

INTERMEDIATE AND LONG TERM OUTCOME OF PATIENTS AFTER DEVICE CLOSURE OF ASD WITH SPECIAL REFERENCE TO COMPLICATIONS

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Background: Device closure of Secundum atrial septal defect (ASD) is an accepted mode of treatment in selected patients with a suitable defect. The major initial concern over the long term outcome has been erosions and more recently development of aortic regurgitation. Objective was to assess the intermediate and long term outcome of patients with device closure of ASD with special reference to complications. **Methods:** Two hundred and four patients with significant Secundum ASD, 16 months to 55 years (median 8 years) were considered for transcatheter closure with the Amplatzer septal occluder from October 1999 to April 2009 with follow up examinations at 1, 3, 6, and 12 months and thereafter at yearly interval. **Results:** Device closure of ASD was done successfully in 202/204 patients. The immediate (first 24-hour) major complications included device embolization (n=4), pericardial effusion (n=1) and 2:1 heart block (n=1). At a mean follow up of 4.9 years (90 days to 9.6 years, median 5.3 years) complete closure was documented in all patients. Two patients (1%) had developed mild aortic regurgitation. Atrial fibrillation occurred in 3 adult patients (1.5%) at a mean of 2 weeks post procedure with complete recovery within 6 months. There were no late embolizations, erosions or thromboembolic events on long term follow up. **Conclusions:** Device closure of Secundum ASD using Amplatzer septal occluder is safe and effective in intermediate and long term follow up with extremely low mortality rate. The risk of development of aortic regurgitation or atrial fibrillation is also very low.

Keywords: Atrial septal defect, Device closure, Cardiac catheterisation, Complications

INTRODUCTION

Device closure of Secundum atrial septal defect (ASD) is an accepted mode of treatment in selected patients with a suitable defect.¹ Immediate and intermediate follow up studies in the literature have reported upon procedural success, degree of residual interatrial shunts and recurrence rate of thromboembolic events.²⁻⁴ There is very limited data on the intermediate term and long term outcome of device closure of ASD with special reference to complications.^{2,3} The major initial concern over the long term outcome has been erosions and more recently development of aortic regurgitation.⁵ Zahid Amin *et al* reported upon the incidence of erosions in immediate and medium term.⁴ There has been a longitudinal follow-up study investigating functional and structural effects on heart valves caused by an implanted closure device. This study reported long-term echocardiographic results after transcatheter closure of interatrial defects (ASD and Patent foramen ovale) in 240 adult patients and found a very high incidence of development or increase in severity of aortic regurgitation (9%).⁵

We report our experience of device closure of Secundum ASD using an Amplatzer septal occluder in 204 consecutive patients with special reference to intermediate term and long term complications. We have already reported our initial experience of device closure of ASD.⁶

PATIENTS AND METHODS

All patients admitted to two tertiary care hospitals in Lahore, Pakistan, from October 1999 to April 2009 with

a significant Secundum ASD, evaluated by transthoracic echocardiography (TTE), were enrolled for transcatheter closure with the Amplatzer septal occluder (AGA Medical Corporation, USA). Evaluation before cardiac catheterization included a standard 12 lead ECG, chest X-ray, and TTE. A 24 hour Holter ECG was done in selected adult patients only with suspicion of arrhythmias. Routine TOE was done in all adult patients over 18 years of age and where possible in children over 10 years of age without general anaesthesia. Informed consent was taken from all the patients or patients' parents where the patient was a minor. The same team of paediatric cardiologists performed the procedures at both hospitals. The study protocol was approved by the hospital's research ethics board.

