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[Original article]

Transcatheter device closure of atrial septal defects in patients above age 60

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Background Closure of an atrial septal defect (ASD) mostly causes reverse remodelling of the right heart, a decrease in pulmonary artery pressures (PASP), and improves functional capacity. However, abolition of the left-to-right shunt may be unfavourable in older patients. This study aimed at evaluating patients older than 60 years who underwent ASD closure.

Methods and results Forty-seven patients (mean age 69 ± 5 years, 19.1% male) with ASD type secundum who underwent transcatheter device closure were included. Echocardiographic data before and after closure were obtained. Follow-up data until the last follow-up visit were retrieved. Age-, gender- and BMI-matched controls were selected.

Before closure, ASD patients had a higher right ventricular end-diastolic diameter (RVEDD), right (RA) and left atrial (LA) dimensions, and PASP when compared to controls. After closure, RVEDD and PASP decreased whereas LVEDD and E/A-ratio increased. RVEDD, PASP, LA dimensions, left ventricular ejection fraction (LVEF) and E/A-ratio were higher than controls. NYHA class improved significantly after ASD-closure. During a median follow-up time of 3.3 years, 6 patients died and 16 were hospitalized because of cardiac events.

Conclusion Device closure in the elderly improved functional capacity, with a decrease, but not a normalization of RV dimensions and PASP, and an increase in LV dimensions, EF and mitral E/A-ratio. Atrial arrhythmias and coronary ischaemic events are common in this population.

Keywords *Atrial septal defect – Amplatzer septal occluder – diastolic function – elderly patients.*

INTRODUCTION

Atrial septal defect (ASD) type secundum is a relatively common congenital heart defect, with an estimated birth prevalence of 1.49 per 1000 and an estimated survival into adulthood of 98%[1,2].

The left-to-right shunt results in a chronic volume overload of the right heart that eventually may lead to increased morbidity (heart failure, arrhythmia, pulmonary hypertension) and mortality[3-7]. Compared to the surgical procedure, transcatheter closure of an ASD causes a faster haemodynamic improvement and fewer complications[8,9]. Therefore it is the treatment of choice in patients who are at increased risk for surgery, particularly older patients. However, there have been reports of procedure-induced heart failure, presumably because of increased LV filling pressures after ASD closure due to an age-related LV diastolic dysfunction[10-12]. Because of differences in ventricular compliance, duration of volume overload and the development of pulmonary vascular lesions, the haemodynamic effects of defect closure may be different in the elderly[13]. Therefore, this study aimed at evaluating patients older than 60 years of age before and after ASD closure.

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METHODS

Patient selection

Patients were selected from the adult congenital heart disease database of our hospital. All patients with an

ASD type secundum who underwent transcatheter device closure after the age of 60 years with an Amplatzer septal occluder (AGA Medical Corp., Golden Valley, MN) between April 2000 and February 2011 were included in the study. Indication of device closure was a haemodynamically significant secundum ASD defined by the presence of right heart dilatation and/or a Qp:Qs > 1.5:1. Patients with device closure other than the Amplatzer septal occluder and patients with chronic atrial fibrillation were excluded. A database of echocardiographic variables on healthy controls is available, which consists of 378 healthy, sedentary adults between 16 and 94 years. Blinded for the echocardiographic results, ASD patients were matched according to age, gender and body mass index (BMI) using this database of healthy controls. The study was approved by the institutional review board of the University Hospitals Leuven.

Data collection

Records of the selected patients were reviewed. Demographic, clinical, electrocardiographic and echocardiographic data were obtained from original case notes, echo protocols and reports of the interventional procedure. Parasternal long-axis M-mode was used to measure posterior wall (PW) and interventricular septum (IVS) thickness. In an apical four-chamber view, the right ventricular (RVEDD), left ventricular end-diastolic diameter (LVEDD), right atrial (RA) and left atrial (LA) dimensions were obtained. Left ventricular ejection fraction (LVEF) was measured using Simpson's biplane method. Pulmonary artery systolic pressure (PASP) was estimated using the Bernoulli equation (four times the tricuspid regurgitation (TR) peak velocity squared). Peak velocity during early diastole (E) and during atrial contraction (A), ratio of E/A, and mitral E deceleration time were obtained from mitral inflow patterns. Regurgitation of mitral, tricuspid and aortic valve was graded semi-quantitatively using colour-Doppler flow mapping on a scale from 0/4 to 4/4. All echocardiographic data were collected prior to the procedure, 1 day and 1 month after the procedure.

