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Early and Mid-term Results of Transcatheter Closure of Perimembranous Ventricular Septal Defect using Amplatzer Ductal Occluder type 1

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Abstract
Objectives: To study the early and midterm results of transcatheter closure of perimembranous VSD using Amplatzer Ductal Occluder type 1.
Methods: Prospective study of one hundred thirteen patients with perimembranous VSD (PMVSD) who referred to catheterization laboratory and underwent transcatheter closure of their defects by using Amplatzer Ductal Occluder type 1 device. Routine right and left heart catheterization was performed with evaluation of the pulmonary and systemic pressure. All the procedures were done under fluoroscopy and transthoracic echocardiography guide. Follow up evaluations were done between 1 month and 12 months after discharge (mean 4.5 ± 1.13 months) with transthoracic echocardiography and 12 lead electrocardiography.
Results: The age of patients range from 2 to 34 years at procedure (mean 10.60 ± 7.31 years), weight range from 10 to 85 kg (mean 32.38 ± 19.70 kg). The mean echocardiographic defect size was 5.69 ± 1.63 mm and the mean angiographic size was 5.89 ± 1.70 mm. The devices size used range from 6/4–16/14 mm. The most common device used was 10/8. The ADOs were successfully implanted in 108 patients (95.6%). The VSD occlusion rate was 85.2% at completion of the procedure, rising up to 90.7% next day at discharge, 93.5% at one month and 97.2% at 6 months during follow-up. Two patients (1.9%) developed CAVB, one case within 24 hours and the other case after 2 days of the procedure, they were admitted in hospital treated by temporary pacemaker implantation, steroids and NSAIDs (high dose aspirin) with complete remission within 5 days.
Conclusion: Transcatheter closure of PMVSD with ADO1 in children is a safe and effective treatment associated with excellent success and closure rates and with no significant adverse events, but long-term follow-up in a large number of patients would be warranted.
Keywords: Transcatheter closure, perimembranous ventricular septal defect, amplatzer ductal occluder type 1

Introduction

Ventricular septal defect (VSD) is a defect in the ventricular septum that separates the left and right ventricles of the heart. The ventricles are a single chamber at about four weeks of gestation but by eight weeks it has been divided into two. Failure of development of any part of the septum results in a defect. It may vary considerably in terms of size and hemodynamic consequences. In adults a VSD may be acquired as a complication of myocardial infarction or trauma.[1] VSDs are the most common congenital heart defect in children, occurring in 50% of all children with congenital heart disease and in 20% as an isolated lesion. The incidence of VSDs has increased significantly with advances in imaging and screening of infants and ranges from 1.56 to 53.2 per 1,000 live births.[2] Factors affecting the developing fetal heart can be associated with development of VSDs. These include genetic conditions (chromosomal, single gene or polygenic) as well as environmental influences.[3] Chromosomal disorder caused by absent or duplicated chromosomes may be associated with VSDs. Recurrence risk in the offspring is that of the chromosomal disorder. If antenatal diagnosis has shown a VSD, it is reasonable to proceed to fetal karyotyping in case of chromosomal abnormality.[3] Single gene disorders are caused by deletions, mutations or duplications within a single gene and there is high risk of recurrence in first-degree relatives. An example is Holt-Oram syndrome.[4] Recurrence risk is estimated to be between 3% and 5%.[3] VSD is also more likely with diabetes in pregnancy.[5] It can occur with fetal alcohol syndrome.[6] There may be an association with maternal use of cannabis.[7] The prognosis for a patient with an isolated VSD is excellent. Most small-to-moderate muscular VSDs can be expected to close spontaneously. Perimembranous defects can also close by apposition of adjacent tissue from tricuspid valve leaflets. Subarterial infundibular VSDs do not close. Spontaneous closure is common in children under a year old but less likely after the age of 2 years. After more than six years almost a third of all perimembranous and just over two thirds of all muscular defects close spontaneously. Generally, perimembranous defects are larger than muscular defects, require surgical intervention more frequently and even when they are small have just over 50% chance of closing spontaneously.[8] The aim of study to study the early and midterm results of transcatheter closure of PMVSD using Amplatzer ductal occluder type I.

