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Right Ventricular Form and Function After Percutaneous Atrial Septal Defect Device Closure

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OBJECTIVES We sought to assess the right heart's response to percutaneous device closure of moderate sized atrial septal defects (ASDs) in adults over a one-year follow-up period.

BACKGROUND Percutaneous ASD device closure is a safe and effective means of reducing or eliminating interatrial shunting. The response of the adult's right heart to device closure is incompletely understood.

METHODS Forty consecutive patients had 40 device implantations (32 with the CardioSeal implant and 8 with the Amplatzer device). The patients were assessed with echocardiography, chest radiography and electrocardiography before the procedure and at 1, 6 and 12 months.

RESULTS The mean ASD size was 13 ± 4 mm, and the device size ranged from 33 to 40 mm for CardioSeal and 12 to 36 mm for Amplatzer. At one month, heart size (49% vs. 46%), four-chamber right ventricular (RV) size (45 vs. 41 mm), paradoxical septal motion (60% vs. 5%), QRS duration (125 vs. 119 ms), PR interval (181 vs. 155 ms) and echocardiographically determined pulmonary artery systolic pressure decreased significantly and was maintained at 12-month follow-up. At six months, right atrial length decreased from 50 to 47 mm. At one year, 29% of patients had persistent RV enlargement.

CONCLUSIONS Right heart morphology undergoes rapid improvement within one month of defect closure, with associated mechanoelectrical benefit. A small number of patients had persistent RV enlargement or pulmonary hypertension, or both, at one year. Our data support the application of transcatheter methods in achieving excellent hemodynamic and anatomic outcomes. (J Am Coll Cardiol 2001;37:2108–13) © 2001 by the American College of Cardiology

Atrial septal defects (ASDs) account for 10% of all congenital heart lesions (1) and represent the third most common congenital cardiac defect seen in adults (2). This lesion is sometimes associated with the development of pulmonary hypertension, congestive heart failure, atrial arrhythmias and impaired aerobic capacity, corresponding with varying degrees of right heart volume overload and decompensation (3–5). Such potential complications have prompted prophylactic closure during childhood or early adulthood. In the later adult years, ASD closure provides symptomatic relief and may prevent the progression of right heart dysfunction (4). Both surgical and catheter occlusion of the defect has been found effective and safe in reducing left to right shunting (6,7). In addition, transcatheter ASD closure has the advantage of avoiding the need for sternotomy, cardiopulmonary bypass and intensive care stay and permits rapid patient recovery, with its associated economic and social benefits (8). However, the response of the adult's right ventricle (RV) after percutaneous defect closure is incompletely understood, with the degree and rate of resolution of RV enlargement, pulmonary hypertension and paradoxical septal motion (PSM) remaining unclear in this group of patients. The focus of this investigation was to describe changes in RV physiology over a one-year follow-up period in adults who had undergone catheter device closure of an isolated ASD.

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METHODS

Patients. Forty consecutive adults underwent secundum ASD device closure at the Toronto General Hospital between April 1, 1997 and December 31, 1999. The functional classes (New York Heart Association) of the patients are summarized in Table 1. Only one patient had documented paroxysmal atrial fibrillation. All patients underwent chest radiography, echocardiography and 12-lead electrocardiography before the procedure and at 1, 6 and 12 months after the procedure. Echocardiography was performed using a standardized protocol by a single senior sonographer (H.E.H.). Echocardiographic, electrocardiographic (ECG) and chest radiographic data were reviewed retrospectively.

