Comparison of Long-Term Complications of Using Amplatzer Ductal Occluder and Ventricular Septal Defect Occluder for Transcatheter Ventricular Septal Defect Closure

Mehdi Ghaderian, Negin Salemi
Pediatric Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

ABSTRACT

Background: Ventricular Septal Defect (VSD) is the most common type of congenital heart disease and perimembranous type is the commonest form of these defects. Trans-catheter management of these defects is a challenging procedure.

Objectives: The purpose of this study was to compare of Trans-catheter closure of perimembranous ventricular septal defect (PMVSD) using Amplatzer Ductal Occluder (ADO) and VSD occluder and their complications and follow-up.

Patients and Methods: Between 2013 and April 2019, 69 patients underwent percutaneous closure of PMVSD using ADO (29 patients) and VSD occluder (40 patients). After obtaining the size of VSD from the ventriculogram at least 2 mm larger than the orifice diameter of VSD at the right ventricular side was chosen. The devices were positioned after verification of the proper device position by echocardiography, aortogram and left ventriculography.

Results: The mean age of patients were 9.07 ± 7.73 years, mean weight 26.12 ± 16.25 kg. The mean defect size of the right ventricular orifice and device sizes were 5.54 ± 1.83 mm 7.72 ± 1.94 mm respectively. Small residual shunts were seen at the completion of the procedure, but they disappeared during follow-up in all but one patient. Two patients had mild AI before the procedure in ADO group that disappeared during the follow-up. The mean follow-up period was 3.3 ± 1.7 years (range 1 to 6 years). Complete atrioventricular block (CAVB) was seen in one patient (VSD occluder) during the procedure that disappeared after the retrieval of the device. Major complication or death was not observed in our study.

Conclusions: Trans-catheter closures of PMVSD with ADO or VSD occluder had similar effects in these patients and are safe and effective treatment associated with excellent success and closure rates. Long-term follow-up in a large number of patients is warranted.

Key words: Amplatzer, patent ductus arteriosus, ventricular septal defect

INTRODUCTION

Ventricular septal defect (VSD) is the most commonly recognized congenital heart disease and has over 20%–30% prevalence of all forms of congenital disease. VSD means there is a defect between the two ventricles and has different classification based on location and size also can be associated with other congenital diseases.\(^{[1,2]}\)

According to the location, defects are either muscular (15%), supra crystal (5%) and perimembranous. PMVSD which is the most common sub type (around 70%). They can undergo spontaneous closure during the first year of life if they have a small diameter. Closure overload of the heart chambers is necessary to prevent...
pulmonary arterial hypertension (PAH), ventricular dysfunction, arrhythmias and aortic regurgitation.

In addition, the surgical approach is associated with morbidity and mortality, but the trans-catheter closure of perimembranous VSDs is an alternative method and is suggested because of shorter hospitalization time, no need for cardiovascular bypass, and sternotomy.[3-6]

Recently, use of Amplatzer device has been introduced. This approach seems to be safer for routine use and had lower complications than surgical approach[7]. Complete heart block associated with device closure of perimembranous ventricular septal defects was the most important complication. However, years ago, by using other Amplatzers such as Patent Ductus Arteriosus occluder, complete heart block complication was reduced [8,9]. In a study 21 patients underwent transthoracic echocardiography (TTE) that protocol and experienced operator; all of them were examined by a standard echocardiographic using ADO and 40 patients with VSD occluder. Patients 29 patients underwent trans-catheter closure of VSD and had symptoms. This study is a long-term follow-up of ventricular septal defect closure in at the Shahid Chamran hospital between 2013 - 2019.

**METHOD**

The Ethics Committee of the Isfahan University of Medical Sciences in Iran approved the study protocol. In this study, all patients who had undergone transcatheter closure of VSD using ADO or VSD occluder between 2013 and 2019 in Shahid Chamran Medical and Cardiovascular Research Center were included. Full and informed consent (or parental) was obtained for this study. Patients in this study had a perimembranous ventricular septal defect and had symptoms.

There were 69 patients: 32 females and 37 males. 29 patients underwent trans-catheter closure of VSD using ADO and 40 patients with VSD occluder. Patients were examined by a standard echocardiographic protocol and experienced operator; all of them underwent transthoracic echocardiography (TTE) that was performed with an Echo 7 Samsung made in Korea machine including M-mode, two-dimensional, and color Doppler. The non-sedated method used for older children and adults and sedated methods for younger children in the quiet and vigilant state. Size and sort of VSD were examined in different views.

