Device Closure of Secundum Atrial Septal Defects in Children <15 kg

Complication Rates and Indications for Referral

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Objectives This study sought to determine institutional complication rates in a previously underreported patient population and discuss referral indications.

Background There has been a trend over the years for referral of younger and smaller patients for "elective" closure of atrial septal defects (ASD). In general, the risks associated with ASD device closure are believed and reported to be relatively low. Complication rates in this group of smaller patients are not well described in the literature for either percutaneous or surgical approaches.

Methods Retrospective review of all patients who underwent elective transcatheter closure of secundum ASD between March 2000 and April 2010. We excluded all children >15 kg, as well as those with complex congenital heart defects. Major and minor complications were predefined and indications for referral were evaluated.

Results We identified 128 patients meeting criteria with a median procedural age of 1.92 years (3 months to 4.92 years), and median weight of 10.8 kg (4.3 to 14.9 kb). There were 7 major (5.5%) and 12 minor (9.4%) complications. Nearly two-thirds of referrals were for right heart enlargement or poor growth. Rate of resolution of residual shunt was 99%. When compared with age, there was no difference in the rate of resolution of right heart enlargement. No clinically significant improvement in growth was observed.

Conclusions Transcatheter ASD closure in small children is highly successful, but with an increase in previously perceived complication rates. In small, asymptomatic patients, deferral of closure until the historically established timeline of around 4 to 5 years of age should be strongly considered.   (J Am Coll Cardiol Intv 2012;5:1178–84) © 2012 by the American College of Cardiology Foundation

Successful nonsurgical closure of atrial septal defects (ASD) was first described in 1974 by King and Mills (1). Numerous studies have since described the safety and efficacy of the percutaneous approach and suggested it to be the preferred method of closure over surgery in certain patients (2–4). 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. It is not uncommon for surgeons and interventionalists to quote a very low major complication rate. This tendency is based on large studies that have evaluated the safety of surgical and percutaneous ASD closure and have returned similar results for major complications. These studies, however, 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 (5–8). The most comprehensive data describing adverse event rates in congenital cardiac catheterization did not stratify results according to patient size (7). Our goal was to determine our institutional complication rates for elective, percutaneous, ASD closure in patients <15 kg, as well as to evaluate the various indications for early referral.

Methods

Study design. Our electronic catheterization database was searched for all patients having undergone a percutaneous secundum ASD closure during a 10-year period (March 2000 to April 2010). The surgical database was also reviewed to identify any patients who may have had an aborted percutaneous closure. We excluded all patients >15 kg as well as those with coexisting complex congenital cardiac defects. Patients with other medical conditions unrelated to the cardiovascular system, genetic abnormalities, and history of prematurity were also included. In all cases, the procedure was carried out under general anesthesia and assisted by fluoroscopy and transesophageal echocardiogram (TEE). Standard catheterization of the right heart was performed as well as calculations of cardiac output, intracardiac shunt, and vascular resistances.

All records were reviewed, including pre-procedure and all follow-up clinic notes, admission and discharge documentation, catheterization reports, electrocardiograms, and Holter/event monitor reports. Echocardiogram reports were reviewed from the time of referral, post-catheterization day 1, follow-up at 1 and 6 months, and if available, a long-term follow-up echocardiogram around 2 years. Additional echocardiogram reports were reviewed as needed if complications occurred. Emergency department documentation was reviewed for a 30-day period following the date of procedure. All complications identified by this process were

cross-referenced with an existing complications database maintained independently of the catheterization lab records. **Study outcomes and definitions.** The primary outcome was rate of complications. Before data collection, complications were predetermined and stratified into major and minor categories (Table 1). If during the data collection process an adverse event was identified that had not previously been considered it was added to the list. Short-term complications were predefined to include anything discovered during the procedure as well as the first 30 days following. Secondary outcomes included procedural success rates, identification of the indications for referral, residual shunt rate, rate of resolution of right heart enlargement (RHE), and patient growth.

Improvement of RHE was based on comparison of the official echocardiogram reports only. The degrees of RHE were originally determined by various, experienced cardiologists' interpretations and reported as mild, moderate, or severe. These were based on M-mode measurements from the parasternal short axis, when available. When not available, a subjective assessment of RHE had been made. We did not attempt to reclassify these original reports with respect to the degree of enlargement.

