CLINICAL RESEARCH

The Impact of Transcatheter Atrial Septal Defect Closure in the Older Population

A Prospective Study

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Objectives We sought to prove that device closure of atrial septal defect (ASD) in older patients not only improves cardiac function but also results in symptomatic relief by improving functional class.

Background Atrial septal defect accounts for approximately 10% of all congenital cardiac defects. It is possible that ASD closure in older patients may derive benefits, though this is not well established. We therefore aim to prospectively assess the clinical status and functional class of older patients after transcatheter ASD closure.

Methods This was a prospective study of all patients age 40 years or more who underwent device closure of a secundum ASD between April 2004 and August 2006. Investigations including atrial and brain natriuretic peptide levels, electrocardiography, chest X-ray, transthoracic echocardiogram, 6-min walk test, and quality of life questionnaire were performed before and at 6 weeks and 1 year after the procedure.

Results Twenty-three patients (median age 70 years, 13 women) had transcatheter device closure of ASD. Median ASD size was 18 mm (range 9 to 30 mm). Median pulmonary artery pressure was 22 mm Hg (range 12 to 27 mm Hg). At 1 year, New York Heart Association functional class improved (p = 0.004) in 16 patients with significant improvement in 6-min walk-test distance (p = 0.004) and physical (p = 0.002) as well as mental health score (p = 0.03). There were no major complications. One year following closure there was a significant change in left ventricular end-diastolic (p = 0.001) and end-systolic dimensions (p = 0.001) and also significant reduction in right ventricular end-diastolic dimension (p < 0.001).

Conclusions Our data demonstrated that ASD closure at advanced age results in favorable cardiac remodeling and improvement of functional class. (J Am Coll Cardiol Intv 2010;3:276–81) © 2010 by the American College of Cardiology Foundation

Atrial septal defect (ASD) is one of the most common forms of congenital heart disease in adults (1), accounting for approximately 10% of all congenital cardiac defects (2,3). The left-to-right shunt through an ASD results in chronic volume overload of the right heart and, if untreated, may lead to atrial arrhythmias (4), right heart failure (5,6), pulmonary hypertension (7), and/or systemic embolism (8). Closure of ASD in children and young adults is recommended with low operative risk and a good long-term prognosis (9–11). Adults with an ASD, although often reporting no symptoms or only mild effort intolerance, may have a significant reduction in cardiopulmonary function during formal exercise testing (12–14). However the benefits of ASD closure in older patients are less clear (15–19), and closure of the defect may be delayed or withheld (20). We therefore prospectively assessed the effects of transcatheter ASD closure on clinical and echocardiographic parameters in older patients.

Methods

Study population. We prospectively studied consecutive patients age >40 years who underwent device closure of a secundum ASD at the Royal Brompton Hospital, London, between April 2004 and August 2006. Patients listed for device closure were those with hemodynamically significant secundum ASD defined by the presence of right heart dilation and significant left to right shunt with calculated Q_p/Q_s ratio ≥1.5 on echocardiogram. The study was approved by the institutional ethics committee and patients provided informed consent before participation in the study. Only those patients unable to perform an exercise test or who declined to give consent were excluded from the study.

Device closure. Transcatheter ASD closure was performed as previously described (21). The Amplatzer septal occluder (AGA Medical, Plymouth, Minnesota) was used in all patients. The Amplatzer septal occluder device size was selected using balloon sizing or intraprocedural echocardiographic assessment of ASD diameter as previously described (22,23).

Study protocol. The following evaluations were performed immediately before ASD closure and at 6 weeks and 1 year after the procedure: full blood count, serum atrial natriuretic peptide and brain natriuretic peptide (24) levels determined by immunoradiometric assay, 12-lead electrocardiogram, chest X-ray, transthoracic echocardiogram, and 6-min walk test (6MWT). Quality of life (QOL) was assessed using the health survey and New York Heart Association (NYHA) functional class.