The initial TTE was done to confirm the diagnosis and then assess the suitability for device closure. Sub costal window was used in young children and thin adolescents to determine the location of the ASD, its diameter and all relevant margins. The length of the interatrial septum was measured in the four chamber view.⁷ Measurements were repeated in patients above 18 yr or where feasible over 10 years through TOE mainly in three views, i.e., four chamber view, short axis view and bicaval view. The inferior vena cava margin, superior vena cava margin, atrioventricular valve margin, superior margin, aortic margin, posterior margin and coronary sinus margin were measured. Recommended echocardiography exclusion criterion (i.e., distance of less than 5 mm from the rim of the defect to the atrioventricular valves, the coronary sinus, or the right

upper lobe pulmonary vein) was used before making a final decision about procedure suitability. All patients with deficient IVC margin were also excluded considering the high risk of embolization. Absent or very deficient aortic rim was not considered as an exclusion criterion. Patients with severe pulmonary hypertension were also excluded from the study. 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. The left ventricular ejection fraction was calculated and RV systolic dysfunction was assessed visually and graded as normal or hypokinetic. After the procedure, residual inter-atrial shunting was examined by colour Doppler. The Amplatzer septal occluder was the only device used. Vascular access was obtained from the femoral vein. After making a complete haemodynamic evaluation, a multipurpose catheter was placed in either left or right upper pulmonary vein.

For the initial series of patients until 2005, the ‘stretched’ diameter of the ASD was measured using a 24 or 34 mm sizing balloon provided by AGA. A device with a waist diameter 1–2 mm bigger than, the stretched ASD diameter was chosen. After the initial series due to over sizing concern, stop flow technique to measure the balloon diameter was used from 2005 onwards.⁷ In patients with stiff margins size, 1–2 mm larger than colour flow diameter of ASD was used instead of balloon sizing.

Right upper pulmonary vein technique was used in all except in very small central ASDs under fluoroscopic and TOE guidance. A secure and stable position of the occluder within the defect was checked by a push-pull manoeuvre (the ‘Minnesota wiggle’). The device and adjacent structures were re-examined by TOE to ensure that there was no encroachment of the device on the atrioventricular valves or the right pulmonary veins or any significant residual shunt. Post procedure, aspirin 3–5 mg/kg/d was continued for 6 months. Warfarin was added to all patients over 40 years of age or with a history of arrhythmia. Before discharge an ECG, a 24 hour Holter study (where relevant), a biplane chest X-ray, and a TTE examination were performed.

Follow up examinations including ECG and TTE were scheduled at 1, 3, 6, and 12 months and

yearly from there after. The follow up examination also included a 24 hour Holter ECG recording in adults or in patients with complaint of palpitation or possible arrhythmia. TOE was only performed where a residual shunt was suspected or there was concern about possible thrombus formation. Early follow-up [mean (SD) 2.3 Mo (1.2 Mo), range 1–6 months] was available in all patients. Late clinical follow-up data was available in 172 (86%) patients.

Demographic profile, ASD size, device size, balloon sizing and balloon assisted techniques, and complications were tabulated and analyzed using SPSS v14. Students t-test or chi squared test was implied for comparing various variables for any statistically significant difference, *p*-value taken significant at <0.05 .

RESULTS:

A total of 217 patients were enrolled for device closure, both adults and children. Thirteen patients were considered unsuitable on TOE or balloon sizing and were excluded. In these patients the defect was either too large for the age and weight of the patient⁶, more than two rims were deficient⁴, there was associated significant mitral regurgitation¹ or patient needed more than one device⁷. Transcatheter ASD occlusion was done in 204 patients.

The age ranged from 16 months to 55 years (median age 8 years). There were 131 females and 73 males (M:F=1:1.8). The body weight of the patients ranged from 10 kg to 97 kg (median 18 kg). On TOE, the maximum defect diameter varied between 10 mm to 36 mm, while the balloon stretched diameter where used varied between 14 mm to 38 mm. Devices implanted varied with waist diameter ranging between 10 mm to 40 mm (Table-1). The procedure time varied between 20–167 min (median 46 min) and the fluoroscopy time between 2.5–60 min (median 8 min). The procedure or the fluoroscopy time was not significantly different in children under 18 years of age when compared to patients 18 yrs and above (procedure time, *p*=0.552; fluoroscopy time, *p*=0.442)

Overall success rate was 98% (202/204). Devices could not be implanted despite multiple attempts and various manoeuvres in 2 patients. In 15 patients with large ASD, the balloon assisted technique was used to hold and stabilise the device across the defect.

