Safety and efficacy of percutaneous device closure of large post tricuspid shunts in pediatric patients with severe PAH at short term and midterm follow up

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Abstract

Background: Transcatheter closure of large post-tricuspid shunts in patients with severe pulmonary arterial hypertension remains a challenging problem. Among this unique subset of patients there is an entire spectrum of severity of pulmonary vascular disease with variable pulmonary vascular resistance and reversibility especially in older children. Aims: The current study was done to assess the safety and efficacy of percutaneous device closure of large post tricuspid shunts in pediatric patients with severe PAH at short and mid term follow up. Methods: A total of 42 pediatric patients underwent transcatheter closure of large post tricuspid shunts with severe PAH. All subjects underwent clinical examination, electrocardiography, chest x-rays and echocardiography before discharge and at 1, 6 and 12 months after the procedure and yearly thereafter. Results: Most of the patients (64%) were having patent ductus arteriosus followed by ventricular septal defect in 8 patients (19.04%), aorto-pulmonary window in 5 patients (12%) and coronary cameral fistula in 2 patients (5%). Cardi-O-Fix VSD occluder was the most commonly used device (45%), Cardi-O-Fix PDA occluder (21%) and Amplatzer duct occluder in 17% patients. Pre-procedural pulmonary artery systolic pressure decreased significantly from mean 81.12 mmHg to mean 43.17 mmHg post procedure over a mean follow-up of 18.5 months. Only two major complications viz; severe aortic obstruction and symptomatic complete heart block were noticed in two children. Conclusions: Our study showed that the transcatheter closure of large post tricuspid shunts in pediatric patients with severe PAH was safe, feasible and efficacious alternative to conventional surgery.

Keywords: Large post-tricuspid shunts, Pediatric Cardiology, Structural heart disease, Transcatheter closure.

Introduction

Numerous studies have reported the incidence of congenital heart diseases across the globe at around 8–12 per 1000 live births [1, 2]. The development of pulmonary vascular disease associated with congenital heart diseases has been largely attributed to adverse vascular remodeling triggered by increased pulmonary blood flow and pressures. The histological hallmarks of pulmonary arterial hypertension namely vasoconstriction, inflammation, thrombosis, impaired apoptosis, unregulated cellular proliferation and fibrosis results primarily due to imbalance of vasomediators, endothelial dysregulation and augmented shear stress [3]. Whether to attempt percutaneous closure in pediatric patients with large post – tricuspid shunts and severe pulmonary hypertension remains largely unexplored and fascinating concept. Among this unique subset of patients there is an entire spectrum of severity of pulmonary vascular disease with variable pulmonary vascular resistance and reversibility especially in older children.

Despite newer advances and evolution of innovative transcatheter techniques, this unique subset of patients poses challenges in terms of patient selection, techniques, complications and long term follow up after percutaneous closure. The current study evaluates the safety and efficacy of percutaneous device closure of...
large post tricuspid shunts in pediatric patients with severe pulmonary arterial hypertension at short term and midterm follow up.

Materials and Methods

After complete evaluation forty two children with large post tricuspid shunts and severe pulmonary arterial hypertension underwent attempted percutaneous device closure between 2008 and 2014 at our centre. The large post tricuspid defect with significant shunting was objectively assessed clinically or by transthoracic echocardiography, namely cardiomegaly on chest xray or evidence of left atrial / left ventricular volume overload. All patients included in the study were having severe pulmonary arterial hypertension defined as invasive pulmonary artery systolic pressure more than 2/3rd of the aortic systolic pressure. All the data was prospectively collected during and after intervention with prior written and informed consent of patients and or parents. Detailed history was taken including any previous history of infective endocarditis. Other associated non-cardiac anomalies were also ruled out. General physical examination, standard twelve lead electrocardiogram, chest x-ray and routine blood investigations including complete blood counts, serum electrolytes, renal function tests and viral markers were done. The oxygen saturation was measured in all four extremities at baseline and on exercise when necessary in all the patients. Those candidates with post exercise oxygen saturation of < 90% were excluded from the study due to the possibility of irreversible pulmonary hemodynamics. All patients with complex co-existing congenital heart defects, baseline left ventricular dysfunction, interstitial lung disease, intracardiac thrombi, malignancy and sepsis were excluded from the study. All patients with proximally located aorto-pulmonary defects, distal spiral defects near pulmonary bifurcation or with complete absence of aorto-pulmonary septum were excluded. Also those patients with ventricular septal defects with aortic rim < 4mm, perimembranous defects with inlet extension, right aortic cusp prolapse with baseline aortic regurgitation were not included in the study.