Device design and implantation. A CardioSeal implant (Nitinol Medical Technologies Inc., Boston, Massachusetts) was used in 33 patients, and an Amplatzer occluder

Abbreviations and Acronyms

ASD	=	atrial septal defect
ECG	=	electrocardiogram or electrocardiographic
PA	=	pulmonary artery
PSM	=	paradoxical septal motion
RA	=	right atrium or atrial
RV	=	right ventricle or ventricular
RVOTD	=	right ventricular outflow tract diameter

(AGA Medical, Golden Valley, Minnesota) was used in 8 patients. The CardioSeal implant consists of four flexible spring-loaded stainless-steel arms covered by two Dacron patches (8). The Amplatzer device, on the other hand, consists of a Nitinol meshwork that assumes a double mushroom shape when deployed, with the central portion of the complex plugging the defect (9). The indication for defect closure in all patients was an increased RV end-diastolic diameter on the echocardiogram or an enlarged heart on the chest radiograph, or both, with or without the presence of symptoms. The procedures were performed under general anesthesia with fluoroscopic and transesophageal echocardiographic guidance. Access was obtained from the femoral vein. A sizing balloon catheter (Meditech Boston Scientific, Mansfield, Massachusetts, or Amplatzer sizing balloon, AGA Medical) was used to determine the so-called stretched diameter of the defect. A suitably sized device was chosen to be twice the size (CardioSeal) or the same size (Amplatzer) as the stretched diameter. The devices were deployed through long sheaths (9F to 11F) using previously described techniques (6).

Two-dimensional echocardiography. All patients underwent transesophageal echocardiography to assess their suitability for the device and subsequently only transthoracic studies, as part of the clinical follow-up. All available transthoracic studies were reviewed retrospectively, and the measurements were verified by an experienced echocardiographer (G.R.V.). On-line measurements were made in the parasternal, apical four-chamber and subcostal views to define the RV and right atrial (RA) sizes, presence of PSM, defect size and number, position and presence of residual shunts after defect closure. Four-chamber views were obtained to document the maximal RV inlet diameter at end diastole, with measurements made at the tips of the tricuspid valve leaflets. On the parasternal long-axis view, the right ventricular outflow tract diameter (RVOTD) was determined as the widest short-axis RVOTD. Four-chamber views were obtained to measure RA size, using the maximal mediolateral diameter (width), as well as the maximal superoinferior diameter (length) of the atrium, (10,11) measured at end systole (Fig. 1). The parasternal long-axis and short-axis views were studied for the presence of paradoxical motion of the interventricular septum. When PSM was evident on any of these views, it was denoted as being present.

Table 1. Intraobserver Variability*

RV dimensions	4.8%
RA dimensions	6.5%
PR interval	4.3%
QRS duration	8.8%
QRS axis	5%
Cardiothoracic ratio	4%

*Expressed as a percentage of the standard deviation of the difference between initial and repeat measurements on the same variable, divided by the mean value of the two measurements.
RA = right atrial; RV = right ventricular.

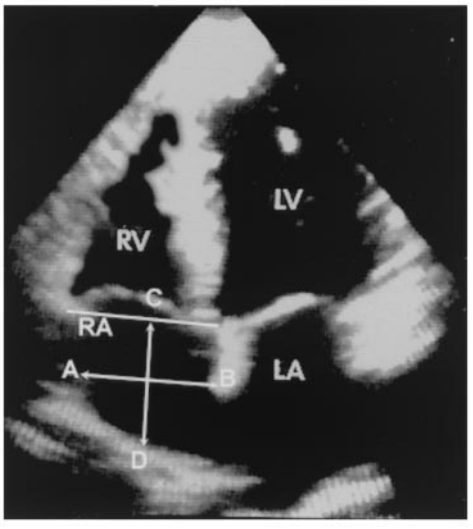

Figure 1. Echocardiographic measurement of RA dimensions at end systole. A↔B = maximal mediolateral dimension (i.e., width of RA); C↔D = superoinferior dimension (i.e., length of RA); LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

Residual shunts were defined by their cross-sectional diameter on the color flow map. Color Doppler settings, including the velocity map scale, were kept constant throughout all studies by the sonographer (H.E.H.) performing the investigation. All echocardiographic studies were performed on the same machine. For accurate shunt identification, multiple echocardiographic views were examined. The widest diameter on any view was identified as the residual shunt size. Shunts were arbitrarily defined as small (<3 mm), moderate (3 to 6 mm) and large (>6 mm) in size. Right ventricular systolic pressure was estimated from tricuspid regurgitation jet velocity, when present (12). All repeat on-line measurements were performed using a Hewlett-Packard Sonos 2500 echocardiograph.