Data collection. Demographic information was collected to include age and weight at the time of the procedure and follow-up. Referral letters/clinic notes were used to identify indications for referral as well as other coexisting medical conditions. Preprocedural transthoracic echo-cardiogram and intraprocedural TEE reports were used to collect data pertaining to the extent of RHE, size of ASD, size of ASD rims (if documented), total septal length, and other coexisting cardiac lesions. Catheterization reports were used to collect all available pressure, saturation, and cardiac output/resistance data, as well as information regarding device type and size. Follow-up information of residual shunting and changes to the extent of RHE were collected from echocardiograms obtained on post-catheterization day 1, 1 month, 6 months, and long-term follow-up.

Statistical analysis. For all patient and procedural data, medians with ranges were calculated for continuous variables and frequencies with percentages for categorical variables. Where there was missing data, the number of nonmissing values was reported for that variable. Growth was compared with respect to weight percentiles before and after device closure (up to a maximum of 14 months follow-up). A mean improvement of >5th percentile in weight was considered clinically significant. The 14-month

Abbreviations and Acronyms

ASD = atrial septal defect(s)

IQR = interquartile range

PH = pulmonary hypertension

RHE = right heart enlargement

TEE = transesophageal echocardiogram

Table 1. Predetermined Major and Minor Complications

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

time frame was chosen to include several patients who were late for their 1-year follow-up.

Results

During the study period, 347 patients had attempted ASD device closure (Table 2). Of these, 139 (40%) met inclusion criteria. We excluded 11 patients that had complex congenital heart defects leaving a final study group of 128 patients. Of these, 77 patients had 135 other comorbidities (Table 3). The median procedural age was 1.92 years (3 months to 4.92 years) and the median weight was 10.8 kg (4.3 to 14.9 kg). The median ASD diameter measured 9 mm (4 to 20 mm) by transthoracic echocardiograms performed in the cardiology clinic and 10 mm (5 to 20.5 mm) by TEE using balloon-inflated, stop-flow technique. The procedural success rate was 98% (125 of 128) with only 1 device removal and 2 patients having their procedure abandoned without a device being placed. The median pulmonary/systemic flow ratio was 1.46 (interquartile range [IQR]: 0.76 to 4.75). The median fluoroscopy time was 17.6 min (IQR: 5 to 68 min). Follow-up ranged from 8 months to 10 years, 9 months, with a mean follow-up time of 5 years, 9 months.

Table 2. General Characteristics

Age	1.92 yrs (3 months−4.92 yrs)
Weight, kg	10.8 (4.3–14.9)
ASD diameter by TTE, mm	9 (4–20)
ASD diameter by TEE, mm	10 (5–20.5)
Qp:Qs	1.46 (0.76–4.75)
Fluoroscopy time, min	17.6 (5–68)
Proportion of patients with comorbidities	60% (77/128)

Values are median (IQR) or % (n/N).

ASD = atrial septal defect; IQR = interquartile range; Qp = pulmonary flow; Qs = systemic flow; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram.

Table 3. Cardiac and Noncardiac Comorbidities

Cardiac	Noncardiac
PDA coiled in same procedure: 14	Prematurity: 31 (range 24–36)
Mild pulmonary valve stenosis: 7	Down syndrome: 19
Restrictive ventricular septal defect: 2	Mild pulmonary hypertension: 14
Right upper pulmonary vein to superior vena cava: 2	Developmental delay: 10
Congenital complete heart block: 2	Other*: 45
Bicuspid aortic valve: 1	
Prior coarctation of the aorta repaired in infancy: 1	

*Other includes: chronic lung disease (8); twin gestation (7); other genetic mutations (5); seizure disorder (5); tracheostomy-dependent (3); cerebral palsy (2); reactive airway disease (2); and 1 each of: obstructive sleep apnea, beta thalassemia trait, autism, congenital hypothyroidism, history of NEC, Necrotizing enterocolitis, Seckel syndrome, VACTERL association, Ehlers-Danlos syndrome, lupus, fetal alcohol syndrome, scoliosis, prior malrotation, club foot.

PDA = patent ductus arteriosus.

Devices used are listed in Table 4. Fourteen patients had multiple defects and/or fenestrated ASD. Eleven of these were closed with an Amplatzer septal occluder device (St. Jude Medical, Plymouth, Minnesota) and 3 with a Gore HELEX septal occluder device (W. L. Gore and Associates, Flagstaff, Arizona), and no patient required multiple devices.

There were 12 short-term minor complications (9.4%), including: transient arrhythmia resolving spontaneously or with only catheter manipulation (2 cases); rebleeding from access site (1 case); transient hypoxemia (2 cases); trivial/small pericardial effusions that resolved spontaneously (4 cases); deployment malfunctions (2 cases); and development of post-procedural lower respiratory tract infection (1 case). There have been no minor complications reported to date beyond day 7 following the procedure.