Method

This is a prospective study done in Ibn Albitar cardiac center for surgery. In this study, include all patients who had undergone transcatheter closure of Perimembranous VSD using ADO1 between January 2015 and January 2016. Patients were examined by a standard echocardiographic protocol and experienced operator; all patients underwent transthoracic echocardiography (TTE) including M-mode, two-dimensional and color Doppler. The standard technique was used to obtain the measurements in a non-sedated for older children and sedated for younger children in quiet and wakeful state. Size and sort of VSD were examined in different standards four chambers, five chambers and parasternal in short and long-axis views. Patients with clinical or echocardiographic evidence of significant left to right shunt whose Qp/Qs was ≥ 1.5 due to isolated PMVSD were selected and included in the

study. Exclusion criteria were (a) VSD associated with any other congenital heart disease which had to be corrected by surgical approach; (b) patients with significant non-cardiac and cardiac co-morbidities and abnormalities that could impact clinical outcome of VSD closure; (c) VSD with sever pulmonary hypertension (Eisenmenger syndrome) and right to left shunt or pulmonary vascular resistance of greater than 8 Woods units [Pulmonary hypertension defend as mean pulmonary artery pressure >25 mmHg at rest or >30 mmHg at exercise due to increase flow or increase resistance, mild pulmonary hypertension when systolic PA pressure; 25–40 mmHg, moderate; when 40–60 mmHg and severe; when]. (d) ventricular septal defect distance (rim) <2 mm away from atrioventricular and semilunar valves; (e) patients with perimembranous VSD and prolapse of an aortic cusp; (f) Patients with malalignment type ventricular septal defects; and (g) contraindication to antiplatelet therapy. Data are expressed as a frequency or percentage for nominal variables. Continuous variables are expressed as Mean ± standard deviation (SD). Analyses were performed by using SPSS Statistics 18.0. *P* value is used, a significant level if it is < 0.05.

Results

One hundred thirteen patients were included in this prospective study. Patients age were ranged from 2 years to 34 years (mean 10.60 years ± 7.31), their weights ranged from 10–85 kg (mean 32.38 kg ± 70). About the sex of patients, 64 patients (56.6%) were females and 49 patients (43.4%) were male, (Table 1). The systolic pulmonary artery pressure ranged from 19 to 85 mmHg (mean 36.13 ± 10.59), in 7 patients (6.2%) the systolic PA pressure was <25 mmHg (normal), in 68 patients (60.2%) ≥ 25–40 mmHg (mild), in 27 patients (23.9%) >40–60 mmHg (moderate) and in 11 patients (9.7%) >60 mmHg (severe), (Table 2). The echocardiography diameter of the defect ranged from 3 to 12 mm (mean 5.69 ± 1.63 mm). The angiographic defect diameters ranged from 3–13 mm (mean 5.89 ± 1.70 mm). *P* value = 0.095 (not significant). In 94 patients (83.2%) the procedure was done under general anesthesia, while local anesthesia was used in 19 patients (16.8%).

Table 1. **Baseline characterstics of study group**

Parameter	Mean ± standard deviation (M ± SD)
Age	10.60 ± 7.31 years
Weight	32.38 ± 19.70 kg
PA pressure	36.13 ± 10.59 mmHg
Echo size	5.69 ± 1.63 mm
Angio size	5.89 ± 1.70 mm
Fluoro time	22.94 ± 7.90 minutes
Procedure time	62.35 ± 22.29 minutes

Table 2. **Systolic PA pressure range of study group**

PA pressure	Number of patients	Percentage
≤25 mmHg	7	6.2%
>25–40 mmHg	68	60.2%
>40–60 mmHg	27	23.9%
>60 mmHg	11	9.7%