Chest radiography. All patients underwent posteroanterior chest radiography, and cardiac size was expressed as a percentage of the total thoracic diameter.

Electrocardiography. Twelve-lead surface ECGs were analyzed for the mean frontal plane QRS axis, the widest QRS duration (from the initial deflection of the QRS complex to where the terminal deflection crosses the baseline, taken in any chest lead with the widest complex and where the deflections are acute enough to permit accurate assessment [expressed in milliseconds]), the presence of RA overload (defined by any combination of peaked p waves, p wave height >2.5 mm in any lead or p wave >1.5 mm in lead

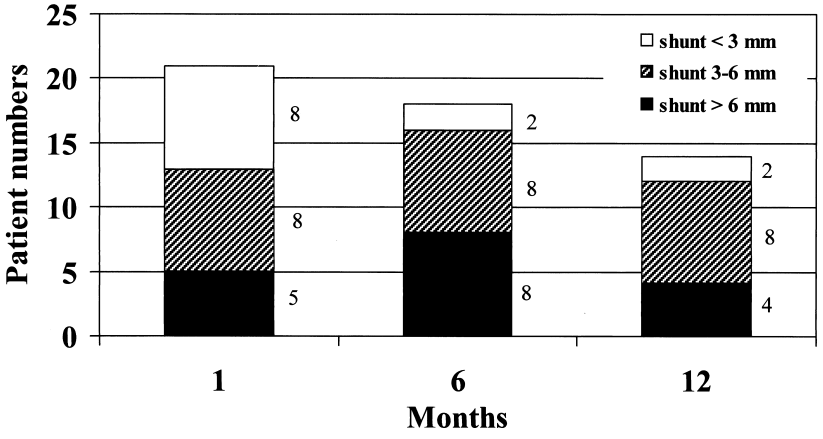

Figure 2. Size of residual shunts over follow-up time.

V_2), the PR interval (measured from the initial deflection of the p wave to the initial deflection of the QRS complex), the R wave height in lead V_1 (height of initial positive deflection of the QRS complex above the baseline value [expressed in millimeters]) and the presence of right bundle branch block (defined by the presence of an "rSR" pattern in lead V_1 or V_2). A single observer made all ECG and radiographic measurements (V.R.).

Statistics. Data are presented as the mean value ± SD for normally distributed data obtained before the procedure and at 1, 6 and 12 months after the procedure. Echocardiographic, ECG and chest radiographic variables at each follow-up period were compared with the preprocedural values; categorical data were presented as a proportion of the total number of patients who had data available during the follow-up period. Continuous variables were compared using paired *t* tests. Categorical variables were compared using either the chi-square or Fisher exact test, as appropriate. For comparisons of the continuous variables (RV size and pulmonary artery [PA] pressure) between patients <40 years old and those ≥40 years old, an independent *t* test was used. For comparisons between baseline and follow-up measurements, the level of significance was adjusted for multiple comparisons ($p = 0.05/3 = 0.017$). To document intraobserver variability, repeat measurements were done in randomly selected patients. A single observer, who had no knowledge of the previous measurements for a particular patient, repeated 30% of ECG, radiographic and echocardiographic measurements on the same study. Intraobserver variability was expressed as a percentage of the standard deviation of the difference between initial and repeat measurements on the same study, divided by the mean value of the two measurements. Our study protocol was deemed ethical by the local Research Ethics Board.

RESULTS

Forty devices were successfully deployed in 40 patients. Their ages ranged from 20 to 71 years (median 38). The female to male ratio was 3:1. Mean ASD diameter was 13 ± 4 mm, and the balloon size stretched at the time of catheterization to 17 ± 3 mm. The device size ranged from 33 to 40 mm (median 40) for the CardioSeal implant and 12 to 40 mm (median 23) for the Amplatzer device. Thirty-eight patients had 1-month, 36 patients 6-month and 28 patients had 12-month follow-up.