Post-procedural events (arrhythmias, coronary ischaemic events, events related with valvular heart disease, hospitalizations for heart failure) and deaths were reviewed until the last follow-up visit.

Statistical analysis

Descriptive data for continuous variables were reported as the mean ± SD. Descriptive data for discrete variables are presented as frequencies. Between-group differences (controls versus patients) were compared using an unpaired *t*-test; a paired *t*-test was used to compare values before and after closure. Frequencies between controls and patients were compared using the chi-square test; differences in pairwise distribution before and after closure were calculated by the Wilcoxon's signed rank test. Uni- and multivariate linear regression analysis was performed to assess the relationship with PASP after device closure of the ASD. All tests were two-sided. A *P*-value of less than 0.05 was considered statistically significant. Analysis was performed using SPSS (version 16.0) for windows.

RESULTS

Baseline characteristics and procedural variables

Forty-seven patients with ASD-type secundum were included. Mean age at repair was 69 ± 5 years (range 60-81 years). Patient characteristics are summarized in table 1. Baseline systolic blood pressure (SBP) was slightly higher in the control group when compared to the ASD group ($P = 0.005$). Transcatheter closure was successful in all patients without any significant procedural complications. Complete occlusion immediately after procedure was achieved in 96% of the patients.

Clinical and echocardiographic data before and after ASD closure

NYHA class improved significantly after ASD closure ($P = 0.019$). Before closure, RVEDD, RA dimensions, and PASP were higher in ASD patients when compared to controls. LA dimensions were higher, whereas LVEDD, LVEF and E/A ratio were similar in both groups (table 2). After ASD closure, RA dimensions decreased to values similar to controls. RVEDD (at 1 month) and PASP remained higher when compared to controls. LVEDD, LVEF, LA dimension and E/A ratio were higher when compared to matched controls (table 2).

Univariate analysis indicated that the degree of tricuspid regurgitation ($P < 0.0001$) and PASP ($P < 0.0001$) before and the degree of tricuspid regurgitation ($P = 0.010$) after ASD closure were related with PASP after ASD closure. Multivariate analysis showed that the degree of tricuspid regurgitation ($P = 0.010$) and PASP ($P < 0.0001$) before closure were independently related with PASP after ASD repair (figure 1).

Co-morbidity and outcome

There were several patients with cardiovascular co-morbidity. Medically treated arterial hypertension was present in 70% of the patients; coronary artery disease in 45%.

Table 1 General characteristics of patients and controls (matched for age, gender, BMI)

	Controls	Patients	P-value
No. of patients	47	47	-
Age (years)	69 ± 5	69 ± 5	0.985
Male gender (%)	19.1	19.1	-
BMI (kg/m^2)	26.9 ± 5.5	26.3 ± 4.8	0.658
SBP (mmHg)	153 ± 20	141 ± 20	0.005
DBP (mmHg)	79 ± 12	79 ± 12	0.965
HR (bpm)	72 ± 13	68 ± 9	0.064
Pre-ECG			
PR-duration (ms)	—	180 ± 32	
QRS-duration (ms)	—	105 ± 17	
ASD			
defect size (mm)	—	18 ± 5	
device size (mm)	—	22 ± 6	
Antihypertensive medication (%)			
0	100	29.8	
1	—	38.3	
2	—	23.4	
3	—	4.3	
4	—	4.3	
Coronary artery disease (%)	—	45	

Values are means ± SD, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, Pre-ECG: pre-procedural electrocardiogram.

During a median follow-up of 3.3 years (range 0.0 - 10.0), 22 events occurred. Six patients died, 1 due to severe aortic stenosis, 1 due to late free atrial wall rupture and in 4 the cause of death was unknown. Seven patients presented with late atrial arrhythmias, five with a coronary ischaemic event, 2 with deterioration because of aortic stenosis and 1 was hospitalized because of right heart failure (table 3). Despite the significant co-morbidity, no subject developed pulmonary oedema following the closure of the defect.

DISCUSSION

This study showed that ASD closure in older patients (> 60 years of age) (i) resulted in functional improvement with a decrease, but not a normalization of RV dimensions and PASP, (ii) caused an increase in LVEDD, LVEF and E/A ratio, and, (iii) post-procedural heart failure appears uncommon despite significant co-morbidity.

