Percutaneous Transcatheter Closure of Atrial Septal Defect in Children younger than 5 years: Initial experience of Sohag University

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Abstract. Objectives: This study was aimed to determine institutional efficacy and safety of percutaneous closure of secundum ASDs in symptomatic children younger than 5 years of age and discuss referral indications. **Methods:** The retrospective study between March 2011 and April 2013, included 24 patients (12 girls, 12 boys) with secundum ASDs measuring more than 8 mm with a hemodynamically significant shunt, resulting in failure to thrive, right ventricular dilatation, or repeated chest infections. Four patients had multiple or fenestrated ASD secundum. Defect size and total interatrial septal length were estimated by transthoracic (TTE) and transesophageal (TEE) echocardiography in 3 views. Procedures were performed under fluoroscopic and TEE guidance without balloon sizing. Patients were followed-up at 1, 3, 6, and 12 months with TTE. Major and minor complications were predefined and indications for referral were evaluated. **Results:** We identified 24 patients meeting criteria with a mean procedural age of (3.6±1.8 years), and mean weight of (13.9±3.1Kg). The mean defect size was 13.6 ± 2.9 mm and mean IAS length was 26.9 ± 6.4mm on TTE and defect size was 14.3 ± 3.5 mm on TEE. The mean device size was 15.7 ± 4.5 mm (range, 9 to 28 mm). The device was placed successfully in all patients including fenestrated ASDs that were closed with a single device placement. No residual flow was seen after device placement in patients. There were one major (4.1%) in form haemopericardium and cardiac tamponade and three minor (12.5%) complications including: transient arrhythmia resolving spontaneously or with only catheter manipulation (2 cases); rebleeding from access site (1 case). Nearly two-thirds of referrals were for right heart enlargement or poor growth. There was significant in the rate of resolution of right heart enlargement after transcatheter closure of ASD II**.** At 6 and 12 months, all the patients were asymptomatic. No cardiac perforation, device erosion, embolization, thrombus formation, or malposition of the device was observed. **Conclusions** Transcatheter ASD closure in small symptomatic children is highly successful and safe. In small, asymptomatic patients, deferral of closure until the 4 to 5 years of age should be strongly considered.
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1. Introduction

An atrial septal defect (ASD) is, due to its frequency, the fourth most common congenital heart disease, appearing in 3.78 of every 10,000 live newborns.[1] The diagnosis of an ASD, with signs of right ventricular volume overload, is an indication for its closure. Although surgical repair of atrial septal defects is a safe and widely accepted procedure with negligible mortality, it is associated with morbidity, discomfort, and a thoracotomy scar as well as the possibility of bleeding, arrhythmia, postpericardiotomy syndrome, and residual left to right shunts across the surgical patch.[2,3]

Successful nonsurgical closure of atrial septal defects (ASD) was first described in 1974 by King and Mills [4]. As the percutaneous approach has evolved over the years, along with the advent of newer devices, a gradual tendency has developed in performing it electively on smaller patients especially when the disease leads to progressive right ventricle enlargement, failure to thrive or repeated chest infections.[5] Indeed, in a study on the change in size of ASD, a significant enlargement of the defect, more than 50% of the initial size, has been detected in 30% of the studied population, which suggests that there is a potential for some of the defects to outgrow a possible transcatheter closure.[6]There are many studies described the safety of surgical and percutaneous ASD closure, were based on older and larger patients than are often referred today. There is very little published data on whether this complication rate holds true for the much younger and smaller patient; what is available is inconsistent in definition of major complications [7-10].

2. Methods:

Patient populations. The present work was designed as a retrospective cohort study that included 27 children less than 5 years of age presenting to our center with ASD secundum between March 2011 to April 2013,. All children completed one year follow up. An informed written consent has been obtained from parents of children.

The occlude. The Amplatzer septal occluder, cribriform ASD occlude and delivery system (AGA Medical, Golden Valley, Minnesota) have been used in our study.

Preimplantation protocol.