There were 7 short-term major complications (5.5%) in 5 patients (Table 5). No medium- or long-term major complications have been reported to date.

1. Patient #1 was a former 32-week gestation girl with no active medical problems. She developed complete heart block upon device deployment, which resolved to 2nd-degree block during the procedure. The decision was made to leave the device in place with in-patient observation for 48 h.

Table 4. Devices Used

Devices	n	Median (Range)
Amplatzer septal occluder (St. Jude Medical, Plymouth, Minnesota)	109	12 (6–25 mm)
Gore HELEX septal occluder (W. L. Gore and Associates, Flagstaff, Arizona)	15	25 (20–30mm)
CardioSeal septal occluder (NMT Medical Inc., Boston, Massachusetts)	3	28 (23–28mm)
Amplatzer multifenestrated "cribriform" septal occluder	1	25 mm

Table 5. Patient Characteristics for Major Complications

Patient#	Age	Weight, kg—Percentile	ASD Size, mm (TEE)	Device Used, n	Qp:Qs	Reason for Referral
1	3 yrs 5 m	11.5—2nd	10	25 HELEX	1.18	Poor weight gain
2	1 yrs 5 m	5.5—2nd	8	10 ASO	1.33	Poor weight gain
3	6 m	4.3—2nd DS*	7	10 ASO	0.76	Pulmonary hypertension
4	4 yrs 3 m	14.7—11th	10	25 HELEX	1.0	Poor weight gain/RHE
5	3 yrs 1 m	14.5—50th	19†	24 ASO	2.5	RHE

*Patient plotted on Down syndrome growth curve. †Defect reported to measure 24 mm by angiography using stop-flow technique.

ASO = Amplatzer septal occluder; DS = Down syndrome; RHE = right heart enlargement; other abbreviations as in Table 2.

a. Event 1: Recatheterization at 48 h for device removal due to persistent high-grade 2nd-degree atrioventricular block.

b. Event 2: Developed complete heart block with hemodynamic compromise requiring cardiopulmonary resuscitation during 2nd procedure for device removal. Patient survived and was referred for future surgical closure.

2. Patient #2 was a former 28-week gestation girl with no other active medical problems. She had device deployment with no intraprocedural complications.

a. Event 3: Stroke. The patient was readmitted on post-catheterization day 3 for seizure activity and focal neurologic deficits. Subsequent workup identified a lesion involving the left medial insular cortex believed to be from an embolic source.

3. Patient #3 was a former 30-week gestation boy with Down syndrome and moderate pulmonary hypertension (PH). He was referred by neonatology out of concern for development of worsening PH and bronchopulmonary dysplasia.

a. Event 4: PH crisis/arrest after device deployment requiring cardiopulmonary resuscitation. Patient survived with the device left in place. He underwent continued neonatal intensive care unrelated to his ASD and was discharged 2 weeks later and continues to do well to this day.

4. Patient #4 was an otherwise healthy girl referred due to poor weight gain and RHE.

a. Event 5: Procedure abandoned secondary to development of complete heart block with deployment of right atrial eyelet of a 25-mm HELEX device. This necessitated pacing the patient for an extended period during the procedure. Before the end of the case, the rhythm resolved to 1st-degree heart block, and the patient was observed overnight. She remained in 1st-degree block up to the time of the second device closure attempt.

b. Event 6: The patient returned 4 months later and had successful deployment of the same 25-mm HELEX device; however, on post-catheterization day 1, new mitral valve regurgitation was discovered by echocardiogram. The device was not felt to be near the mitral valve apparatus and was therefore left in place. The regurgitation has persisted and remains mild.

5. Patient #5 was an otherwise healthy girl referred for RHE.

a. Event 7: Procedure abandoned secondary to development of complete heart block with attempted device deployment of a 24-mm Amplatzer septal occluder device. Although the defect measured 19 mm by TEE, it was noted to measure 24 mm by fluoroscopy. Successful deployment proved difficult with the device repeatedly prolapsing into the right atrium. During these attempts, the patient developed complete heart block and shortly after converted to a stable 2nd-degree Wenckebach block. Continued attempts to deploy the device led to Cobra deformation. Due to the deployment malfunction as well as the persistence of the heart block, the device was removed.

b. She was observed overnight, and she remained in a stable 2nd-degree heart block at the time of discharge. This was resolved at the time of a 1-week follow-up appointment.

c. At the family's continued wishes to avoid surgery, she returned 1 year later (>15 kg) and had successful deployment of a 22-mm Amplatzer septal occluder without complications.