Table-1: Comparison of the two groups of patients (n=204)

PROPERTIES	Up to 18 Years	>18 Years	Statistical difference
No of patients	115	89	
Mean age Years	10 (95% CI 6.2–13.7)	32 (95% CI 25.9–38.1)	
Male	43	30	
Female	72	59	
Male to female ratio	1:1.7	1:2	<i>p</i> =0.65
Mean ASD size on TOE	18.7 mm (95% CI 16.4–21.0 mm)	25.5 mm (95% CI 22.6–28.5 mm)	<i>p</i> =0.10
Mean ASD size on balloon sizing	22.5 mm (95% CI 21.3–23.6)	28.3 mm (95% CI 25–31.6)	<i>p</i> =0.142
Mean Device size used	22 mm (95% CI 21–23)	28 mm (95% CI 26–30)	<i>p</i> =0.028
Balloon Assisted technique used in	7	8	<i>p</i> =0.59

Table-2: Complications of device closure of ASD (n=200)

Complications	No (%)
Major Complications	
Death	1 (0.5%)
Embolization required surgical retrieval	2 (1.0%)
2:1 heart block	1 (0.5%)
AF	3 (1.5%)
Minor Complications	
Mild Aortic regurgitation	2 (1.0%)
Pericardial effusion	1 (0.5%)
SVT	1 (0.5%)
Residual Shunt	3 (1.5%)
Bleeding required transfusion	1 (0.5%)

Malformation of the Amplatzer occluder during deployment occurred in seven cases ('cobra head' configuration) and led to a prolonged procedure and prolonged fluoroscopy time. The device could be retrieved into the long sheath and redeployed and defect was closed successfully.

Malposition or embolization of the device occurred in four patients. In two patients device embolized immediately after deployment. Atrial septal defects were of large size in both patients relative to the size of device used. In both patients devices were successfully retrieved by transcatheter technique and ASDs were closed with the larger device in these patients. In rest of the two patients, device embolized after procedure in next 24 hours and both patients underwent surgical removal of the device and ASD closure (Figure-1).

All patients were assessed for a residual defect at the time of discharge. By the time of discharge, 24 hours after ASD closure, the rate of residual leakage had decreased to less than 4% (n=8). During further follow up examinations the complete closure rate was achieved in 98% (n=200/202).

ECG abnormalities associated with transcatheter closure i.e. supraventricular tachycardia (SVT) occurred in 6 cases (2.9%) during procedure which settled with adenosine or verapamil in all. Atrial fibrillation occurred in three cases (1.5%) during procedure, all were adult patients. Two patients recovered immediately and in one patient treatment

could be discontinued after 6 months. One patient developed 2:1 heart block during procedure (0.5%) in our early experience. He is in follow up for last nine years but never had been symptomatic and can increase heart rate on exercise during Holter monitoring.

One patient (0.5%) complained chest pain after the procedure and on echocardiography there was small pericardial effusion. Patient was managed conservatively and effusion improved in next 72 hours. TOE confirmed no evidence of perforation or erosion. One patient with inherited cardiomyopathy died after 15 days of device closure in low cardiac output and multi organ failure. No patient without any associated lesion died on follow up.

In young children undergoing device closure of ASD, despite of the concerns regarding large profile of the device, it flattened nicely and assumed a fairly slim configuration at serial follow up in all cases (Figure-2). Two patients (1%) developed aortic regurgitation on long term follow up (9-12 Mo). The regurgitation jet emerged in the centre of the aortic valve and was mild in both patients. 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.

