Transcatheter device closure of atrial septal defects in patients aged 40 years and older

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Objective. To evaluate the safety and effect of transcatheter device closure in ostium secundum atrial septal defects (ASD II) in patients aged 40 years and older.

Methods. Retrospective single-centre study concerning 47 consecutive ASD transcatheter occlusion procedures performed between January 1999 and December 2008. Electrocardiography, echocardiography and clinical assessments of the patients were conducted pre- and post-intervention and at follow-up.

Results. Of the 130 patients who were referred for interventional ASD closure, 47 were 40 years and older and all of them actually had the device inserted. There were no major complications during the intervention. Mean follow-up time was 15 ± 15 months. During follow-up, three patients needed surgical reintervention because of device embolisation ($n=2$) or dislocation ($n=1$). Of the patients with severe right ventricular (RV) dilatation, more than half (58%) had no or mild dilatation at last follow-up. Reduction of RV dilatation was not related to age. Pulmonary hypertension was present in 63% before the procedure and was reduced to 38% at follow-up. NYHA class improved in all age groups, also in

patients over 60 years of age. In two of the three patients who died during follow-up, no cause of death could be established, but both had responded well to treatment regarding the echocardiographic and clinical findings.

Conclusion. Transcatheter device closure of ASD is a successful and effective treatment, also for patients aged 40 years and older. Patients showed regression of right ventricular enlargement and an improvement in functional class. (Neth Heart J 2010;18:537-42.)

Keywords: Atrial Septal Defect; Transcatheter Closure Device, Follow-up

Patients with a secundum atrial septal defect (ASD) are often asymptomatic until the second-to-third decade of life. The most common presenting symptoms at adult age are palpitations and exercise intolerance manifested as either exertional dyspnoea or fatigue, which increased with age.¹ More serious complications are typically seen in older patients with previously unrecognised ASDs who have been exposed to large left-to-right shunting for a long period. This prolonged shunting may cause cardiac dilatation and subsequent right heart failure. Atrial arrhythmias may also occur.²

Patients with a haemodynamically significant ASD could be offered medical treatment or elective closure of the ASD. Surgical repair of ASDs in middle-aged and elderly patients increases long-term survival and decreases functional deterioration when compared with medical therapy. Surgery also appears to prevent deterioration of the patients in NYHA functional class.³ While surgical correction has been practised for many decades with very good long-term results, percutaneous device closure of secundum ASD is accepted as an alternative to surgical closure provided the location of the defect is favourable (centrally placed). Transcatheter closure seems to have a similar efficacy in the long term^{4,5} but it is less invasive, shows less complications,⁶ requires shorter hospital stay and is less expensive.⁷

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Figure 1. Right ventricular dimensions before treatment and at follow-up.

Besides the device's proven safety, the transcatheter procedure avoids a thoracotomy and thereby a scar and the need for longer rehabilitation, which makes device closure very attractive to patients.^{4,5,7-12}

However, the treatment of an ASD in the older age group is still controversial.¹³ Some early studies were interpreted to show no major benefit if closure was performed in adulthood.^{14,15} Although, based on more recent analysis, it would be appear that ASDs should be closed when they are identified, irrespective of the patient's age and symptoms.^{4,7,16-19}

The aim of this study was to evaluate the results of transcatheter closure of ASDs in patients from 40 years of age with emphasis on procedure-related complications, right ventricular dimensions and functional capacity.

Methods

Study population

Between January 1999 and December 2008, 130 adult patients underwent percutaneous ASD closure of whom 52 patients were ≥ 40 years at the time of closure. Indications for referral were clinical symptoms of dyspnoea, fatigue ($n=36$) and/or palpitations ($n=28$) in combination with a left-to-right shunting defect with right-sided heart dilatation discovered by transthoracic (TTE) and/or transoesophageal (TEE) echocardiogram. For the purpose of this study we contacted all patients who were still alive and all of them gave informed consent for this study and to participate in the follow-up questionnaire.