In 10 patients (8.8%) there were two PMVSDs and 103 patients (91.2%) with one defect. In 105 patients (92.9%) shows PMVSD with no extension, while 3 patients (2.7%) had inlet VSD extension and 5 patients (4.4%) with muscular extension. In 77 patients (68.1%) there were aneurysmal tissue formations with PMVSD, while 36 patients (31.9%) had PMVSD with no aneurysmal tissue formation including all those with inlet and muscular extension. The procedure was successful (device inserted and released) in 108 of 113 patients (95.6%) {including all PMVSDs with aneurysmal tissue}, (Figure 1). Sixteen patients (14.8%) had small angiographic and echocardiographic residual shunts develop immediately after release of device, six of them (5.5%) had residual shunt through device and 10 patients (9.3%) had true residual shunt (from another defect). There were 5 patients (4.4%) underwent failure procedure, two of them with perimembranous to inlet extention, it was impossible to obtain a stable position of the device, which was retrieved before unscrewing it (so from 3 patients with inlet extension, 2 patients show procedure failure). In one patient there was Aortic Valve contact with significant new onset Aortic Valve regurgitation. In one patient the guide wire (size 0.021 inch) looped around the TV surroundings after snaring it, couldn't be moved and fractured there who then referred for surgical removal of the guide wire piece that girts the TV surroundings. One patient developed CAVB when crossing the defect, resuscitation had been done successfully and the procedure was aborted, (Table 3). Fluoroscopy and total procedural times ranged from 15–60 minutes (mean 22.94 ± 7.90 minutes) and from 30–150 minutes (mean 62.35 ± 22.29 minutes) respectively. The fluoroscopy time and procedure time were shorter in patients with larger defects ≥7 mm (mean fluoro time and procedure time were 17.6 min and 42.7 min, respectively). Devices used (device diameter/length in mm) were 10/8 in 46 patients (39.7%), 8/6 in 43 patients (37.1%), 12/10 in 13 patients (11.2%), 6/4 in 7 patients (6%), and 16/14 in 2 patients (1.7%); so the most common device used was 10/8 mm, (Figure 2). About attempts to close the defect during procedure, (attempt mean the number of

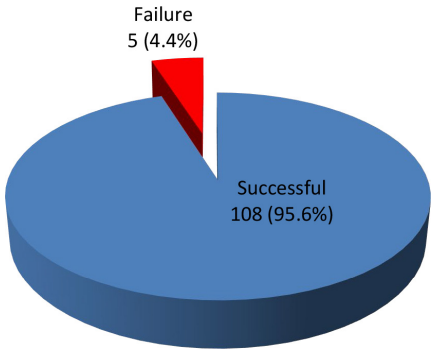

Fig. 1 **Success of procedure and failure.**

Table 3. **Causes of closure failure**

Causes of failure	No. and percentage
PMVSD-inlet	2 patients (1.7%)
New onset significant AR	1 patient (0.9%)
Guide wire girts around TV	1 patient (0.9%)
CAVB	1 patient (0.9%)
Total no. and percentage	5 patients (4.4%)

crossing the VSD and deployment device). In 93 patients (86.1%) one attempt was done successfully, in 14 patients (13%) the defect was closed after second attempt (10 by changing the device size and 4 by repositioning the device) and one patient (0.9%) after 3 attempts (two time by repositioning the device and third time by changing the device), (Figure 3). The complications were occurred in different age groups and different body weights, (Table 4). Two patients (1.9%) developed CAVB, one of them was 9 years' old who developed CAVB within 24 hours of the procedure, the other was 6 years' old who developed CAVB after 2 days of the procedure; they were admitted in hospital treated by temporary pacemaker implantation, receiving steroids for 5 days and NSAIDs (high dose aspirin) with complete remission within 5 days. Trivial to mild new onset AR was detected by aortogram in 6 patients (5.6%) immediately after release of device. Mild new onset tricuspid regurgitation was detected by echocardiography on next day in 8 patients (7.4%). No patient developed vascular complications, device embolization or death and all were discharged home next day after evaluation by echocardiography and electrocardiography.