Among the various indications (Table 6), nearly two-thirds of the referrals were for either RHE or poor growth.

Table 6. Primary Indications for Referrals and Frequencies of Referrals

Primary Indication for Referral	Frequency, %
Right heart enlargement	34
Poor growth	29
Pulmonary hypertension	15
Frequent upper respiratory tract infection	8
Other*	8
Incidental finding	5
Lower respiratory tract infection	1

*History of chronic lung disease, acute life-threatening event, and cyanosis.

In our study, the rate of resolution of RHE by the following morning was 50% (n = 126); at 1-month follow-up, it was 88% (n = 103); and it improved to >92% (n = 79) by long-term follow-up at 12 to 24 months (Fig. 1). There was no difference when we compared the resolution rates of right atrial versus right ventricular enlargement. There was a 52% rate of complete resolution of the atrial level shunt by post-catheterization day 1 (n = 124), which further improved to 99% at long-term follow-up of between 12 and 24 months (n = 115).

Of 37 patients in the sample specifically referred for poor growth, we evaluated a subset of 22 patients for which there was sufficient follow-up data, and were otherwise completely healthy, for growth improvement. These patients were all the result of full-term births and had no other past medical history or diagnoses. The median age of this group was 17.5 months (9 to 59 months), median weight at time of procedure of 9 kg (6.7 to 14.9 kg), and median follow-up time of 8.5 months (3 to 14 months). Among the 22 patients, 1 patient decreased in growth percentile at 6-month follow-up; 8 patients remained the same after a mean follow-up of 9 months; and 11 patients had an increase of only 1st to 6th percentile at mean follow-up of 9 months. There were only 2 patients that met clinically significant criteria for weight gain, which we predefined as an improvement of at least 1 SD. One patient, a 56-month-old girl increased from the 10th to 25th percentile in weight at 14-month follow-up. The second, a 17-month-old boy increased from the 3rd to 20th percentile in weight at a follow-up of 1 year. In this subset of patients, residual shunt across the defect had resolved in 20 of 22 patients (91%) by 1-month follow-up, and in 21 of 22 (95%) by 6-month follow-up.
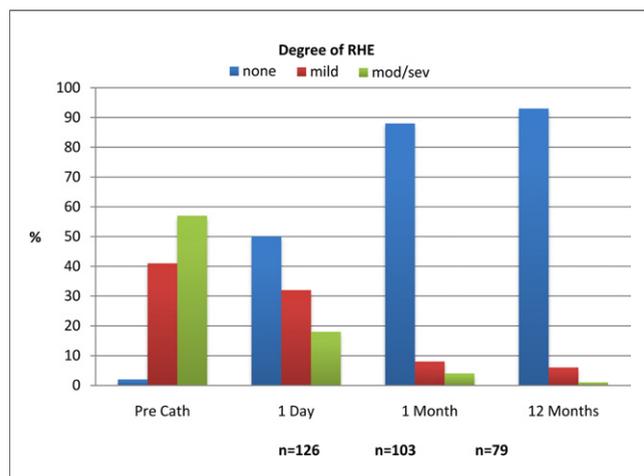
Figure 1. Changes in RHE

Changes in the improvement of right heart enlargement (RHE) over a 12-month follow-up period. mod = moderate; PreCath = pre-catheterization; sev = severe.

Discussion

Historically, the recommendation for elective ASD closure from surgical literature was to wait until around 4 years of age (9). Numerous previous studies have shown a fairly high rate of spontaneous closure of ASD <8 mm in the first few years of life (10–13), and rarely as late as adolescence (14). Due to the known high rates of spontaneous closure in the first year of life, it has been written, "One should be careful about proceeding too rapidly to close an ASD in an asymptomatic young patient" (15). The median ASD diameter of 10 mm in our study suggests that many of these smaller defects may have, in fact, closed spontaneously had we not intervened. It has been shown that some ASD can enlarge over time, even to the extent of outgrowing percutaneous closure capability (16); however, this typically occurs in older children and was not a factor in our study.

As the technology and experience surrounding percutaneous device closure of ASD has progressed, 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 ample evidence to suggest percutaneous closure is preferred with respect to decreased morbidity and length of hospital stay (2). Our aim was to assess if closing these defects earlier poses a greater risk for the smaller patients. Our results indicate a major complication rate higher than previously reported in any interventional literature. Although it is possible we are being too conservative in our definitions of complications and their severity, we feel it necessary to underscore the importance of appropriate patient selection and timing of closure.