The inclusion criterion was: Perimembranous ventricular septal defect (PMVSD), mean pulmonary arterial pressure less than 2/3 of systemic arterial pressure, evidence of a significant left-to-right shunt through the VSD (> 1.5 / 1) and one or more of the following data: (a) prominent cardiomegaly and lung congestion on standard chest X-ray; (b) left atrial to aortic ratio > 1.5 in long-axis parasternal view examination by echocardiography defined as left atrial enlargement; (c) left ventricular overload and enlargement in echocardiography; (d) frequent respiratory infections in past medical history and/or failure to thrive; (e) Infants selected for trans catheter VSD closure that weighed ≥ 10 kg.

The exclusion criteria were: (a)VSD associated with any other congenital heart disease which had to be corrected by surgical approach; (b) patients who have a mean pulmonary pressure greater than 2/3 of systemic blood pressure ;(c) body weight less than 10 kg;(d) Eisenmenger syndrome and right to left shunt or pulmonary vascular resistance of greater than 8 Woods units m2; (e) patients with PMVSD and an aortic cusp prolapse; (f) sepsis and (g) contraindication to antiplatelet therapy.

The procedure was performed under general anesthesia and standard routine protocol. Femoral vein and arterial line were obtained and then each patient were given 80- 100 IU/kg heparin in two divided doses (50 IU/kg at first and 30- 50 IU/kg during the procedure) to maintain activated clotting time more than 200 sec. Intravenous antibiotic with 50 mg/kg Cefazolin was administered for prophylaxis during the procedure and three subsequent doses 8 hours during the following 24 hours. Standard right and left cardiac catheterization and angiography were performed and data were gathered. During the cardiac procedure angiographies and catheterization data including size and type of VSD, its relation to the aorta and being of an aneurysmal formation of VSD were obtained from the ventriculogram in left-anterior-oblique (LAO) in different views and also right-anterior-oblique (RAO) views for relation to the pulmonary artery.

The pulmonic part of the ADO device or VSD occluder was suggested to be 2 mm larger than the narrowest VSD diameter on the right side measured by ventriculography. Afterward, a 0.035-inch Terumo guide wire was placed across the VSD using a 4 or 5 French curved end-hole catheter (Judkins right coronary, Cobra) or manually cutting a pigtail catheter to adjust the needed angle from the right ventricle (RV) and then either branch of the pulmonary artery or superior or inferior vena cava.

At the next step, the wire was snaring with one of the different snares and withdrawn to exteriorize it
through the femoral vein and establishing a long wire loop from the femoral artery to the femoral vein. Over this wire, an appropriate long sheath was advanced from the femoral vein across the VSD by standard protocol to the tip of the sheath was in the descending aorta or in the left ventricle.

Then the dilator from the femoral vein and the catheter and guidewire was removed from the arterial line. Measurement of VSD diameter was repeated; ventriculogram was done. The device was implanted while the device was attached to the cable and then was advanced to the tip of the sheath during fluoroscopy.

At this time, the retentive disc of the device was deployed, and the cable, delivery sheath, and device were pulled back as one unit under fluoroscopy until the retentive disk was placed at the LV side of VSD not interfering with aortic valve cusps. Ventriculography, aortography, and echocardiography were performed to confirm the proper device position and to confirm the absence of aortic regurgitation.

The tubular frame of the device was deployed by pulling the sheath into the right ventricle, and the right side of the device was deployed in the appropriate position. The device was released by turning the cable after verification of the proper device position [Figure 1]. Aortogram, left ventriculogram, and TTE were done before releasing the device for evaluation of early complications.

Complete blood cell counts (CBC) and echocardiography were done 4–6 h later because of early complications such as occult hemorrhage, pulmonary complications, and pericardial effusion. Vital signs monitoring was done during the first 24 hours. The patients were monitored with 12-lead electrocardiogram for 24 hours and also repeated with echocardiography one day, one month, three months, six months, and then annually after the device implantation.

After discharge, all patients received clopidogrel 1 mg/kg for three days and then 0.5 mg/kg for at least 1 month, acid salicylic acid (ASA) 3–5 mg/kg for six months, and heparin 50 IU/kg every six hours for the first day by the control of clotting tests. All patients were discharged 24 hours after the procedure. Prophylaxis for endocarditis was done for the first six-months if needed and discontinued at the six-month follow-up by echocardiography if the defect was completely occluded and had no residual shunt.

**Statistical analysis**
Data are expressed as a frequency or percentage for nominal variables. Continuous variables are expressed as Mean ± standard deviation (SD). Analyses were performed using SPSS Statistics 25.0 (SPSS Inc., Chicago, Ill, USA). Statistical significance was defined as a P-value <0.05.