Transthoracic echocardiographic studies were performed according to the American Society of Echocardiography guidelines (25). Left ventricle (LV) M-mode measurements and right ventricular (RV) diastolic dimensions were made in parasternal long-axis view and RV inlet measurement in the apical 4-chamber view. Ventricular filling was assessed using pulse-wave Doppler, with the sample volume positioned at the level of the tricuspid and mitral valve tips, including deceleration time analysis. Doppler tissue imaging (DTI) was performed and both systolic (s) and diastolic waves, early (e) and atrial (a), were recorded at the tricuspid and mitral valve annular level. Left and right atrial volumes were measured by planimetry in 4-chamber view.

Quality of life (QOL) was assessed using the SF-36v2 Health Survey (2nd version) (QualityMetric, Inc., Lincoln, Rhode Island). This health survey was used for the first time to assess health-related QOL outcomes after ASD closure. This questionnaire has been suggested for the evaluation of a wide variety of medical interventions (26), as it is not disease- or treatment-specific (27). Each questionnaire was given to the patient for an hour to complete, and data were entered into a Web-based patient tracking service.

Statistical analysis. R version 2.9.2 (AT&T Bell Laboratories, Murray Hill, New Jersey), with packages nlme and glmmAK was used for statistical calculations. Data are expressed as mean ± SD, or median with range, as appropriate. Changes in the continuous parameters over time were analyzed using a mixed-model linear regression analysis, with patients as a random effect and time as a fixed effect. Change in functional (NYHA) class was assessed using a cumulative logit model for ordinal response (MCMC sampling, 40,000 iterations, burn-in 10,000). A p value <0.05 was considered statistically significant.

Abbreviations and Acronyms

6MWT = 6-min walk test

ASD = atrial septal defect

DTI = Doppler tissue imaging

LV = left ventricle

NYHA = New York Heart Association

QOL = quality of life

RV = right ventricle

Results

A total of 23 patients (13 women; median age 68 years, range 50 to 91 years) underwent ASD closure (Table 1). Median ASD size was 18 mm (range 9 to 30 mm) and median device size was 24 mm (range 16 to 36 mm). Median Q_p/Q_s ratio was 2.2 (range 1.5 to 3). Median pulmonary artery pressure was 23 mm Hg (range 12 to 27 mm Hg). Three patients had mean pulmonary artery pressures >25 mm Hg. None of the patients showed signs of pulmonary hypertension at 1-year follow-up echocardiogram.

Device delivery and implantation were successful without procedure-related complications in all patients. Five patients (21%) were in atrial fibrillation at the time of implantation. One patient developed transient atrial fibrillation after the procedure that reverted to sinus rhythm after treatment with flecainide. Two patients had 2 devices implanted at the same procedure due to the presence of multiple defects. Four patients had minor groin hematoma at the puncture site. One patient developed chronic renal failure and died suddenly 24 weeks after device closure from an unexplained cause.

Table 1. General Characteristics of Patients

No. of patients	23
Mean age, yrs	69 (43–92)
Sex, M/F	10/13
Hypertension	7 (30)
Hypercholesterolemia	6 (26)
Ischemic heart disease	3 (13)
Chronic renal failure	1 (4)
ASD size, mm	18 (9–30)
ASO device size, mm	24 (10–36)
Mean PA pressure, mm Hg	22 (12–27)
Q_p/Q_s ratio	2.2 (1.5–3)
Procedure time, min	65 (41–110)
Fluoroscopic time, min	14.6 (7–33)

Values are n (%), median (range), or n.
ASD = atrial septal defect; ASO = Amplatzer septal occluder; PA = pulmonary artery; Q_p = pulmonary flow; Q_s = systemic flow.