Historical data

The following items were collected: gender, date of birth, age, height and weight, the presence of

diabetes mellitus, hypertension, stroke/TIA, heart failure in the past, smoking and medication. Heart rhythm before closure was classified as sinus rhythm, paroxysmal atrial fibrillation or flutter and persistent atrial fibrillation or flutter. Echocardiographic data were obtained: the right ventricular (RV) dimensions (normal and mildly, moderately or severely dilated) and tricuspid regurgitation (absent, mild, moderate or severe).²⁰ Pulmonary hypertension was defined as a tricuspid regurgitation flow velocity $>2.8 \text{ m} \cdot \text{s}^{-1}$, without the presence of pulmonary stenosis. Associated cardiac abnormalities were documented. The physical condition of patients, which was obtained by anamnesis, was categorised according to the NYHA functional class.

Intervention data use

The following data were recorded: duration of the intervention, use of heparin and anticoagulants during intervention, balloon stretched defect size, the Op/Qs ratio with oxymetry using the Fick principle, the tricuspid regurgitation flow velocity and type and size of device. Presence of a residual shunt the day after device placement assessed by TEE, use of anticoagulants after the intervention and the occurrence of complications during the intervention were also recorded. The complications are divided in major and minor according to the classification scheme used by Khairy et al.²¹

Follow-up data

For follow-up the patient records were used. Electrocardiograms and echocardiograms were reviewed. Late complications were collected. Status was retrieved by contacting the civil registry. A written questionnaire was sent to obtain information on current clinical condition and the personal experience of the intervention.

Data analysis

Continuous data are expressed as mean $\pm$ standard deviation (SD) and baseline and follow-up was compared by the paired Student's t-test. For the comparison of categorical variables the χ^2 test was used. The level of statistical significance was two-sided and set at $p < 0.05$. Statistical analysis was performed with SPSS version 15.0.0 for Windows.

Results

Of the 52 patients who were referred for interventional ASD closure, 47 patients actually had the device inserted (figure 1). In five patients surgical closure was preferred due to fenestrated defects and very large defects. These patients were excluded from further analysis.

Baseline characteristics are presented in table 1. The mean age at intervention was 58 ± 13 years. All patients included had a single defect. The mean

Table 1. Baseline characteristics of all patients undergoing transcatheter closure of secundum atrial septal defect.

Characteristics	Patients (n=47)
Female sex	37 (79%)
Age at the time of closure (years)	
- Mean (SD)	58±13
- Range	40-79
BMI at the time of closure	
- Mean (SD)	25±4
- Range	18-37
Diabetes mellitus	4 (9)
Hypertension	24 (51)
Pulmonary hypertension	29 (62)
Stroke / TIA	5 (11)
Heart failure	13 (28)
Smoking	13 (28)
Medication usage	
- Oral anticoagulants	13 (26.5)
- Antiplatelet drugs	8 (17)
- Beta-blockers	20 (42.6)
- ACE inhibitors	10 (21.3)
- Diuretics	9 (19.1)
- Statins	5 (10.6)
- Cardiac glycosides	6 (12.8)
- Other medications	23 (48.9)

Values are presented as numbers (%) unless otherwise stated. Age is the age at intervention and is measured in years; SD=standard deviation; BMI=body mass index, TIA=transient ischaemic attack.

size of the defect was 19 ± 5 mm (n=46). The RV was dilated in all patients and 29 patients (63%) presented with TI >2.8 m/s. Mild aortic insufficiency was found in 30% (n=14) and mild mitral insufficiency was found in 62% (n=29) of the patients. Only 23% (n=11) of the patients were in NYHA class I. Table 2 presents more information about electrocardiographic, echocardiographic and NYHA functional class data.

Intervention

All procedures were guided by transoesophageal echo (TEE) or intracardiac echo (ICE). TEE was performed in the patients treated before January 2003 and ICE was performed thereafter, when the AcuNav catheter (Acuson Corporation, Siemens Medical Solutions USA, Inc.) became available. The mean procedure time was 105 minutes $\pm$ 43 (n=44). Over the years, the average intervention

Table 2. Data pre- and post-intervention.