Closure of the ASD resulted in reverse remodelling with a significant reduction in RA and RV dimensions, and a decrease in PASP. However, there was no normalization of RV dimensions and PASP and the degree of tricuspid regurgitation did not change significantly one month after closure. These findings are consistent with previous reports investigating an older population

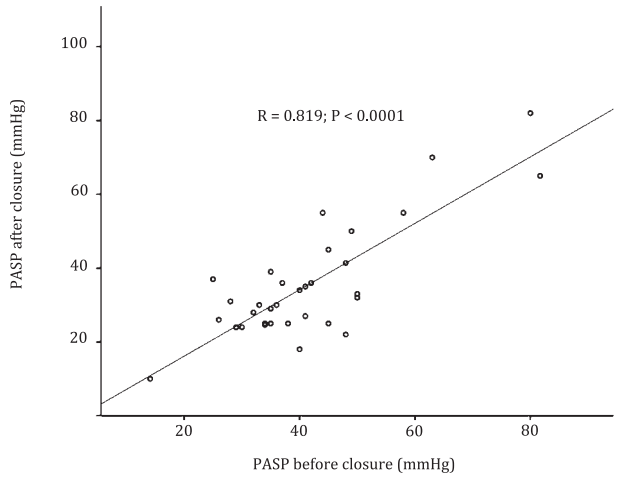

Fig. 1 Relationship between PASP before and after ASD closure

showing that late ASD repair results in incomplete RV remodelling without normalization of PASP[14-18]. As pulmonary artery pressure is determined by flow and resistance, a persistently elevated PASP after closure suggests the presence of pulmonary vascular lesions with increased pulmonary vascular resistance[13,19]. Therefore, given the close correlation between PASP before and after closure, abnormal PASP values before repair should be taken into account as they cannot be solely attributed

Table 2 Clinical and echocardiographic parameters: comparison with controls and effect of ASD-repair

	Controls	Pre-closure	Post 24 h	Post 1 month
Clinical data				
NYHA I (%)	—	34	—	69.7*
NYHA II (%)	—	46.8	—	21.2*
NYHA III (%)	—	19.1	—	9.1*
Echocardiographic data right ventricle				
RV end diastolic diameter (mm)	33.8 ± 5.8	45.2 ± 6.7 ¥	37.0 ± 13.3 *	40 ± 7.4 *¥
RA diameter (mm)	48.8 ± 6.4	55.8 ± 8.3 ¥	53.8 ± 9.5 *	51.7 ± 8.4*
PA systolic pressure (mmHg)	24.5 ± 6.4	41.4 ± 14.5 ¥	35.9 ± 17 *¥	40.4 ± 19.1¥
TR 0/4 (%)	34.8	4.7	—	3.4
1/4 (%)	47.8	25.6	33.3	48.3
2/4 (%)	17.4	39.5	40	27.6
3/4 (%)	—	27.9	22.2	13.8
4/4 (%)	—	2.3	4.4	6.9
Echocardiographic data left ventricle				
LV end diastolic diameter (mm)	41.8 ± 4.5	42.1 ± 6	44.9 ± 7.4 *¥	46.3 ± 5.4 *¥
LA diameter (mm)	35.6 ± 5.1	50.2 ± 11.2 ¥	54.7 ± 11.3 ¥	53.7 ± 8¥
IVS diameter (mm)	11.3 ± 2.4	11.2 ± 2.4	10.6 ± 2.5	11.2 ± 2.5
PW diameter (mm)	10.1 ± 1.7	10.4 ± 2.1	10.0 ± 2.0	9.7 ± 2.2
Ejection fraction (%)	62.8 ± 3.4	63.4 ± 7.6	65.5 ± 7.9 v	67.8 ± 10.1¥
Mitral inflow pattern				
E mitral (cm/s)	68.2 ± 18.7	67.5 ± 22.1	78.3 ± 24.5 ¥	82.3 ± 25.3¥
A mitral (cm/s)	81.4 ± 21.3	72.2 ± 16.2	65.4 ± 18.6 ¥	68.4 ± 18.3¥
E/A mitral	0.87 ± 0.28	0.90 ± 0.22	1.31 ± 0.56 ¥	1.27 ± 0.62 *¥
Mitral E deceleration time (ms)	243 ± 65.3	201 ± 47.8 ¥	218 ± 52.7	230 ± 46.9
MR 0/4 (%)	34.8	11.4	—	10.0
1/4 (%)	47.8	52.3	47.7	40.0
2/4 (%)	17.4	27.3	43.2	40.0
3/4 (%)	—	9.1	6.8	10.0
4/4 (%)	—	—	2.3	—
AR 0/4 (%)	82.6	42.4	50	51.9
1/4 (%)	8.7	39.4	34.2	29.6
2/4 (%)	8.7	18.2	15.8	14.8
3/4 (%)	—	—	—	3.7