All interventions were carried under general anesthesia with inspiratory oxygen regulated between 40% & 55% during the procedure. The balloon occlusion of the defect was carried out in all patients having pulmonary artery systolic pressure more than 90 percent of the aortic systolic pressure and fall of more than 20 percent of baseline pulmonary systolic pressure after balloon occlusion was considered significant and suggestive of reversible pulmonary hemodynamics.

The complete clinical and indoor hemodynamic evaluation was done in all post procedure patients just before discharge and thereafter every three monthly followed by annual follow up. All the patients were given endocarditis prophylaxis and antiplatelets in form of aspirin 5 mg/kg/day orally for 6 months. Those children with ventricular septal defect after procedure were additionally prescribed oral steroids in tapering doses over 2 weeks and duration was extended in patients who develop conduction disturbances after the procedure.

Statistical Analysis- Quantitative data were expressed as mean ± SD (range). A paired t test was performed as indicated to compare two mean values. P < 0.05 was set as the level of statistical significance.

Results

Patient-related variables- Forty two selected patients with large post tricuspid shunts underwent attempted transcatheter closure with successful completion in 41 patients (97.60%). There were 15 male and 27 female patients. The age ranged from 4 months to 17.5 years (7.34 ± 4.98). The weight varied between 4 kg upto 50 kg (17.31 ± 11.09). Most of the patients (64%) were having patent ductus arteriosus followed by ventricular septal defect in 8 patients (19.04%), aorto-pulmonary window in 5 patients (12%) and coronary cameral fistula in 2 patients (5%). The defect size on two-dimensional echocardiography varied from 3mm upto 13.5mm (7.70 ± 2.63). The pre-procedural right ventricular systolic pressure on echocardiography ranged from 60 mmHg to 140 mmHg (78.76 ± 16.84).

Cardiac catheterization- The mean preprocedural pulmonary artery and aortic pressures were 81.12 ± 19.02 mmHg and 121.78 ± 18.30 mmHg respectively (Table I). Out of 16 patients in whom balloon occlusion of defect was performed during procedure, five were in age group 5 to 10 years and eleven patients were >10 years of age. The balloon occlusion was successfully performed for 15 min in all the patients with constant monitoring of pulmonary artery systolic and aortic systolic pressures. Most commonly used (45%) occluder device was Cardi-O-Fix VSD Occluder (Starway Medical Technology Inc., Beijing) followed by Cardi-O-Fix PDA occluder (21%) and Amplatzer duct occluder (17%) of patients.
The size of Cardi-O-Fix VSD Occluder (Starway Medical Technology Inc., Beijing) used ranged from 6mm to 16mm while size of duct occluders ranged from 6 x 4 to 18 x 16 mm. The mean post-procedural pulmonary artery systolic pressures were 43.17 ± 15.29 mmHg (p < 0.001). The mean fluoroscopy time of all procedures was 14.40 ± 6.92 min while mean device/defect ratio was 134 ± 19.79 in percentage. During final angiogram there was mild residual shunt through the defect in four patients which got diminished during follow up evaluation.