Immediately after device closure, residual shunts were detected in 29 patients (73%), 28 occurring in those patients with a CardioSeal device. Residual interatrial shunts occurred in 21 patients (53%) at one month, 18 patients (50%) at six months and 14 patients (54%) at one year. Residual shunt sizes ranged from 2 to 8 mm (median 5) (Fig. 2). Functional class improved after defect closure (Fig. 3).

Electrocardiographic analysis revealed a significant decrease in the PR interval (181 ± 8 vs. 155 ± 2 ms, $p < 0.001$) and QRS duration (125 ± 2 vs. 119 ± 2 ms, $p = 0.001$) at one month, and at six months, RA overload became reduced significantly to 0% ($p < 0.001$). The mean frontal plane QRS axis declined from 63 ± 33° to 54 ± 26° ($p = 0.027$) at six months, reaching significance at one year (57 ± 21°, $p < 0.001$). R-wave height in lead V_1 did not change significantly during the one-year follow-up.

On the echocardiogram, mean four-chamber RV size and mean RVOTD decreased significantly by one month to within the normal limits (45 ± 8 vs. 41 ± 6 mm, $p < 0.001$ and 39 ± 7 vs. 34 ± 5 mm, $p = 0.004$, respectively); normal ranges for four-chamber RV size and RVOTD were 26 to 43 mm and 18 to 34 mm, respectively (10). At one year, 8 (29%) of 28 patients had an enlarged RV (four-chamber view), compared with 23 (62%) of 37, before ASD closure ($p > 0.001$). At one-year, the size and incidence of residual interatrial shunts did not differ between those who had an enlarged postprocedural RV and those who did not have an enlarged RV. Mean right atrial length (superoinferior diameter) showed a trend toward shortening at one month (52 ± 7 vs. 50 ± 6 mm, $p = 0.081$) and reached significance at six months (47 ± 5 mm, $p < 0.001$). Normal values for RA length are indicated in Table 2 (10). Right atrial width (mediolateral diameter) did not change significantly with

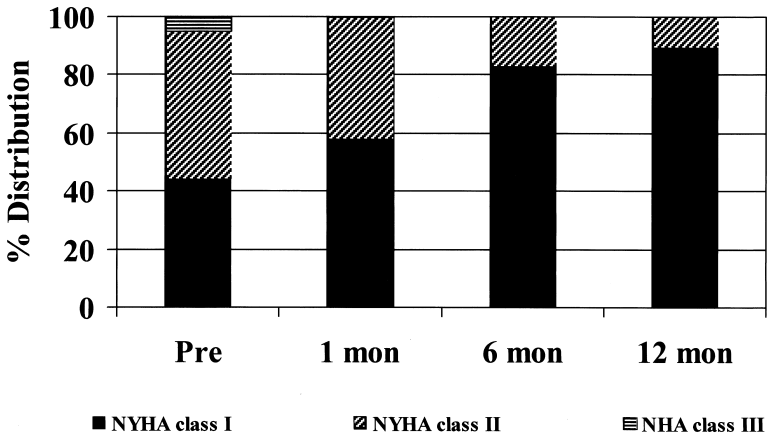

Figure 3. Distribution of New York Heart Association (NYHA) functional classes over duration of follow-up. Mon = interval (months) between procedure and follow-up date; Pre = before atrial septal defect closure.

time. Estimated systolic PA pressures also followed a progressive course of decline in the first year after the procedure, achieving significance at one month (Table 2). Before the procedure, 23 (62%) of 37 patients had systolic PA pressures >35 mm Hg; at one month, 17 (45%) of 38 patients, at six months, 9 (27%) of 33 patients and at 12 months, only 8 (29%) of 28 patients had systolic PA pressures elevated >35 mm Hg. Patients >40 years old at the time of device implantation had significantly higher systolic PA pressures before ASD closure (42 ± 11 vs. 31 ± 8 mm Hg, p = 0.001) and one year later (41 ± 4 vs. 31 ± 12 mm Hg, p = 0.032). Four-chamber RV size did not differ significantly, however. Paradoxical septal motion was present in 21 (58%) of 36 patients before implantation, 2 (5%) of 37 patients at one month, 4 (12%) of 33 patients at six months and in none at 12 months. The results are summarized in Table 2.