Before intervention

<i>Electrocardiography (n=47)</i>	
- Sinus rhythm	28 (60)
- Paroxysmal AF	14 (30)
- Continuous AF	5 (10)
<i>Echocardiography</i>	
RV dilatation (n=47)	
- Absent	0 (0)
- Mild	5 (11)
- Moderate	12 (25)
- Severe	30 (64)
TI (n=47)	
- Absent	5 (11)
- Mild	19 (40)
- Moderate	19 (40)
- Severe	4 (9)
TI velocity (n=46)	2.9 ± 0.6
PTI (n=46)	36 ± 13
PRV (n=46)	43 ± 15
Pulmonary hypertension	29 (63)
<i>NYHA (n=47)</i>	
- NYHA I	11 (23)
- NYHA II	16 (34)
- NYHA III	20 (43)

Follow-up

<i>Electrocardiography (n=41)</i>	
- Sinus rhythm	24 (59)
- Paroxysmal AF	10 (24)
- Continuous AF	7 (17)
<i>Echocardiography</i>	
RV dilatation (n=34)	
- Absent	9 (26)
- Mild	14 (41)
- Moderate	9 (26)
- Severe	2 (7)
TI (n=40)	
- Absent	11 (28)
- Mild	16 (40)
- Moderate	11 (28)
- Severe	2 (4)
TI velocity (n=30)	2.7 ± 0.7
PTI (n=30)	31 ± 16
PRV (n=34)	37 ± 16
Pulmonary hypertension	13 (38)
<i>NYHA (n=41)</i>	
- NYHA I	26 (63)
- NYHA II	13 (32)
- NYHA III	2 (5)
- NYHA IV	0 (0)

Data are presented as numbers (percentages) or mean $\pm$ standard deviation. Follow-up data are obtained from last follow-up. AF=atrial fibrillation, RV=right ventricle, TI=tricuspid regurgitation, PTI=pressure difference over the tricuspid valve, PRV=right ventricular systolic pressure, PHT=pulmonary hypertension, NYHA=New York Heart Association.

duration decreased from 133 ± 36 to 78 ± 30 minutes. Of the 47 interventions, nine (19%) were performed under general and 38 (81%) under local anaesthesia. Patients received full heparinisation during the procedure and from January 2004 onwards patients were also preloaded with clopidogrel. Qp:Qs was 2.3 ± 0.7 , the maximal stretched defect size measured with balloon sizing was 20 ± 6 mm and the mean TI velocity was 2.9 ± 0.4 m/s. An Amplatzer ASD occluder (AGA Medical Corporation, Golden Valley, MN) was used in 45 cases with mean size of 24 ± 6 mm. One patient received a Starflex (NMT Medical, Inc., Boston) 28 mm occluder and one patient an Amplatzer 18 mm PFO occluder. A 24-hour follow-up TTE was performed showing a small residual shunt in 16 (34%) and a large residual shunt in one patient (2%). The defects were closed completely in 30 patients (64%). All patients received six months of aspirin treatment after the procedure. As a result of a shift in anticoagulation regime, six months of clopidogrel was added to the aspirin treatment from January 2004 ($n=33$). When patients had previously been taking oral anticoagulants because of atrial arrhythmias, they continued this regime after the intervention and the antiplatelet medication was not given.

Immediate complications

Device closure was technically successful in all 47 patients. During the procedure there were no major complications such as mortality or embolisations. Minor complications occurred in four patients (9%): one patient developed a femoral arteriovenous fistula which required closure and three patients developed transient atrial arrhythmias during the procedure which required electrical cardioversion. Four additional patients had minor bleeding at the puncture site post intervention.

Follow-up

The mean follow-up time was 15 ± 15 months. Three patients died during follow-up, at the ages of 79, 73 and 67, one, four and seven years after the intervention, respectively. The 79-year-old patient who died in the first year after treatment was taking oral anticoagulants because of atrial arrhythmias. He died suddenly without a known cause. At his last follow-up this patient had mild dilatation of his right heart and there was no residual shunt. Also in the second patient who died suddenly four years after treatment, follow-up had showed a trivial residual shunt and a mild right ventricular dilatation. This patient was not on oral anticoagulants. The third patient died because of subdural haematoma after head trauma. This patient was taking oral anticoagulants because of atrial arrhythmias.