Table-I: Demographic, Hemodynamic and Angiographic data of pediatric patients with large post-tricuspid shunts who underwent successful percutaneous closure.

| Parameter                      | Mean (SD)   | Range       | Median |
|--------------------------------|-------------|-------------|--------|
| Age(years)                     | 7.34 (4.98) | 4m-17.5yr   | 7      |
| Weight (kg)                    | 17.31 (11.09) | 4.50       | 14     |
| Qp/Qs                          | 2.7 (0.55)  | 1.6-4       | 2.5    |
| Fluoroscopy time (min)         | 14.40 (6.92)| 5-40       | 12     |
| Defect size (mm)               | 7.70 (2.63) | 3-13.5      | 7      |
| PASP (pre) mmHg                | 81.12 (19.02)| 60-131    | 75     |
| Aortic systolic pressure (mmHg)| 121.78 (18.30)| 90-185    | 117    |
| PASP (post) mmHg               | 43.17 (15.29)| 18-86    | 42     |
| Follow up (months)             | 18.15 (10.82)| 1.5-60    | 18     |

Complications-There were only two major complications which included one case of severe aortic obstruction due to retention disc of device leading to life threatening hypotension. This patient was having large patent ductus arteriosus which was closed with Cardi-o-Fix muscular vsd occluder of 16mm size but was later removed and defect was closed surgically. The second patient developed symptomatic complete heart block which was treated with dual chamber pacemaker. This patient was having large high muscular vsd which was closed with 14mm Amplatzer muscular vsd occluder. All the other complications were minor including fever, transient vascular complications, transient arrhythmias, transient reversible left ventricular dysfunction etc. All the arrhythmias except in one patient were transient and reverted to sinus rhythm with conservative therapy. Local vascular complications included transient loss of distal pulsations in most patients and common femoral artery thrombosis in one patient which recovered with medical management. None of the patients showed any evidence of worsening of the pulmonary hypertension, device migration or device embolization. At the time of the last follow-up, all the patients were either asymptomatic or in the New York Heart Association - class I. There was no evidence on any device impingement on left pulmonary artery or aortic obstruction during the follow up visits in any of the patients.

Discussion

Infants and children with large post-tricuspid shunts and severe pulmonary hypertension are a unique subset of patients. Most of the defects are correctable with reversible pulmonary hypertension except the older children with minimal or no reversibility of pulmonary hemodynamics.

Surgery has been the traditional method of choice of closure of large post-tricuspid shunts in children with severe pulmonary hypertension with inherent risks of arrhythmias, residual shunts, wound infection, reoperation, post pericardiotomy syndrome, residual pulmonary hypertension etc. Pediatric patients with large post-tricuspid shunts are a high risk subset of patients with higher morbidity and mortality after correction as compared to the conventional patients. Surgical effects of congenital ventricular septal defect associated with pulmonary hypertension are dependent on the recovery of postoperative pulmonary hypertension which in turn depends of age of the patient. Evolution of different surgical techniques with time includes simple ligation [4], division and suturing without CPB [5], division and suturing with CPB [6], transpulmonary artery closure using CPB [7], trans-window closure (anterior sandwich patch closure) [8], trans-aortic direct closure [9] to trans-aortic patch closure of the defect using CPB and arresting the heart [10].
Percutaneous closure of defect is having advantages of significant less discomfort, avoidance of CPB, shorter duration of hospital stay and psychological benefit. In patients with hypertensive ductus, the pulmonary arteries and the ductus arteriosus are large, thin-walled and friable. These vascular structures are prone to hemorrhage at surgery which is the prime cause of operative mortality in these patients [11,12].

Numerous studies have been conducted in the past evaluating the safety and efficacy of transcatheter approach in such patients albeit with high risk of complications [13-28]. This is one of the largest and most comprehensive single centre study till date to evaluate the safety and efficacy of transcatheter closure of large post tricuspid shunts in pediatric patients. This unique subset of patients presents with varying severity of symptoms ranging from totally asymptomatic infant to older children with full blown picture of Eisenmenger syndrome. In this study appropriate patients were selected for transcatheter closure after the temporary closure of the defect to decide on contribution of left to right shunt to pulmonary arterial hypertension and subsequent fall in pulmonary artery pressures.