Discussion

Surgical repair generally a safe procedure for PMVSD but have potential risks including heart block in 1–5%, significant residual shunt in 1–10%, the necessity for reoperation in 2% and death in 0.6–5% of the patients. Furthermore, infections, tachyarrhythmias and neurologic complications may occur.[4,9] Perimembranous VSDs are located near the conduction tissue and aortic valve, and if there is an aneurysmal tissue around the VSD, it makes its morphology even further complex.[10] In this study, the age of patients was ranged from 2 years to 34 years (mean 10.60 years ± 7.31), their weights ranged from 10–85 kg (mean 32.38 kg ± 19.70), approximately similar to

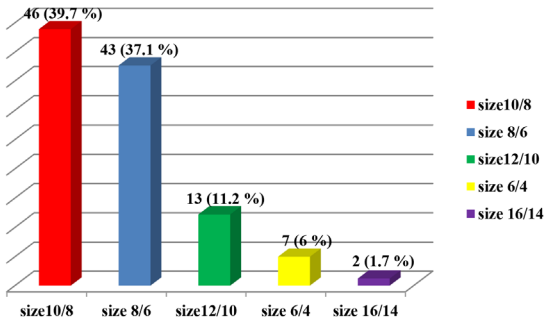

Fig. 2 **The size of devices used.**

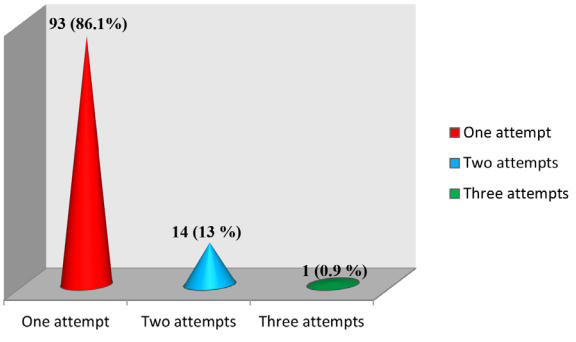

Fig. 3 **Number of attempt.**

Table 4. **The types of complications**

Type of complications	Number	Percentage	Fate
Mild TR	8	7.4%	Completely disappeared
Mild AR	6	5.6%	Disappeared in 4 patients
CAVB	2	1.9%	Completely disappeared

study reported by Lee SM et al.,[11] which include the age ranged from 3 years to 42 years (median 7 years) and their weights ranged from 18 kg to 60 kg (median 27 kg). Female gender percentage (56.6%) was slightly higher than male, a result accedes with that reported by Lee et al.,[11] who was found that female gender percentage (60.2%). The mean defect size by echocardiography was (5.69 ± 1.63 mm) and by angiography was (5.89 ± 1.70 mm), the difference statistically not significant (*P* value = 0.095), approximately similar to study reported by Ghaderian M et al.,[12] in which the mean defect size was (4.5 ± 1.6 mm) and the *P* value > 0.075 (statistically not significant). The mean PA pressure in this study was (36.13 ± 10.59 mm Hg), similar to study reported by Gianfranco Butera et al.,[13] in which the mean PA pressure was (38 ± 9), while in study reported by Lee SM et al.,[11] the mean PA pressure was (22.11 ± 6), this differences may be related to number of cases included in each study, which were 113 patients, 104 patients and 21 patients, respectively. The Amplatzer ductal occluder type I devices was successfully implanted in 108 of 113 patients (95.6%) in this study, which is nearly same result of study that done by Nguyen Lan Hieu,[14] who reported that ADO-I was successfully implanted in 128 of 133 patients (97%) and less than the results reported by Ghaderian M. et al.,[12] who reported (100%) successful rate (in his study, all cases selected were with VSDs ≤7 mm in diameter). This differences may be related to the selection of cases with smaller defects candidate to transcatheter device closure. There were 5 patients (4.4%) underwent failure procedure in this study, two of them with perimembranous to inlet extention. which is nearly same result of study that done by Nguyen Lan Hieu,[14] who reported that there were 2 of 133 patients underwent failure procedure due to big defects with inlet extention, this because it was impossible to obtain a stable position of the device. The accuracy rate of device size selection was (90.7%) including those with VSD ≤7 mm measured by angiography and echocardiography and those with aneurysmal tissue, such high accuracy rate was also obtained by El Said et al.,[15] (96.2%). So that both angiography and echocardiography can be used for measuring the defect size for selection of suitable device. Regarding fluoroscopy and total procedural time in this study ranged from 15–60 minutes (mean 22.94 ± 7.90 minutes) and from 30–150 minutes (mean 62.35 ± 22.29 minutes), respectively, while in study done by Yoosef M. et al.,[16] the mean fluoroscopy time was 15.4 ± 8.7 minutes (range: 9.7–38.5 minutes) and the mean procedure time was 43 ± 14.3 minutes (range: 38–80 minutes). The most common device used was 10/8 mm in 46 of 108 patients (39.7%), same result obtained by Nguyen Lan Hieu,[14] in which the most common device used was 10/8 in 52 of 128 patients (40.6%). Complete closure was found to be (85.2%) at completion of the procedure, (90.7%) next day after the procedure, (93.5%) at 1 month and rising up to (97.2%) during follow up. which is nearly same result of study that done by Yoosef M. et al.,[16] who reported that complete closure was found to be (82.5%) at completion of procedure, (87.3%)