Table 2. Changes in Health Status, Rhythm, and Cardiothoracic Ratio

	Pre-Closure (n = 23)	6 Weeks (n = 23)	1 Year (n = 22)	p Value
NYHA functional class				<0.0001
I	2 (9%)	11 (48%)	17 (78%)	
II	16 (70%)	9 (39%)	3 (13%)	
III	5 (22%)	3 (13%)	2 (9%)	
QOL				
Mental health score	46 ± 10.7	47 ± 10.8	53 ± 5.1	0.007
Physical health score	47 ± 6.7	48 ± 7.4	53.8 ± 5.1	<0.0001
6MWT distance, m	400 ± 106	451 ± 102	493 ± 89	0.001
CT ratio	0.57 ± 0.05	0.56 ± 0.06	0.54 ± 0.07	ns
QRS duration, ms	108 ± 40	106 ± 45	106 ± 17	ns

CT = cardiothoracic; NYHA = New York Heart Association; QOL = quality of life; 6MWT = 6-min walk test.

At baseline, 16 (70%) patients were in NYHA functional class II and 5 (22%) were in NYHA class III and average 6MWT distance was 400 m. Following ASD closure, a significant improvement in 6MWT distance (Fig. 1) was observed (94-m increase in average at 1 year [p = 0.001]). This was associated with an improvement in NYHA class, present as early as 6 weeks and maintained at 1-year follow-up (NYHA I: 77%, 17 of 22, p < 0.0001) (Table 2).

Low SF-36v2 survey scores were obtained at baseline for mental and physical health (Table 2) in our population, with almost two-thirds of patients scoring well below average in both (28). A significant improvement in both the mental (p = 0.007) and physical score (p < 0.001) was seen over the period of 1 year after the procedure. At 1 year, only 13 of mental and physical scores were below average.

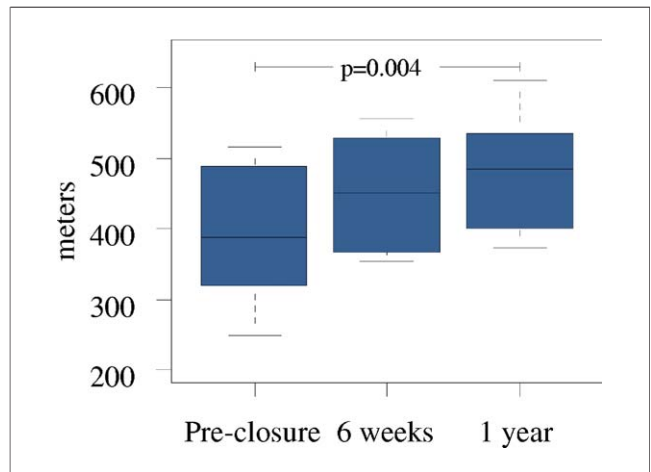Comparison of RV and LV dimensions are as shown in Figure 2. Right ventricular end-diastolic and inlet dimen-

sions, as well as right atrial volume decreased significantly (p < 0.001 for all) (Table 3). No significant change in tricuspid annular plane systolic excursion was found. Right ventricular DTI data are also shown in Table 3; similarly, systolic DTI velocities at tricuspid annular level did not show any significant improvement.

There was a significant increase in LV end-diastolic and end-systolic dimensions after ASD closure (Table 4), with the greatest change seen in the first 6 weeks. Similarly, there was significant improvement in global LV systolic function (mean LV ejection fraction: 65%, 76%, and 82%, pre-closure, at 6 weeks, and at 1 year, respectively, p < 0.0001). There was a borderline reduction in LV long-axis function with no reduction in systolic DTI velocities. After an initial rise in atrial natriuretic peptide levels at 6 weeks, this decreased at 1 year, albeit not reaching statistical significance (Fig. 3).

Discussion

In this study, we have demonstrated that ASD closure is technically feasible with a high success rate and can be performed at low risk in the older population. We observed significant improvement in symptoms and functional ability with favorable cardiac remodeling in an older population after transcatheter ASD closure. The most clinically relevant finding of our study was the increase in exercise capacity as indicated by the 23.5% increase in 6MWT distance and the improvement in QOL as assessed by the SF-36v2 survey and NYHA functional class.