All patients were evaluated with transthoracic two-dimensional and color Doppler echocardiography with multiple subxyphoid and precordial windows. Each of the following criteria had to be fulfilled prior to inclusion: (1) the presence of an ostium secundum ASD with left to right shunt; (2) a distance of >5 mm from margins of the defect to the mitral and tricuspid valves, superior vena cava, right upper pulmonary vein, and coronary sinus; (3) dilation of right atrium and right ventricle indicating right ventricular overload; (4) ASD size >8 mm; and (5) adequate interatrial septal length, measured mainly by multiplane transthoracic echocardiography (TTE).

Routine examination before catheterization included a standard 12-lead electrocardiography (ECG), a chest x-ray, and a transthoracic echocardiography (TTE). Complete blood counts, prothrombin time (PT), prothrombin concentration (PC), partial thromboplastin time (PTT), and international normalized ratio (INR) were performed to exclude bleeding disorders.

Technique

After obtaining a written informed consent, trans-catheter closure of ASD was planned using are Amplatzer septal occluder devices (St. Jude Medical, Plymouth, Minnesota).

All patients received intravenous claforan injection (50 mg/kg) and Unysun (100mg/Kg) 30 min before the procedure. Intravenous heparin was injected (100mg/Kg) to achieve therapeutic level of anticoagulation (activated clotting time ACT>250 s).

Multiplane TEE using Vivid S5 ultrasound systems (GE Medical systems, Horton, Norway) was performed in each patient after endotracheal intubation and assisted ventilation under general anesthesia. Dimensions of the defect were measured in various imaging planes. The maximal diameter of the defect was measured using atrial end-diastolic frames in 0°, 45, 90°, and 135°. A minimum diameter was also obtained from other imaging planes. In the presence of a very floppy and mobile rim, measurement of defect diameter was made between steadier and firm rims and the color flow jet width across the defect was also measured to provide supplementary information. The largest dimension was used to select device size.

Depolyment of device occurred under fluoroscopic view LAO cranial (35°, 30°) (Fig.1) and TEE guidance.

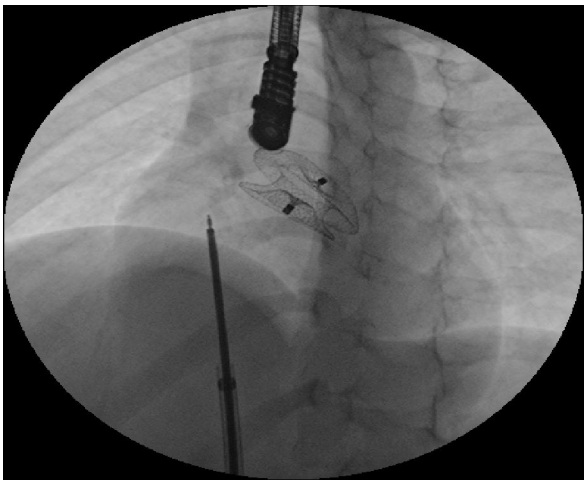

Fig.1.LAO cranial view shows good position of device after deployment.

In several patients with a large defect and/or deficient rims, deployment of the device from the upper pulmonary vein (left or right) was generally performed. When the position of the device was not well visualized on TEE images, particularly the posterior inferior rim, transthoracic subcostal echocardiography was used as adjunct to TEE to monitor device position especially during deployment.

Following the procedure, patients were monitored for 24 h and echocardiographic evaluation was done after 24 h. Patients were discharged 48 h after the procedure. Low dose of aspirin (3–5 mg/kg/day) was given for 6 months and clopidogrel (2 mg/kg) was given for 2 months. Infective endocarditis prophylaxis was advised for 6 months after the device implantation.

Follow-up transthoracic echocardiography obtained on postcatheterization day 1, 1 month, 3months, 6 months, and on long-term.

Device size selection. The device size 1-2 mm larger than the ASD diameter was selected with particular emphasis on the size of the left atrial disc and the IAS length, especially in those small children. The device size more than 3-4mm than the ASD diameter was selected in presence of floppy septum. Two cribriform devices 25mm and 30mm were chosen in two patients with fenestrated interatrial septum.

Statistical analysis.

Data were analyzed using the statistical package for social sciences version 15 (SPSS Inc).For all patient and procedural data, mean and standard deviation were calculated for continuous variables and frequencies with percentages for categorical variables.