Intraobserver variability. The data are summarized in Table 1.

DISCUSSION

Despite the preponderance of residual atrial shunts, these data demonstrate that in the adult patient with a moderate sized secundum ASD, there is a significant decrease in cardiac size by one month after catheter closure. Closure of the ASD results in volume unloading of the right heart and an early reduction in cardiac size. The RV size continued to decline so that the mean size on the four-chamber view was within normal limits at one month and was maintained at 6 and 12 months. At one-year follow-up, only a third of patients demonstrated persistent RV enlargement. Berger et al. (13) demonstrated a reduction in end-diastolic RV volume on the echocardiogram early after device closure in 23 patients, as well as in 24 patients after surgical ASD closure, similar to the findings we demonstrated at one month. They did not examine RA size. Gatzoulis et al. (5) demonstrated a significant reduction in the cardiothoracic ratio three to six months after surgical ASD closure; in

Table 2. Summary of All Data

	Before Procedure	1 Month	p Value	6 Months	p Value	1 Year	p Value
CTR (%)	49 ± 7	46 ± 7	< 0.001*	47 ± 8	< 0.001*	48 ± 7	< 0.001*
RA overload on ECG	4/33 (12%)	3/36 (8.3%)	0.385	0/32	< 0.001*	0/25	< 0.001*
QRS axis	63 ± 33°	60 ± 28°	0.027	54 ± 26°	0.027	57 ± 21°	< 0.001*
PR interval (ms)	181 ± 8	155 ± 2	< 0.001*	151 ± 2	0.061	147 ± 2	< 0.001*
QRS duration (ms)	125 ± 2	119 ± 2	0.001*	109 ± 1	< 0.001*	104 ± 1	< 0.001*
R wave in lead V_1 (mm)	2.5 ± 1.5	2.4 ± 1.7	0.769	2.3 ± 1.6	0.413	1.8 ± 1.3	0.413
RV size (mm)							
Four-chamber normal 26–43	45 ± 8	41 ± 6	0.003*	37 ± 5	< 0.001*	37 ± 6	< 0.001*
RVOTD (mm)							
Normal 18–34	39 ± 7	34 ± 5	0.004*	33 ± 6	0.001*	33 ± 6	0.066
RA length (mm)							
Normal 34–49	52 ± 7	50 ± 6	0.081	47 ± 5	< 0.001*	47 ± 6	0.027
Patients with PSM	21/36 (60%)	2/37 (5%)	< 0.001*	4/33 (12%)	< 0.001*	0/27	< 0.001*
Systolic PA pressure >35 mm Hg	23/37 (62%)	17/38 (45%)	0.016*	9/33 (27%)	< 0.001*	8/27 (29%)	< 0.001*

*Significant p values. The p values reflect pairwise comparisons between preprocedure and follow-up measurements. Data are presented as the mean value ± SD or number (%) of patients.

CTR = cardiothoracic ratio; PA = pulmonary artery; PSM = paradoxical septal motion; RA = right atrial; RV = right ventricular; RVOTD = right ventricular outflow tract diameter.

addition, they demonstrated an initial increase in the cardiothoracic ratio early after repair, believed to be related to cardiopulmonary bypass, which was not evident in our nonsurgical cohort.