Closure of ASD is often considered nonbeneficial in older patients because few data exist on symptomatic relief gained after device closure in older patients. Our study provides further evidence that transcatheter device closure of ASD in adults over the age of 40 years is not only safe and effective, but also results in symptomatic relief by improving functional class and 6MWT distance with favorable cardiac

Figure 1. Improvement in 6MWT

Improvement in 6-min walk test distance (6MWTD) (p < 0.0001).
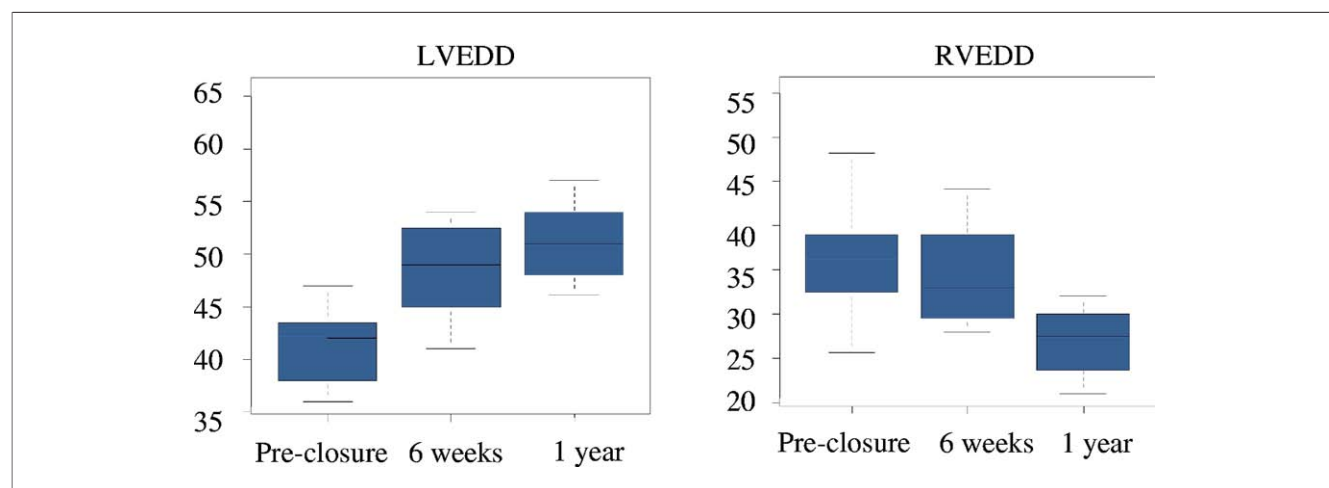
Figure 2. Comparison of LV and RV Diastolic Dimensions

Comparison of left ventricular (LV) (p < 0.001) and right ventricular (RV) (p < 0.001) diastolic dimensions. LVEDD = left ventricular end-diastolic dimension; RVEDD = right ventricular end-diastolic dimension.

remodeling. Our study group has shown significant improvement in both 6MWT distance and NYHA class after ASD closure. The 6MWT is a simple clinical tool, which is useful in the serial evaluation of patient status (29,30). In highly symptomatic patients, it provides information similar to cardiopulmonary exercise testing and has an independent prognostic value (31). Similarly, NYHA functional class is also a predictor of survival in heart failure patients (32).

Our study group mostly had less than average mental and physical health scores, and this reflects the compromised functional status at baseline. Both of these scores showed significant improvement over the 1-year period.

We demonstrated that despite longstanding RV dilation from volume overloading, there is still potential for improvement in RV size and possible improvement in functions (33) even at an advanced age. Closure of ASD resulted in cardiac remodeling with a significant reversal of the right to left volumetric imbalance. These changes were evident within a few weeks following closure and continued at 1 year. Pascotto et al. (10,34) has shown that cardiac remodeling starts very shortly after transcatheter ASD closure in relatively young populations (mean age 22 ± 18 years) and that most of the cardiac remodeling appeared within a few weeks of closure. Conversely, in our older study cohort (median age 68 years) we observed that most of the improvement in RV size took place beyond 6 weeks from ASD closure.