**RESULTS**
There were 8 adult patients (age≥18 years). Also, Table 1 shows demographic, general, clinical and analytical data of the patients. The size of the VSD on angiography was larger in adult patients compared with children. The appropriate position of the device was demonstrated by angiography and TTE and in 66 of 69 patients (95.6%), the defect successfully closed. One patient with VSD Occluder had an AV block that did not disappear and his hemodynamic was became worse during the procedure so the patient underwent surgical approach.

Seven patients had transient arrhythmias during the procedure as a premature atrial contractor (PAC) and premature ventricular contraction (PVC) in both groups with ADO and VSD Amplatzers. In one patient during the angiography, we found out that the VSD was not appropriate for trans catheter closure so he became a candidate for surgery. After the procedure in the post-Cath phase, he lost consciousness and rapidly deteriorated. H-s pupils became fixed and mydriatic. A CT scan was performed immediately and unfortunately, he had a massive intraventricular hemorrhage (IVH) and progressed to brain death, although he had normal ACT and normal clotting exams before and during the procedure.

There were no other major complications such as device embolism, retroperitoneal bleeding, lethal arrhythmia, and vascular injuries [Table 2]. The

![Figure 1: Ventriculogram (a) and aortogram (b) before and after ventricular septal defect (c) and patent ductus artery device closure (d) (at first patent ductus artery and then ventricular septal defect were closed, respectively, in the same procedure)](image-url)
VSD occlusion rate was 65.7% at completion of the procedure, rising up to 79.5% at discharge, and 96.4% during follow-up. During the follow-up, our patients had no complications such as late arrhythmias, device embolism, hemolysis, and bacterial endocarditis. Two patients had mild aortic insufficiency (AI) because of proximity VSD and aortic valve. In both of them, we used ADO and during the follow-up AI became better and one year later, none of them had significant AI.

**DISCUSSION**

The current study reports results and follow-up findings in 69 children who underwent transcatheter closure of VSD using Amplatzer PDA and VSD occluder. As VSD is one of the congenital heart diseases, it has undergone an evolution of treatment. Surgical techniques were used to close VSDs from many years ago but there were many complications such as residual VSD and a perioperative mortality rate of 0.5% and other complications. Trans-catheter closure of VSDs was introduced as an alternative method for surgical closure, however, this method like other interventional procedures, have some immediate, short-term or long-term complications.

One of the most important complications of intravenous VSD closure may be complete heart block, which has been reported with the rate of about 1%-20%. Complete heart block is due to the close contiguity of the perimembranous VSD to the atrioventricular conduction system. The most important cause of this complication is the right side of HIS bundle in ventricular septum being under pressure by the disk of Amplatzer, or it can also cause the beginning of fibrosis at the time of closure of this defect or long afterwards by surgery or interventional approaches. Therefore, by using other kinds of amplatzers as ADO because of the smaller right part disk, the pressure on the atrioventricular node has been decreased.

In this study, by evaluating 69 VSD closure using ADOs and VSD occluders and comprehension the result of their procedure by follow-ups, we realized that using ADO has lower complication rate than using VSD amplatzers for VSD closure. Also in other studies have shown that using the ADO to close muscular VSDs because of the lack of right ventricular retention disk is an ideal method and in the post procedure follow-up patient had no major complications using ADOs. In another study, no AV block was reported and only some events like device embolization which could have been prevented by absolute sizing. In another study two patients out of 49 patients had transient various degrees of heart block and one case who admitted 6 months after procedure with dyspnea and electrocardiography revealed complete atrioventricular block, and the TTE revealed a 20-mm-sized pericardial effusion as the only major complication.

Table 1: Demographic comparison of ventricular septal defect affected cases between Amplatzer ductal occluder and ventricular septal defect occluder group

| Variable               | ADO group (n=29) | VSD occluder group (n=40) | P  |
|-----------------------|------------------|---------------------------|----|
| Age (years)           | 8.37±5.80        | 9.61±8.91                 | 0.5|
| Female/male           | 11/18            | 19/21                     | 0.23|
| Weight (kg)           | 25.56±16.88      | 26.53±15.98               | 0.81|
| PA pressure (mmHg)    |                  |                           |    |
| Systolic              | 20.51±5.26       | 22.00±7.82                | 0.38|
| Diastolic             | 12.37±3.11       | 12.62±4.17                | 0.79|
| Mean                  | 16.51±3.87       | 17.32±5.67                | 0.51|
| Hemoglobin            | 12.54±1.41       | 12.39±0.75                | 0.55|
| Fluoroscopy time, min | 16.41±3.22       | 17.56±6.84                | 0.37|
| Total angiography time, min | 45.12±5.31 | 49.32±6.14                | 0.45|
| VSD size at right ventricle, mm | 5.63±1.81     | 5.47±1.86                | 0.71|
| Size of device (orifice at right ventricle), mm | 7.75±2.01 | 7.70±1.92                  | 0.90|