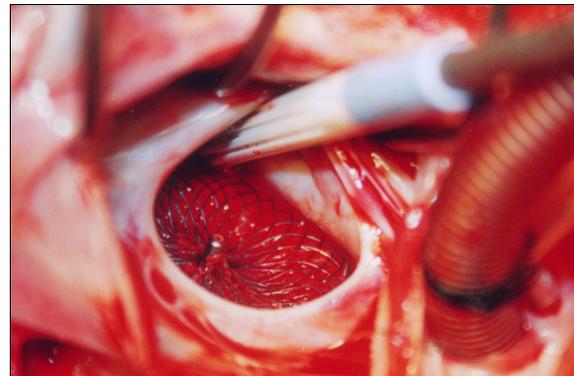


Figure-1: Per-operative view of the device being seen through the Secundum ASD lying entirely in LA

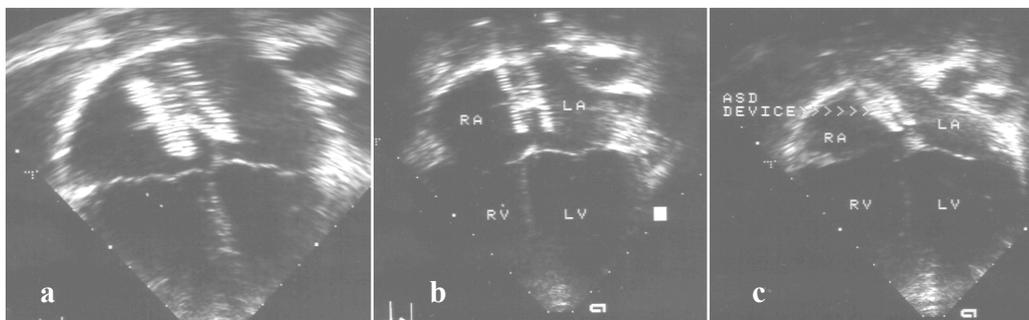


Figure-2: Shape of the device: a) immediately after the device closure, b) at 6 months, and c) at 3 years follow up

DISCUSSION

Interventional ASD closure is now widely practiced and has replaced surgical ASD closure in majority of patients with Secundum ASD.^{1,2} It has certain advantages as short procedure time, cosmetic benefits, reduced pain and reduced hospital stay. However, technical complications with occasional deaths have been reported. Improvements in design have made the devices retrievable, and reduction in the size of the introduction systems allows interventional treatment even in young patients. This study was a single team experience from two tertiary referral cardiac and paediatric centres from a developing country with limited resources.

The reported significant complications of device closure include cardiac perforations, device malposition or embolization, residual shunts, vascular trauma, thrombus formation, atrioventricular valve regurgitation, aortic regurgitation, atrial arrhythmias, infective endocarditis and sudden death.^{4,5} Cheesa M reported upon 417 patients undergoing device closure of ASD.³ Two different devices were used: the CardioSEAL/STARFlex in 159 patients and Amplatzer device in 258. They reported 36 complications in thirty four patients (8.6%). Ten patients underwent surgical closure as device malposition occurred in three and device embolization in seven (1.7%). Two patients in this group were reported having late complications: embolization to left leg one year after implantation of an Amplatzer device and a sudden death 1.5 year later. The reported sites of embolization include right ventricle, pulmonary artery, left ventricle, arch of aorta and peripheral vessels. In our series, embolization rate was 2%, similar to previously reported series. In 2 patients, the early embolization occurred to RV where both were removed and repositioned. Surgical intervention was required in 2 patients where embolization had occurred 12–24 later, one each to LA (Figure-2) and RV. There were no late device embolizations or malposition.