Left ventricular systolic function also improved soon after closing the ASD and removing the RV volume overload. In patients with an ASD, shunting of blood into the right heart invariably affects LV filling, akin to a "steal phenomenon." Our results support the phenomenon of ventricular interdependence (35) associated with RV volume overload and the "reverse Bernheim's effect" in which the septum bulges into the LV cavity leading to impaired LV filling. Following device closure, left to right shunt is abolished and

Table 3. Changes in RV Echocardiographic Parameters

	Pre-Closure (n = 23)	6 Weeks (n = 23)	1 Year (n = 22)	p Value
RVDD, mm	36 ± 8	34.2 ± 6.3	26.9 ± 4.5	<0.0001
RV inlet, mm	48 ± 8.1	45.6 ± 9.8	33 ± 4.5	<0.0001
RA volume, ml	126.1 ± 62.4	80.2 ± 45.5	58.9 ± 18.6	0.0004
TAPSE, mm	21.8 ± 5.7	23 ± 4.6	23 ± 3.2	0.51
DTI RV, cm/s				
s	13.6 ± 2.8	12 ± 3.3	12.9 ± 3.3	0.09
e	9.1 ± 2.5	8.9 ± 2.5	9.8 ± 2.9	0.61
a	15 ± 3.2	13.2 ± 5.3	12.4 ± 3.3	0.03

a = atrial wave; DTI = Doppler tissue imaging; e = early wave; RA = right atrium; RV = right ventricle; RVDD = right ventricular diastolic dimension; s = systolic wave; TAPSE = tricuspid annular plane systolic excursion.

Table 4. Changes in LV Echocardiographic Parameters

	Pre-Closure (n = 23)	6 Weeks (n = 23)	1 Year (n = 22)	p Value
LVEDD, mm	41.4 ± 4.4	48.4 ± 5.2	51 ± 4.2	<0.0001
LVESD, mm	26.8 ± 3.4	28.1 ± 4	30.8 ± 4.5	0.0001
LV inlet, mm	38 ± 3.6	39.4 ± 3.2	43 ± 2.8	<0.0001
LVEF, %	64.9 ± 8.2	76.4 ± 8.1	82 ± 6.1	<0.0001
LA volume, ml	84.3 ± 37.4	80.9 ± 34.6	82.6 ± 34.1	0.53
MAPSE, mm	16.8 ± 3.5	14.9 ± 3.7	14.5 ± 2.6	0.04
DTI LV, cm/s				
s	11.9 ± 3.3	9.5 ± 2.5	9.8 ± 2.3	0.10
e	9.9 ± 2	8.6 ± 1.9	9.2 ± 2	0.33
a	12.3 ± 2.9	11.2 ± 3.2	10.4 ± 3.1	0.01