ADO: Amplatzer ductal occlude, VSD: Ventricular septal defect, PA: Pulmonary artery

Table 2: Complications comparison of ventricular septal defect affected cases between Amplatzer ductal occluder and ventricular septal defect occluder group

| Complications          | ADO group (n=29) | VSD occluder group (n=40) | P  |
|------------------------|------------------|---------------------------|----|
| Arrhythmia             | 3                | 4                         | NS |
| Death                  | -                | -                         | NS |
| Vascular injury        | -                | -                         | NS |
| Emboli                 | -                | -                         | NS |
| Retroperitoneal bleeding | -       | -                         | NS |
| CHB                    | 2                | 1                         | NS |
| AI                     | 2                | 2                         | -  |

CHB: Complete heart block, ADO: Amplatzer ductal occlude, VSD: Ventricular septal defect, NS: Not significant, AI: Aortic insufficiency
complete congenital atrioventricular block (CAVBL) persisted, and a permanent pacemaker was implanted.\textsuperscript{[19]} In the current study during the follow-up, we had not any pericardial effusion and it could be due to immunologic reaction.

In some studies using steroids for reversing or preventing the CAVB was mentioned, and in one study, there was a reported case of CAVB relapse that required pacemaker implantation after using ASA and steroid to initial reversal management.\textsuperscript{[13,18-24]} but the occurrence of CAVB is not completely predictable and it can appear after years.\textsuperscript{[24]} Occurrence of AVB could be resulted as fibrosis, it could be happened during the years, and use of steroids did not show prevention of this complication.

As our study and other studies of percutaneous VSD closure using the ADO reported, the rate of VSD closure was about more than 93% at the last follow-up, so the appropriate closure is confirmed.\textsuperscript{[25,26]}

Limitation
One of our limitations was the hard accessibility to patients for follow-ups. Because these methods have been used for a few years, long-term follow-up in these patients is required to confirm these studies. In addition, larger and multi-center studies are also required to confirm of using these amplatzer and long-term complications.

CONCLUSION
Closing of VSD with ADO seems to have fewer specific side effects than the previous amplatzers. The experience of the operator will play an important role in preventing complications. Our study during follow-ups confirmed trans-catheter closure of VSDs using ADO is effective, and multiple studies confirm using of these amplatzers. This method can be used instead of VSD amplatzers by using the appropriate size and position and considering the transient arrhythmias.