There was no in-hospital or early mortality in our study which stands out in stark contrast to that in various surgical series previously reported ranged from 1.3% in recent studies to 47.36% in earlier studies. However one case of late mortality was reported in which death resulted from a non-cardiac cause after eleven months of successful follow up and resolution of pulmonary pressures to baseline. There were only two major complications (4.76%) which included one case of severe aortic obstruction due to aortic retention disc of large device leading to life threatening hypotension. This patient was having large patent ductus arteriosus which was closed with 16mm Cardi-O-Fix muscular vsd occluder but was later withdrawn and defect was closed surgically electively. The second patient with large high muscular vsd was closed with 14mm Amplatzer muscular vsd occluder and developed symptomatic complete heart block after sixty months of device deployment. The patient underwent dual chamber pacemaker later on. There were transient arrythmias in form of intermittent sinus pauses, junctional rhythm, atrial and ventricular pre excitation in five patients which recovered conservatively. Interestingly majority of minor and all major complications occurred with large sized Cardi-O-Fix VSD occluders (Starway Medical Technology Inc., Beijing). There was no correlation of minor complications with age, weight, delivery system used in patients.

There were no cases of significant aortic regurgitation in our study during follow up visits in spite of the use of larger and more bulky occlusion devices. This can be attributed to cautious exclusion of patients with insignificant aortic rims on transthoracic echocardiography. One patient with patent ductus arteriosus had bicuspid aortic valve with severe aortic stenosis and moderate valvular aortic regurgitation which persisted after successful ductal occlusion. The incidence of residual shunting was 7.14% at discharge which decreased to 2.38% at mid term follow-up. There was higher use of Cardi-O-Fix VSD occluder device (Starway Medical Technology Inc., Beijing) and Amplatzer muscular ventricular septal defect occluder device (St. Jude Medical Inc., Minnesota, USA) in patients with larger defects and higher Qp/Qs values. Most (97.62%) patients had complete closure with no evidence of device embolization, migration, wire fracture, thromboembolism, residual shunting or endocarditis. Mild obstruction to descending thoracic aorta was observed in one patient but with no hemodynamic consequences and resolved on follow-up. There was transient left ventricular systolic dysfunction in five patients immediately post-procedure. All patients were treated conservatively with inotropic support and digoxin supplements.

Due to left ventricular volume overload there is left ventricular remodeling with increase in cardiac output according to Frank-Starling law which maintains systemic circulation. Due to transcatheter closure of defect, there is immediate decrease in preload and left ventricular end diastolic diameter alongside stationary left ventricular end systolic diameter which leads to reduction in muscle fiber stretch and fractional shortening of left ventricle [29]. There is increase in left ventricle afterload immediately after closure due to isolation of low-resistance pulmonary circulation from the left ventricle outflow circulation [29,32].

There is complete and often spontaneous resolution of left ventricle systolic dysfunction in children in contrast to adults with similar hemodynamics due to longer duration of volume overload and consequently more extensive and irreversible changes in left ventricle in adults compared to children [29-32]. There was a consistent decrease in the pulmonary pressures immediately after intervention and over short and intermediate term follow-up (Figure 1).
Conclusions

This study shows that the transcatheter closure of large post-tricuspid shunts in pediatric patients with severe pulmonary hypertension is safe, feasible and efficacious alternative to surgery. Holistic evaluation of such patients using spectrum of clinical examination, non-invasive tests and if needed cardiac catheterization leads to optimal selection of such patients who would benefit from percutaneous closure. It has excellent results in experienced hands with minimum morbidity and almost no mortality. Sudden decrease in preload with in left ventricle afterload leads to transient and often completely reversible left ventricle systolic dysfunction in some patients. Careful attention should be paid in catheterization laboratory in infants due to higher predisposition to pulmonary stenosis and aortic outflow obstruction after device deployment.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Abbreviations

CPB – Cardio-pulmonary bypass
PASP – Pulmonary artery systolic pressure

Conflict of Interest: The authors declare that they have no conflict of interest. Informed consent was obtained from all individual participants included in the study.

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