In some ventricles with prolonged volume loading, RV morphology does not completely return to normal (14,15). In our study, 29% of patients had persistent RV enlargement at one year. Pearlman et al. (14) investigated this phenomenon of persistent RV enlargement after ASD closure in a surgical cohort of 31 patients. Similar to our group, 23% of their patients had persistent RV enlargement and tended to be older patients (i.e., >25 years old at the time of operation). Despite the fact that 95% of our cohort was >25 years old, most RVs returned to normal size by one year in a time-related manner. Those who had persistent RV enlargement tended to be >40 years at the time of device implantation, suggesting an impaired ability of the RV to remodel after prolonged volume loading, or the aged state per se. We were unable to demonstrate a relationship between the incidence and size of residual interatrial shunts and the persistence of RV enlargement. Pearlman et al. (14) also demonstrated that only one of their study patients had a significant residual left to right shunt on oximetry, and they concluded that residual shunts did not contribute to the observed persistent right heart abnormality. During the first six months after ASD closure, there was a corresponding significant decline in the presence of RA overload, PR interval and QRS duration on the ECG. These mechanoelectrical changes presumably reflect better intra-atrial and intraventricular conduction properties subsequent to volume unloading of both right heart chambers and may potentially reduce the substrate for late atrial arrhythmia (3), as has been demonstrated in patients with a partial right heart bypass and single-ventricle physiology (16). Gatzoulis et al. (5), in their adult surgical cohort, also demonstrated an early reduction in the QRS duration, but did not report changes in the PR interval or RA enlargement by ECG criteria.

Abnormal septal motion began to normalize by one month in a significant percentage of patients, and the process continued over the one-year follow-up period. Abnormal septal wall motion is caused by displacement of the interventricular septum toward the left ventricle, as the RV becomes progressively volume-loaded (1). During ventricular systole, the septum moves "paradoxically" toward the RV as the left ventricle contracts. An abrupt reduction in RV volume is most likely responsible for the restoration of normal wall motion. This process may not be complete, and some authors have demonstrated permanent changes in RV wall motion abnormality (14,15).

A reduction in estimated systolic PA pressures also followed a progressive normalizing trend. By one year, only 29% of patients had pressures elevated >35 mm Hg. At late follow-up, Oelberg et al. (12) demonstrated persistent elevation in rest systolic PA pressures in 16% of their patients, and some patients only demonstrated abnormal elevation of PA pressures during exercise. These findings suggest a proportion of patients have permanently elevated pulmonary vascular resistance before ASD closure.

Intraobserver variability. We have documented accurately the degree of intraobserver variability for echocardiographic, radiographic and ECG measurements. Intraobserver variability was <10% for all of the echocardiographic and radiographic measurements, with the greatest variability demonstrated in RA measurements (6.5%). Right atrial dimensions, however, decreased by >10% at six months, more than that expected by chance alone. Intraobserver variability was <5% for all ECG measures, with the exception of QRS duration, which was 8.8%. Despite this higher variability, QRS duration had declined by 10% at six months and 16% at one year, again more than anticipated by variability alone. We therefore believe that the decline in echocardiographic, ECG and radiographic dimensions reflects a true improvement in right heart size.

Study limitations. This study was a retrospective analysis using echocardiographic, ECG and radiographic means to describe changes in right heart physiology after device closure of an ASD. Because of the nongeometric shape of the RV, quantitation of RV volume is difficult by echocardiography. Thus, RV dimensions are utilized as a surrogate for RV size. Our data were collected over a one-year period only, and during that time, considerable normalization in virtually all variables was demonstrated. Longer follow-up is imperative to elucidate further changes in RV physiology. Larger multicenter patient cohorts would permit more detailed assessment of risk factors for impaired RV remodeling late after ASD closure.

Conclusions. In adults undergoing transcatheter ASD closure, there was a significant reduction in RA and RV sizes and PSM, with corresponding mechanoelectric improvement in the PR interval, ECG RA overload pattern, mean frontal plane QRS axis and QRS duration early after the procedure. Systolic PA pressures followed a slower decline over one year. Twenty-nine percent of patients demonstrated persistent elevation of PA pressures (they tended to be >40 years of age). Similarly, 29% of patients had impaired right heart remodeling at one year, corresponding to published data on patients who have undergone surgical repair. We conclude that device closure of ASDs in adults leads to early improvement, with subsequent continued improvement in RV and RA physiology. We believe our data support the increasing practice and body of knowledge in support of nonsurgical closure of isolated secundum ASDs in selected adults.

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