3. Results

Demographic data and preprocedure transthoracic echocardiography

During the study period, 27 patients had attempted ASD device closure (Table 2). The patients included 13girls and 14 boys. We excluded 3 patients, two of them that had severe floppy septum and multiple fenestrations and the third female child (1.5 years, 9KG) had relatively large defect needed large device(18mm) more one and half of her weight so the procedure was postponed. Of these, 9 patients of 24(37.5%) had other comorbidities (Table 3).

Four patients had pulmonary valve stenosis, two patients needed pulmonary valvuloplasty during procedure. One had restrictive VSD. Four patients had non cardiac disease; two had Down syndrome, one had noonan syndrome and the last one had kyphioscoliosis. Four patients (12.5%) had audible systolic murmurs of pulmonary valve stenosis. and one patient (4.2%) had harsh holosystolic of VSD. Plain chest x-ray revealed cardiomegaly in 22/24 patients (91.7%), mainly right atrial (RA) and right ventricular (RV) dilatation.

The mean procedural age was 3.2±1.3 and the mean weight was 13.9±3.1 Kg. The mean ASD diameter measured 13.6±2.9mm by TTE and RV measurements were taken by 2-dimensional examination using parasternal long-axis view. Right ventricular end diastolic diameter (RVEDD) was 1.8±1.4cm. Mean IAS length was 26.9 ± 6.4mm.All patients had sufficient rims (>5 mm) except deficient aortic rim in 15/24(62.5%).

Transoesophageal echocardiography and procedure

TEE confirmed the diagnosis of isolated ASD and revealed a mean ASD size of 14.3±3.5mm on TEE.. Sufficient ASD rims were observed in all cases except deficient aortic rim.

Four cases out of 24 (16.6%) had a fenestrated ASD (two separate ASDs with interatrial septal [IAS] tissue in between); the first case had 11 mm and 5 mm ASDs with 4.5 mm of IAS tissue, while the second had 18 mm and 7 mm ASDs separated by 6 mm of IAS tissue. IAS aneurysm was detected in 3case (12.5 %).

Mean device size used was 15.7 ±4.6 mm (range, 9 to 28 mm). Device placement was successful in all patients including the 4patients(2 girls and 2 boys) with fenestrated ASDs, which were closed with a single device (16 mm and 28 mm)in two cases and two cases were closed by Cribriform ASD occluder (25,30mm). The mean procedure time was 54.7 ± 16.3 minutes. No case of embolization was recorded.

Three patients having their procedure abandoned after TEE examination without a device being placed in early experience of transcatheter closure of ASD. The median pulmonary/systemic flow ratio was 2.2±0.6. The mean fluoroscopy time was 22.6±14.3min and the procedure time was 37.4±16.8min.

All devices used are Amplatzer septal occluder devices (St.Jude Medical, Plymouth, Minnesota). Four patients had multiple defects and/or fenestrated (16.6%) ASD, two of them had floppy septum with multiple fenestrations and closed by cribriform types of device 25mm and 30mm and two of them had two adjacent defects with distance less than 7mm which closed by one device. fifteen of these patients (62.5%) had deficient aortic rim, and one patient required change device by larger device due to prolapse of device through defect. Four patients required right pulmonary vein technique.

No residual flow was detected by intra-operative TEE and color flow Doppler after device deployment (Figure 1).

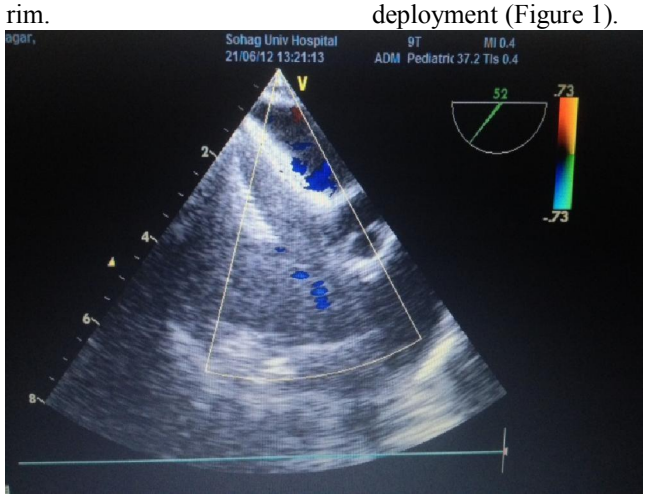

Fig1.TEE after device deployment no residual shunt

In our study, the rate of resolution of RHE by the following morning was 58% (n =14); at 1-month follow-up, it was 83% (n =20); and it improved to 96% (n =23) by long-term follow-up at 12 months.