Values are means ± SD; RV: right ventricle, RA: right atrium, PA: pulmonary artery, TR: tricuspid regurgitation, LV: left ventricle, LA: left atrium, IVS: interventricular septum, PW: posterior wall, E: peak mitral inflow velocity during early diastole, A: peak mitral inflow velocity during late diastole, MR: mitral regurgitation, AR: aortic regurgitation.

*** $P < 0.05$, compared to before ASD repair**

¥ $P < 0.05$, compared to controls

to increased flow in older patients. Interestingly, PASP was also related to the degree of tricuspid regurgitation (even after controlling for RV EDD), a mechanism which may protect the RV against pressure loading.

Abolition of the left-to-right shunt resulted in increased LVEDD and LVEF, indicating ventricular interdependence with improved LV filling[15,17,20]. LA dimension, however, remained elevated. This favourable LV remodelling appears to be an early post-interventional effect and to some extent independent of RV remodelling, as reported previously[17,21]. Indeed, a major concern in some older patients is the risk of acute left ventricular dysfunction immediately after transcatheter closure, leading to symptomatic pulmonary oedema[11,22]. Unlike the effect of ASD closure in children and younger adults[23-25], it appears that some older patients are at risk of developing high left ventricular filling pressures after ASD closure due to an age-related LV diastolic dysfunction[12].

In this study, before ASD repair, mitral E deceleration time (DT) was shorter and E/A ratio similar when compared to controls. However, after ASD repair, DT was similar, whereas E/A ratio increased and became higher when compared to controls. A relatively impaired LV

compliance, because of adverse ventricular interdependence caused by RV volume overload before closure, may lead to a shorter DT[26]. In this study, LV filling appears to improve after ASD repair with an increase in E/A ratio. The values observed in our study are not compatible with restrictive filling patterns and there were no cases of left ventricular heart failure after closure, although patients had significant co-morbidity, reinforcing the fact that this may be an uncommon complication[27]. However, if there is suspicion of severe diastolic left ventricular dysfunction in an older patient, a temporary balloon occlusion of the defect should still be performed to identify a masked left ventricular restriction[10]. If mean left atrial pressure increases above 10 mmHg during ASD occlusion, intravenous anti-congestive conditioning therapy seems to be effective in preventing congestive heart failure immediately after ASD closure[22].

Finally, older ASD patients have significant co-morbidity. As expected, patients more frequently developed atrial arrhythmias after closure[7,28,29]. Coronary artery disease is also quite frequent in this age group with ASD. Therefore, co-morbidity should always be considered and investigated when transcatheter ASD closure is performed in an older population.

Study limitations

This paper has the limitations of a retrospective study design. Selection bias may have occurred as this was a single-centre study and patients with chronic atrial fibrillation were excluded. Interobserver variability of echocardiographic measurements was not performed. There were no invasive haemodynamic measurements available after ASD closure. Echocardiographic evaluation did not include tissue Doppler Imaging (TDI) data, which is a major limitation in evaluating LV myocardial relaxation, filling pressures and regional function. This study provides no long-term results.

Table 3 Follow-up patients post-closure ASD

Events (total)	22
1. Arrhythmias	7
– Atrial fibrillation (4)	
– Atrial flutter (2)	
– IART (1)	
2. Coronary artery disease	5
– CABG (1)	
– PTCA (3)	
3. Aortic stenosis	2
– Surgery (1)	
4. Right heart failure	1
5. Atrial rupture	1
6. Death	6
– Aortic stenosis (1)	
– Atrial rupture (1)	
– Unknown cause (4)	

IART: intra-atrial re-entry tachycardia, CABG: coronary artery bypass graft, PTCA: percutanuous transluminal coronary angioplasty.

CONCLUSIONS

Transcatheter device closure in the elderly causes an improvement in functional capacity, with a decrease, but not a normalization of RV dimensions and pulmonary artery pressures, and an increase in LV dimensions and EF. Mitral E/A ratio increased after device closure, which suggests normalization of filling patterns. These patients have significant co-morbidity during follow-up, including coronary ischaemic events and atrial arrhythmias.

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