LA = left atrium; LVEDD = left ventricular end-diastolic dimension; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic dimension; MAPSE = mitral annular plane septal excursion; other abbreviations as in Table 3.
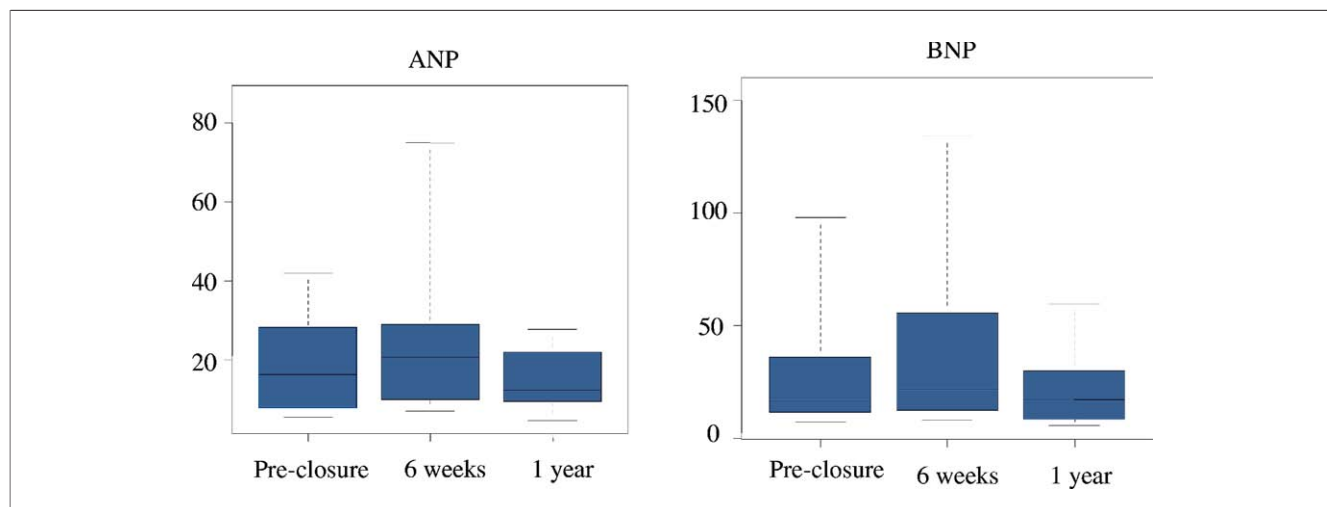
Figure 3. Change in ANP and BNP Over 1 Year

Change in atrial natriuretic peptide (ANP) (p = 0.11) and brain natriuretic peptide (BNP) (p = 0.14) levels over 1 year.

LV filling is improved resulting in an increase in LV dimensions and ejection fraction. A similar trend was found in a recently published study (36). The improvement in LV function was most marked in the first 6 weeks after ASD closure, suggesting that LV remodeling occurs early and plateaus thereafter (37).

Improvements in LV function are likely to be a major determinant of the early improvement in NYHA functional class seen after ASD closure. It is of interest that the improvement in LV size and function appears to occur earlier than in the RV. This may suggest that LV remodeling is independent of RV remodeling.

Schubert et al. (38) have shown that ASD closure in some elderly patients may be associated with a transient increase in left atrial pressure and subsequent pulmonary edema due to an underlying "stiff" LV. However, in our cohort, no cases of pulmonary edema occurred and no significant new arrhythmias were noted during the 1-year follow-up. Similarly no patient developed signs of diastolic dysfunction or mitral regurgitation following ASD closure. Arrhythmia persisted in all patients, when present before the procedure.

No major adverse cardiovascular events related to the procedure were observed in the first 3 months after closure in our patients, which is in contrast to what has been reported for surgical ASD closure in patients >40 years of age (39). In our study, an 81-year-old man died 24 weeks after ASD closure, of causes that were unrelated to the procedure. His ASD was 21 mm in size and was closed with 24-mm ASO device with no technical difficulty. He was in NYHA class III before the closure. He was last reviewed 18 weeks before his death. At that time, he was in NYHA class II and his health scores had also shown improvement from baseline. Echocardiogram at that time showed a well-placed device without any complications. He had chronic atrial fibrillation and chronic renal failure and had been on hemodialysis for the last 4 years. A necropsy examination was not performed, and his death was presumed to have been caused by myocardial infarction.

Study limitations. This was a nonrandomized single-center cohort study, on a relatively small group of consecutive patients undergoing percutaneous ASD closure. Larger, randomized comparisons are required to establish the efficacy of ASD closure in this older adult population.

Conclusions

Our data demonstrate that transcatheter ASD closure is technically feasible and results in favorable cardiac remodeling and significant improvement in functional class and QOL in older patients.

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