next day at discharge rising up to (96.4%) during follow up. This finding may be related to the small micro-displacement of the occluder and the insufficiently covered irregular defect. This may suggest that more precise selection of patients who require such interventions is required and on base of fenestrated PMVSD we should close the larger defect giving chance for the adjacent smaller defect for closure spontaneously.

In this study 2 patients (both of them ≤ 9 yrs old) developed CAVB (1.9%), one of them within 24 hours and the other after 2 days of the procedure; they were admitted in hospital treated by temporary pacemaker implantation, receiving steroids and NSAIDs (high dose aspirin) with complete remission within 5 days, approximately similar to study reported by Mahimarangaiah J et al.,[17] from India who reported 2 of 126 patients (1.6%) developed CAVB (both of them < 10 yrs old), one of them developed soon after deployment, treated with temporary pacing, and one developed late onset CAVB after 15 months treated with permanent pacemaker implantation. Similar complication reported by Lee SM et al.,[11] in one of 41 patients (2.4%), who was 6 years old, treated by temporary pacing and steroid with complete remission. CAVB may be due to pressure tension on conduction system by the device. Shah SMA et al.,[18] reported that the incidence of CAVB after surgical closure of PMVSD was 10 of 103 patients (9.71%), in which the incidence was 2 of 33 patients (6.1%) and in a study of Ralf Holzer et al.,[19] who revealed 6 of 77 patients (7.7%) with complete heart block and two patients with right bundle branch block. So the incidence of CAVB after transcatheter closure of muscular VSD, after surgical closure of VSD and after transcatheter closure of PMVSD using Amplatzer Membranous VSD Occluder is higher than that in transcatheter closure of PMVSD using ADO-I. In this study 8 patients (7.4%) had new onset mild Tricuspid Valve regurgitation detected on next day, completely disappeared at one month follow up, compared to study done by Mahimarangaiah J et al.,[17] who was shown 2 of 126 patients (1.6%) were presented with new-onset tricuspid regurgitation, completely disappeared at one month follow up, while there was no TV impairment reported by Nguyen Lan Hieu.[14] The new onset tricuspid regurgitation occur more in patients with long procedure time could be due to excessive manipulation. Follow up period (mean 4.5 ± 1.13 months) showed no significant complications such as device embolization or malposition, thrombus or clot formation, hemolysis or thromboembolism, or cases of infectious endocarditis, a result agree with that reported by Merajie M. et al.,[12] and El Said et al.[15] The lack of observed hemolysis is probably related to the absence of sizeable residual shunts and the appropriate alignment of the device. Death was not observed in this study while in studies done by Bol-Raap et al.,[20] and Mavroudis C et al.,[14] reported that the mortality rate after surgical closure of PMVSD was 5%.

Conclusion

Transcatheter closure of PMVSD with ADO1 in children is a safe and effective treatment associated with excellent success and closure rates and with no significant adverse events, but long-term follow-up in a large number of patients would be warranted.

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