Acknowledgments
We wish to express our gratitude to the staff of the Department of Pediatric Cardiology, Child Growth and Development Research Center, at Isfahan University of Medical Sciences.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Mavroudis C, Dearani JA, Anderson RH. Ventricular septal defect.
2. Carminati M, Butera G, Chessa M, De Giovanni J, Fisher G, Gewillig M, et al. Transcatheter closure of congenital ventricular septal defects: Results of the European Registry. Eur Heart J 2007;28:2361-8.
3. Nygren A, Sunnergardh J, Berggren H. Preoperative evaluation and surgery in isolated ventricular septal defects: A 21 year perspective. Heart 2000;83:198-204.
4. Revankar VR, Varghese TG, Papanna M. An interesting case report of unexpected vsd device embolization and its challenging retrieval. Heart India 2015;3:76.
5. Deal BJ, Mavroudis C, Backer CL. The role of concomitant arrhythmia surgery in patients undergoing repair of congenital heart disease. Pacin Clin Electrophysiol 2008;31 Suppl 1:S13-6.
6. Visconti KJ, Bichell DP, Jonas RA, Newburger JW, Bellinger DC. Developmental outcome after surgical versus interventional closure of secundum atrial septal defect in children. Circulation 1999;100:II145-50.
7. Lock JE, Block PC, McKay RG, Baim DS, Keane JF. Transcatheter closure of ventricular septal defects. Circulation 1988;78:361-8.
8. Rigby ML, Redington AN. Primary transcatheter umbrella closure of perimembranous ventricular septal defect. Br Heart J 1994;72:368-71.
9. Predescu D, Chaturvedi RR, Friedberg MK, Benson LN, Ozwara A, Lee KJ. Complete heart block associated with device closure of perimembranous ventricular septal defects. J Thorac Cardiovasc Surg 2008;136:1223-8.
10. Lee SM, Song JY, Choi JY, Lee SY, Paek JS, Chang SI, et al. Transcatheter closure of perimembranous ventricular septal defect using amplatzer ductal occluder. Catheter Cardiovasc Interv 2013;82:1141-6.
11. Ghaderian M, Merajie M, Mortezzaein H, Aarabi M, Mohammad Y, Shah Mohammadi A. Efficacy and safety of using amplatzer ductal occluder for transcatheter closure of perimembranous ventricular septal defect in pediatrics. Iran J Pediatr 2015;25:e386.
12. Mavrodis C, Backer S. Pediatric Cardiac Surgery. 3rd ed. USA: Mosby; 2003.
13. Schwalm S, Hijazi Z, Sugeng L, Lang R. Percutaneous closure of a post-traumatic muscular ventricular septal defect using the Amplatzer duct occluder. J Invasive Cardiol 2005;17:100-3.
14. Shah JH, Sariayya SP, Nikam TS, [ha M]. Transcatheter Device Closure of Perimembranous Ventricular Septal Defect in Pediatric Patients: Long-Term Outcomes. Heart Views. 2020 Jan-Mar;21(1):17-21.
15. Walavalkar V, Maiya S, Pujar S, Ramachandran P, Siddaiiah S, Sronck B, et al. Percutaneous device closure of congenital isolated ventricular septal defects: A single-center retrospective database study amongst 412 cases. Pediatr Cardiol 2020;41:591-8.
16. Brown KN, Kanamthareddy A. Catheter Management of Ventricular Septal Defect. StatPearls [Internet]. [Last updated on 2019 Sep 18].
17. Lin A, Mahle WT, Frias PA, Fischbach PS, Kogon BE, Kanter KR, et al. Early and delayed atrioventricular conduction block after routine surgery for congenital heart disease. The Journal of thoracic and cardiovascular surgery. 2010;140(1):138-60.
18. Nguyen HL, Pham QT, Doan DD, Dinh LH, Tran HB, Sharmin S, et al. Percutaneous closure of perimembranous ventricular septal defect using patent ductus arteriosus occluders. PLoS One. 2018 Nov 15;13(11):e0206335.
19. Yalonetsky S, Lorber A. Late high degree atrioventricular block after percutaneous closure of a perimembranous ventricular septal defect. Cardiology in the young. 2009;19(3):298-300.
20. Butera G, Gaio G, Carminati M. Is steroid therapy enough to reverse complete atrioventricular block after percutaneous
perimembranous ventricular septal defect closure? Journal of Cardiovascular Medicine. 2009;10(5):412-4.

21. Walsh MA, Bialkowski J, Szukutnik M, Pawielec-Wojtalik M, Bobkowski W, Walsh KP. Atrioventricular block after transcatheter closure of perimembranous ventricular septal defects. Heart. 2006;92(9):1295-7.

22. Narin N, Pamukcu O, Tuncay A, Baykan A, Sunkak S, Tasci O, Uzum K, Saltik L. Percutaneous Ventricular Septal Defect Closure in Patients Under 1 Year of Age. Pediatr Cardiol. 2018 Jun;39(5):1009-1015.

23. Koneti NR, Penumatsa RR, Kanchi V, Arramraj SK, Bhupathiraju S. Retrograde transcatheter closure of ventricular septal defects in children using the Amplatzer Duct Occluder II. Catheterization and Cardiovascular Interventions. 2011;77(2):252-9.

24. Pamukcu O, Narin N, Baykan A, Sunkak S, Tasci O, Uzum K. Mid-term results of percutaneous ventricular septal defect closure with Amplatzer duct occluder II in children. Cardiol Young 2017;27:1726-31.

25. Zhao PJ, Yu ZQ, Gao W, Li F, Fu LJ, Liu TL, et al. Efficacy of the transcatheter closure of perimembranous and muscular ventricular septal defects with the Amplatzer duct occluder II. Zhonghua Xin Xue Guan Bing Za Zhi 2012;40:817-20.

26. Koneti NR, Sreeram N, Penumatsa RR, Arramraj SK, Karunakar V, Trieschmann U. Transcatheter retrograde closure of perimembranous ventricular septal defects in children with the Amplatzer duct occluder II device. J Am Coll Cardiol 2012;60:2421-2.