Our study is unique in that we attempted to predefine complications before data collection. We considered a wider variety of major and minor complications than have been generally applied. This is contrary to previous studies that only list death, stroke, or device erosion as major complications. Though the Bergersen et al. study does include a comprehensive listing of complications, it does not stratify patients and the complications according to patient size (7,17). In 1 study of 52 patients, the investigators reported no major complications, yet discussed 2 device embolizations that were classified as minor complications (6). 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 (5). Finally, 1 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% (8).

Our interpretation of these data and that of the literature is neither to recommend against percutaneous closure of ASD in small children, nor to suggest they should be closed

surgically. However, these data do make us pause to thoroughly review the indications for closure in these patients considering the risks are somewhat higher than typically perceived.

One indication for closure of ASD has always been clinical evidence of right ventricular volume overload and worsening RHE. Although this develops early in childhood, the short-term clinical implications are unclear. Yet, 34% 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 (18,19), which our study corroborates. In fact, in our study, just over one-half of all patients experienced improvement of RHE as early as by the following morning. This was similarly shown in a recent study of adult ASD closure using volumetric analysis of atrial size before and after ASD closure (19).

Another indication that has historically been considered acceptable for elimination of any intracardiac shunt has been documentation of lower respiratory tract infections. Our referral patterns indicate this seems to have broadened to include referral of infants due to excessive colds and upper respiratory tract infections in the newborn period that did not require treatment. In fact, in our study of 128 patients, there was only 1 patient with a single documented bacterial pneumonia before referral. The same patient went on to have 2 more documented bacterial pneumonias in the 2 years following his ASD closure.

Poor growth and failure to thrive is another reason these patients are commonly sent for intervention; this accounted for 29% of our referrals. It is important to point out that consistent growth along any percentile is normal and must be differentiated from a plateau, or decline, in growth velocity. Historically, patients with true growth failure exhibit an extensive medical history involving prematurity, chronic lung disease, and many other medical problems, often, including congenital heart disease. Although a left-to-right shunt may be contributing to growth failure, other confounders exist; cardiac shunts associated with growth failure are more classically high-pressure volume-loading lesions, such as a ventricular septal defect or patent ductus arteriosus.

Some studies have recently shown some benefits may exist in eliminating any left-to-right shunt in symptomatic infants with bronchopulmonary dysplasia with respect to respiratory physiology (20,21); however, they did not show any improvement in growth over a 12-month follow-up period (20). There are, unfortunately, no consistent data in the literature to confirm any benefit to growth after ASD closure in an otherwise asymptomatic patient. The few studies that do suggest a possible benefit had such an extended follow-up period that it would be imprecise to infer a correlation solely upon the elimination of the ASD (21,22). Although Lammers et al. (21) suggested that growth and development improved in nearly all patients, their conclusions were not uniformly accepted (23).

There is no evidence that an isolated secundum ASD will cause such a significant increase in metabolic demand in infants and young children as to cause a decline in growth. Our study also suggests that no clinically significant improvement in growth exists, in otherwise asymptomatic and healthy small children, following ASD closure.

Study limitations. This is a retrospective study. Despite the fact that this study is the largest yet reported, population size remains small and more research is needed in this area. Our cohort is very heterogeneous, making it difficult to have a control group. We chose as a comparison to our data the complication rates found in the literature. No direct comparison to older patients who underwent device closure or small patients who underwent surgical closure was performed. Finally, our assignment of complications to either major or minor categories is clearly subjective, however does follow closely with recent literature for future recommendations regarding classification of complications (18).

Conclusions

Percutaneous ASD closure in children <15 kg is effective with a 98% procedural success rate, a 1% rate of residual leak, and a >92% rate of resolution of RHE. Although safe, there is, perhaps, an overall greater risk of complications than previously perceived, which is largely due to variations in prior classification. Growth velocities appear largely unaffected by percutaneous ASD closure in small, otherwise asymptomatic patients. There will undoubtedly be circumstances whereby an attempt will be appropriate at a younger age, and that decision should continue to be deferred to the performing physician for the symptomatic patient. For the truly elective small patient without comorbidities that could be exacerbated by the shunt physiology, including those with poor growth as their sole indication or those with only RHE on echocardiogram, deferral of closure until the historically established timeline of around 4 to 5 years of age should be strongly considered.

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