Three patients (6%) needed surgical reintervention. Two of them had embolisation of the device to the

Figure 2. New York Heart Association (NYHA) class before treatment and at follow-up.

pulmonary artery detected at two and seven weeks of follow-up. In the third case, the device was not well positioned with a large residual shunt requiring surgery at 20 months of follow-up. The devices were removed surgically without complications and the defects were closed successfully. Follow-up data on these three patients were obtained until the date of surgery.

Electrocardiography

Electrocardiographic findings were recorded in 41 patients and showed sinus rhythm in 24 (59%) and atrial fibrillation in 17 (41%). Changes in rhythm before and after intervention are described in table 2.

Echocardiography

Echocardiographic results before and after catheterisation are presented in table 2. Of the patients with severe dilatation before intervention, 58% ($n=11/19$) had no dilatation to mild dilatation at follow-up and 37% ($n=7/19$) had moderate dilatation. Severe dilatation persisted in only one patient (5%). No predictive value of age at intervention was found on reduction in RV dimension and in pressure difference over the tricuspid valve ($p=0.2$ and 1.0 respectively). Shifts in RV dimensions are presented in figure 1. TI velocity of >2.8 m/s decreased from 63% before to 38% after the procedure.

NYHA functional class

The questionnaires were answered by 88% of the patients: 63% were asymptomatic at last follow-up. A comparison between NYHA class before and after intervention is presented in figure 2. There was no association between age and improvement in NYHA functional class ($p=0.2$).

Discussion

Controversy still exists regarding closure of ASD in the older age group.¹³ These patients had had their ASD for a very long time and discussion persists whether an effect on symptoms or improvement in RV dimension can be expected. However, we found a great reduction in RV dimension after device closure. Nearly all patients, regardless of age at closure, showed improvement. In our study, age at intervention is also not related to the degree of improvement in the NYHA class or to the degree of decrease in pressure over the tricuspid valve.

Only a few studies have reported percutaneous ASD closure in patients aged over 40 years.^{11,16,17} Also these studies showed satisfactory results, with substantial reduction of symptoms, an improvement in functional and exertional capacity and significant haemodynamic improvement. Other authors found that age at closure did not significantly influence the potential to reduce RV dimension.^{14,18,19}

Also patients who are asymptomatic or mildly symptomatic should be offered defect closure, because the natural course of untreated atrial septal defects often leads to a shortened life expectancy compared with healthy subjects.²² Dyspnoea on exertion occurs in 30% of patients by the third decade and in over 75% of patients by the fifth decade.¹ If left unrepaired, the majority of patients will experience symptoms and will have a shorter life span compared with patients who undergo closure.¹¹ Brochu et al. showed that even adult ASD patients classified as asymptomatic showed a significant increase in their functional capacity after percutaneous closure. Although in our study 57% of the patients were in NYHA class I or II preclosure we observed an improvement in exercise capacity and a decrease in RV size with our patient population being even older.

No major complications occurred during the hospital stay, which is consistent with the reports in literature.²² The percutaneous approach for ASD closure in elderly patients may have reduced periprocedural morbidity and mortality compared with surgical approach.^{16,23} However, during follow-up two cases of device embolisation without clear acute clinical symptoms and one case of not well positioned device have been recorded warranting for surgical intervention. Literature indicates that malposition and embolisation are indeed the commonest reasons for surgical reintervention.²⁴ In our study, three patients died during follow-up. All of them were over the age of 65 years. The patient who died in the first year after treatment had long-standing volume overload of the right heart and died suddenly. He was on oral anticoagulants because of atrial arrhythmias. There was no cause of death established, thus it can not be excluded that

the death was a result of the treatment. However, catheterisation and follow-up were without any complications. Moreover, this patient responded very well to treatment. At last follow-up this patient had mild dilatation of his right heart and there was no residual shunt. Before treatment this patient had severe dilatation and severe atrial shunt. The other two patients died years after treatment, and also they had no complications during or after treatment and responded very well to the treatment; they both had showed a reduction from severe to mild right heart dilatation.

Conclusion

Transcatheter device closure of ASD is a successful and effective treatment for patients of 40 years of age and older. The great majority of older patients experienced regression of RV volume and a clear improvement of the NYHA class. These improvements are present irrespective of age at closure or preclosure RV dimension. Even patients who were asymptomatic or mildly symptomatic before the procedure showed benefit from defect closure. ■

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