10. Brenner LD, Caputo GR, Mostbeck G, Steiman D, Dulce M, Cheitlin MD, *et al.* Quantification of left to right arterial shunts with velocity-encoded cine nuclear magnetic resonance imaging. J Am Coll Cardiol 1992;20:1246-50.
11. Galie N. Classification of patients with congenital systemic to pulmonary shunts associated with pulmonary arterial hypertension: Current status and future dirctions. In: Beghetti M, Barst RJ, Naeije R, editors. Pulmonary arterial hypertension related to congenital heart disease. Munich: Elsevier; 2006. p. 11-3.
12. Moss AJ, Adams FH, Emmanouilides GC, Riemenschneider TA. Moss' heart disease in infants, children and adolescents. Baltimore, Md, USA: Williams and Wilkins; 1989.
13. Rudolph AM, Nadas AS. The pulmonary circulation and congenital heart disease. Considerations of the role of the pulmonary circulation in certain systemic-pulmonary communications. N Engl J Med 1962;267:968-74.
14. Ellis FH Jr, Kirklin JW, Callahan JA, Wood EH. Patent ductus arteriosus with pulmonary hypertension. An analysis of cases treated surgically. J Thorac Surg 1956;31:268.
15. Campbell M. Patent ductus arteriosus; some notes on prognosis and on pulmonary hypertension. Br Heart J 1955;17:511-33.
16. Kjellberg SR, Mannheimer E, Rudhe A, Jonsson B. Diagnosis of Congenital Heart Disease, 2nd ed. Chicago: Year Book Publishers; 1959. p. 546
17. Wood P. Pulmonary hypertension with special reference to the vasoconstrictive factor. Br Heart J 1958;20:557-70.
18. Yamaki S, Ishidoya T, Osuga Y, Arai S. Progressive pulmonary vascular disease after surgery in a case of patent ductus arteriosus with pulmonary hypertension. Tohoku J Exp Med 1983;140:279-88.
19. Ji Q, Feng J, Mei Y, Wang X, Cai J, Sun Y, *et al.* Transcatheter closure of adult patent ductus arteriosus with severe pulmonary hypertension. Hypertens Res 2008;31:1997-2002.
20. Yu ML, Huang XM, Wang JF, Qin YW, Zhao XX, Zheng X. Safety and efficacy of transcatheter closure of large patent ductus arteriosus in adults with a self-expandable occluder. Heart Vessels 2009;24:440-5.
21. Dimopoulos K, Peset A, Gatzoulis MA. Evaluating operability in adults with congenital heart disease and the role of pretreatment with targeted pulmonary arterial hypertension therapy. Int J Cardiol 2008;129:163-71.
22. Bhalgat PS, Pinto R, Dalvi BV. Transcatheter closure of large patent ductus arteriosus with severe pulmonary hypertension: short and intermediate term results. Ann Ped cardiol 2012;5:135-40.
23. Thanopoulos BD, Tsaousis GS, Djukic M, Al Hakim F, Eleftherakis NG, Simeunovic SD. Transcatheter closure of high pulmonary artery pressure persistent ductus arteriosus with the Amplatzer muscular ventricular septal defect occluder. Heart 2002;87:260-3.
24. Cook S, Rutz T, Meier B. New Amplatzer Duct Occluder II for antegrade closure of patent ductus arteriosus. Kardiovaskuläre Medizin 2009;12:313-4.
25. Anil SR, Sivakumar K, Philip AK, Francis E, Kumar RK. Clinical course and management strategies for hemolysis after transcatheter closure of patent arterial ducts. Catheter Cardiovasc Interv 2003;59:538-43.
26. Benson LN. The arterial duct: its persistence and its patency. In: Anderson RH, Baker EJ, Macartney FJ, Rigby ML, Shinebourne EA, Tynan M, editors. Paediatric Cardiology. 3rd ed London: Churchill Livingstone; 2009. p. 887-8.
27. Mullins CE. Complications of diagnostic and therapeutic cardiac catheterizations. In: Cardiac catheterisation in congenital heart disease: Pediatric and adult. Blackwell Futura; 2006. p. 912.

Access this article online

Quick Response Code:

Website: www.annalspc.com