There was one major complication based on classification of complication in tab.1, in form of haemopericardium and caediac tamponade which detected in 24 hours after device deployment in male child (4.5 years, ASD size 9 mm and closed by device 10mm). The cause of haemopericardium was not detected as no perforation seen by transthoracic echocardiography. The haemopericardium required pericardiocentesis once and close observation. No accumulation occurred and no device removal.

There were 3 short-term minor complications (12.5%), including: transient arrhythmia resolving spontaneously or with only catheter manipulation (2 cases); rebleeding from access site (1 case). There have been no minor complications reported to date beyond day 7 following the procedure. No medium- or long-term major complications have been reported to date.

Table 1. Predetermined Major and Minor Complications	
Predetermined Major Complications	**Predetermined Minor Complications**
Death Cardiac or respiratory arrest Stroke Device erosion Device embolization Need for emergent surgical procedure Need for recatheterization for device removal Significant pericardial/pleural effusion requiring intervention Persistent dysrhythmia or potential lethal intraprocedural arrhythmia requiring cardioversion/resuscitation Any new valvular insufficiency or pulmonary vein obstruction Need for transfusion due to significant bleeding Permanent limb injury	Transient arrhythmia resolving with only catheter manipulation Rebleeding from access site (not necessitating transfusion) Significant access site hematoma Prolonged, transient limb paresthesia Transient hypoxemia during procedure Trivial pericardial/pleural effusions Deployment malfunctions Development of post-procedural lower respiratory tract infection

Table 2. General Characteristics	
Number	24
Gender(F/M)	12/12
Age(years)	3.6±1.7
Weight(Kg)	13.9±3.1
ASD diameter by TTE, mm	12.6±2.9
ASD diameter by TEE, mm	14.3±3.5
IAS lenght	29.4±3.7
Device size	15.7 ±4.6 mm (range, 9 to 28 mm)
Qp:Qs	2.2±0.6
Fluoroscopy time, min	6±2.5min

ASD_atrial septal defect; Qp_pulmonary flow; Qs_systemic flow;IAS interatrial septal
TEE _ transesophageal echocardiogram; TTE _ transthoracic echocardiogram.

Table 3. Cardiac and Noncardiac Comorbidities	
Cardiac	**Non cardiac**
Pulmonary valvuloplasty in severe pulmonary valve tenosis:2 **Mild pulmonary valve stenosis: 2** **Restrictive ventricular septal defect: 1**	Down syndrome:2 Noonan syndrome:1 Kyphoscoliosis:1

Table 4. Primary Indications for Referrals and Frequencies of Referrals	
Primary Indication for Referral	Number and Frequency, %
Right heart enlargement	(17)70,8%
Poor growth	(13)54,1%
Frequent respiratory tract infection	(10)41,7%

Among the various indications (Table 4), nearly 17 patients (70.8%) of the referrals were for RHE, 13 patients (54.1%) for poor growth and 10 patients (41%) for frequent respiratory tract infections.

At 6-month follow-up, patients were asymptomatic. No cardiac perforation, pericardial effusion, infective endocarditis, device erosion, embolization, thrombus formation, or malposition of the device was observed. Three out of 24 patients (12.5%) developed mild insignificant mitral regurgitation, detected by TTE 1day after closure that resolved spontaneously at 6-month follow-up.

4. Discussion

Historically, the recommendation for elective ASD closure from surgical literature was to wait until around 4 years of age [(11)]. Numerous previous studies have shown a fairly high rate of spontaneous closure of ASD <8 mm in the first few years of life [(12–14)], and rarely as late as adolescence [(15)].