Perforation is the most feared complication described in literature.^{7,8} Cardiac perforations related to technique 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.^{8–11} The anterosuperior atrial wall and adjacent aorta are uniquely vulnerable sites. Perforations have occurred even after six months of implantation. Divekar *et al* in a retrospective review found 24 events with Amplatzer device.⁸ Ten patients were under 18 years of age. Late cardiac events occurred in 66%, 25% presented weeks later (longest three years). Amin^{4,7} reviewed the risk factors that may lead to erosion of Amplatzer septal occluder and recommended ways to minimize the risk of perforation. Patients with deficient

aortic rim and/or superior rim may be at a higher risk for device erosion. Oversized Amplatzer septal occluder can also increase the risk of erosion. A total of 28 cases (14 in United States) of adverse events were reported to AGA Medical Corporation. Deficient aortic rim was seen in 89% patients. The incidence of device erosion in the United States reported in this study was 0.1%.^{4,7} They have suggested that defect should not be overstretched during balloon sizing and a small pericardial effusion at 24 hours should be followed closely. Majority of our patients for some unknown reason have a deficient aortic margin. Another important observation in our study was small left atrial size. Both these factors had no effect in long term. Balloon sizing was a routine in our initial patients but later on, stop flow technique was used to avoid over sizing. Only one of our patients (0.5%) developed pericardial effusion at 24 hours. This was observed closely and resolved spontaneously. There was no perforation in our long term follow up.

Residual shunts are more frequent with percutaneous closures than with surgical closures. Various devices have variable incidence of residual shunts mainly related to their design. Rao *et al* reported residual shunts in 45% of patients on colour Doppler with buttoned device¹² while Worms *et al* found residual shunt in 37% patients with Sideris device¹³. The incidence is very low with Amplatzer septal occluder^{1,2,5,9} and this was the case in our series too where only three of our patients had a small leak immediately post procedure which resolved on long term follow up.

Thrombus formation is another important concern and the incidence of thrombus formation was 1.2% in ASD patients and 2.5% in patent foramen ovale patients in a study of 1000 patients who underwent percutaneous device closure.¹⁴ Post-procedure atrial fibrillation and persistent atrial septal aneurysm were significant predictors of thrombus formation. The Amplatzer device with Nitinol wire covered with expanded poly tetrafluoroethylene fabric is less thrombogenic than Cardio SEAL and Star FLEX devices, which have a metallic framework with Dacron fabric.¹⁴ All patients in our study group were started on Aspirin in antiplatelet dose immediately after the procedure while all adults above 40 years or those with a history of an arrhythmia were also anticoagulated with Warfarin for 6–12 months. Three patients (1.5%) had post procedure atrial fibrillation, one requiring long term medication. However, none of our patients developed evidence of thrombus formation in immediately or late follow up.

Despite low peri- and post-procedural complication rates, there are a few reports of sudden deaths in patients after device closure of ASDs. Cheesa M described deaths in two out of thirty four patients.³ In

most cases, erosion with a consecutive cardiac tamponade was proven or suspected.⁴ Anatomic variant coronaries may also be a reason for post interventional fatalities, as ASD patients usually have no coronary angiography on a routine basis. Scholtz *et al* has reported an unusual complication of systolic compression of left coronary artery by left atrial disc on angiogram in a patient with single coronary artery originating from right aortic sinus. This case emphasizes the importance of adequate peri-interventional cardiac imaging to prevent procedure-related complications.¹⁵ There was one death in our series in a child with inherited cardiomyopathy which may have been deteriorated by device closure of ASD but we did not have any deaths in intermediate and long term otherwise. Our inclusion criteria was rather stringent as the family bore the cost of the device in majority of cases and losing a device or needing a second one was a major financial challenge. These strict inclusion criteria could partly explain such low incidence of complications in our series.

CONCLUSION

Device closure of Secundum ASD using Amplatzer septal occluder is safe and effective in intermediate and long term follow up with extremely low mortality rate. The risk of development of aortic regurgitation or atrial fibrillation is also very low.

LIMITATIONS

Our centres are tertiary referral centres with patients being referred from all over Pakistan and Afghanistan. Therefore, not all patients are followed up in our hospital. As a consequence late follow-up data were available in 178/204 (86%) patients. However, baseline characteristic of patients lost to follow-up were similar to those of the group of patients with late follow-up data.

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