As the technology and experience surrounding percutaneous device closure of ASD has progressed especially in reduction in the size of the delivery systems, along with numerous studies concluding it to be safe and the preferred method over surgery, referrals for younger patients have become more frequent. There is strong evidence to suggest percutaneous closure is preferred with respect to decreased morbidity and length of hospital stay [(16)]. Our aim was to assess if closing these defects earlier has a greater risk for the smaller patients. Our results indicate a major complication rate was high(4.1%) as previously reported by large study of transcatheter closure of ASD in 128 small patients by Btakian, *et al.,* which major complication was 5.5% [(17)].

In one study of 52 patients, the investigators reported no major complications, yet discussed two device embolizations that were classified as minor complications [(8)]. Alone, these 2 would account for a nearly 4% major complication rate, which is more similar to our results. Another study of 48 patients <5 years old and median weight of 15 kg also reported no major complications, but did not specifically stratify adverse events [(7)]. Finally, another study suggested an absence of increased complication risk in children <20 kg, but 1 patient out of their sample of 31 required surgical retrieval of the device; a major complication rate of 3.2% [(10)].

In the present series, transcatheter closure was performed in 24 patients with mean age 3.6 ±1.7 years and the mean weight was 13.9±3.1 Kg. The size of ASD in TTE was 13.6±2.9mm and in TEE was 14.3±3.5mm. The Mean device size used was 15.7 ±4.6 mm (range, 9 to 28 mm). Successful closure was achieved in all. Residual shunt was absent. Our results are in accordance with the results reported in many other interventional pediatric cardiac centers around the world[(7,8,17)]

All devices used are Amplatzer septal occluder devices (St.Jude Medical, Plymouth, Minnesota) Four patients had multiple defects and/or fenestrated (16.6%) ASD, closed by cribriform types of device 25mm and 30mm another two patients were closed by single device.This was similar to study by Btakian, *et al.,* [(17)] in which fourteen patients had multiple defects and/or fenestrated ASD and were closed by single device but two types of devices used; eleven of these were closed with an Amplatzer septal occluder device 3 with a Gore HELEX septal occluder device.

In Butera, *et al.,* [(7)] study five patients with multiple ASDs had successful transcatheter closure; a single device was used in three patients, and simultaneous placement of two devices was needed in two subjects.

Balloon sizing was considered as the gold standard for measuring ASD size, but in our study ASD were closed successfully by trans-catheter closure techniques without balloon sizing depending on good imaging of TEE and a device 2-4mm larger than the biggest diameter was chosen.

Non balloon sizing technique of transcatheter closure ASD in our study was in accordance with the study by Rasha, *et al.,* [(16)] in which Percutaneous transcatheter closure of children younger than two years was performed under TEE guidance. Also Amin and Daufors, closed ASD by a device that was 2–4 mm larger than intracardiac echocardiographic (ICE) diameter was chosen[(18)]. Recently, 3D TEE has been used to aid selection of device size[(19)].

This was in contrast to large study by Btakian, *et al.,* [(17)] of ASD closure in small children in which balloon-inflated, stop-flow technique was used.

One indication for closure of ASD has always been clinical evidence of right ventricular volume overload and worsening RHE. 70% of the patients in our study were referred due to echocardiographic evidence of progression of RHE from mild to moderate. There have been numerous studies that have shown nearly complete resolution of right ventricular enlargement following secundum ASD closure [(20,21)]. In fact, in our study, just over more than half of all patients (58%) experienced improvement of RHE as early as by the following morning. This was similarly shown in a large study of transcatheter closure of small children [(17)] and in a study of adult ASD closure using volumetric analysis of atrial size before and after ASD closure [(21)].

Study limitations:

Some limitations exist in the present study. These include the relatively small number of patients and the relatively short period of follow up. More

studies with large number of patients are needed to analyze the incidence of complication of transcatheter closure of ASD in this age group. Finally, our assignment of complications to either major or minor categories is subjective, however it follows closely the recent literature for future recommendations regarding classification of complications [(9)].

Conclusions

Percutaneous ASD closure in symptomatic children younger than 5 years is safe and effective with a 100% procedural success rate under only TEE evaluation without balloon sizing. Although it was safe to close ASD younger than 5 years, there was a greater risk of complications than previously perceived, which is largely due to variations in prior classification so closure of ASD should be delayed to age of 4 to 5 years in asymptomatic patients.

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