ORIGINAL ARTICLE

Short and Mid-Term Outcomes of Percutaneous Ostium Secundum Atrial Septal Defect Closure in a Single-Centre Adult Population within the National Program of Percutaneous Procedures in Adults with Congenital Heart Disease

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ABSTRACT

Background. Atrial septal defect (ASD) is the most common congenital heart defect diagnosed in adulthood, causing a left-to-right shunt with subsequent right ventricle (RV) volume overload, increased pulmonary flow and overloading of the pulmonary circulation. Surgical or percutaneous closure of ASD is associated with reverse right heart remodelling, improved functional class and exercise capacity, irrespective of age. In the present study we aimed to assess the short and mid-term outcomes of ASD closure in terms of hemodynamic response, cardiac remodelling and clinical data in a population of adult patients with ostium secundum ASD eligible for percutaneous closure.

Methods. Patients with ostium secundum ASD referred to our institution from November 1st 2017 to September 30th 2021 were assessed for percutaneous closure within the National Program for percutaneous procedures in adults with congenital heart disease. All patients underwent a clinical and echocardiographic evaluation; demographics and biological data were collected. A transoesophageal echocardiography was available for all patients in order to assess the feasibility of percutaneous closure.

Results. The study population included 37 adult patients (29 women, mean age 43.5 ± 14.4 years) and 33 age- and gender-matched healthy volunteers. Eight patients had a history of supraventricular arrhythmias. The ASD patients had a significant RV and right atrial (RA) dilation, a higher pulmonary artery (PA) size and systolic pressures, a smaller left ventricle diastolic diameter. At least 1 follow-up visit data was available in 23 patients and the mean follow-up was 12 ± 8 months. The functional class significantly improved after ASD closure; 4 patients presented with supraventricular arrythmias after ASD closure. Data showed a significant decrease in RV and RA size after the ASD closure, the RV longitudinal function parameters also decreased. At the follow-up visit, the PA trunk diameter and the systolic PAP were significantly lower (p <0.001) compared with the pre-procedural values. The LV end-diastolic diameter increased after ASD closure. The reverse remodelling of the right chambers was similar in patients aged less and more or equal to 60 years, but the decrease in estimated systolic PAP was higher in older patients.

Conclusion. In adult patients with ostium secundum ASD, percutaneous closure leads to significant changes in functional class and echocardiographic parameters of right and left heart size and RV function and in pulmonary artery size and pressure. The beneficial effect seems to be similar in patients younger and older than 60 years.

Keywords: atrial septal defect, percutaneous closure, right ventricle, pulmonary artery.

REZUMAT

Premise. Defectul septal interatrial (DSA) este cel mai frecvent defect cardiac congenital diagnosticat la adult, determinând un șunt stânga-dreapta și suprasarcina de volum a ventriculului drept (VD), creșterea fluxului pulmonar și supraîncărcarea circulației pulmonare. Închiderea chirurgicală sau percutană a DSA se asociază cu revers-remodelarea cavităților drepte, ameliorarea clasei funcționale și a capacității de efort, indiferent de vârstă. În acest studiu, ne-am propus să evaluăm rezultatele pe termen scurt și mediu ale închiderii DSA din punct de vedere al răspunsului hemodinamic, remodelării cardiace și efectelor clinice într-o populație de pacienți adulți cu DSA tip ostium secundum eligibili pentru închidere percutană.

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Metode. Pacienții cu DSA tip ostium secundum adresați Institutului de Urgență pentru Boli Cardiovasculare „Prof. Dr. C. C. Iliescu" între 1 noiembrie 2017 și 30 septembrie 2021 au fost evaluați pentru închiderea percutană a DSA în cadrul Programului Național pentru proceduri percutane la pacienți adulți cu boli cardiace congenitale. Toți pacienții au fost evaluați clinic și ecocardiografic și datele demografice și biologice au fost colectate. O ecocardiografie transesofagiană a fost disponibilă pentru fiecare pacient pentru evaluarea fezabilității închiderii percutane.
Rezultate. Populația de studiu a inclus 37 de pacienți adulți (29 de femei, vârsta medie 43,5 ± 14,4 ani) și 33 de voluntari sănătoși similari ca vârstă și sex. 8 pacienți aveau antecedente de aritmii supraventriculare. Pacienții cu DSA prezentau o dilatare semnificativă a VD și a atriului drept (AD), dimensiuni și presiune sistolică crescute ale arterei pulmonare (AP) și un diametru telediastolic mai mic al ventriculului stâng. Cel puțin o vizită de urmărire a fost disponibilă pentru 23 de pacienți și durata medie de urmărire a fost 12 ± 8 luni. Clasa funcțională s-a ameliorat semnificativ după închiderea DSA; 4 pacienți au prezentat aritmii supraventriculare după închidere. Datele au arătat o reducere semnificativă a dimensiunilor VD și AD după închidere; parametrii de funcție longitudinală VD au scăzut. La vizita de urmărire, diametrul AP și PAP sistolică au fost semnificativ mai mici (p <0,001) comparativ cu valorile pre-procedurale. Diametrul VS telediastolic a crescut după închiderea DSA. Revers remodelarea cavităților drepte a fost similară la pacienții cu vârsta mai mică și mai mare de 60 de ani, dar scăderea PAP sistolice estimate a fost mai mare la pacienții mai vârstnici.
Concluzii. La pacienții adulți cu DSA ostium secundum, închiderea percutană determină modificări semnificative ale clasei funcționale și ale dimensiunilor cordului drept și stâng și funcției VD, precum și ale dimensiunilor și presiunii AP. Efectele benefice par să fie similară la pacienții cu vârsta mai mică și mai mare de 60 de ani.
Cuvinte cheie: defect septal atrial, închidere percutană, ventricul drept, artera pulmonară.

INTRODUCTION

Atrial septal defect (ASD) is the most common congenital heart defect diagnosed in adult-hood, accounting for 25-30% of newly diagnosed congenital heart diseases.[1] This defect causes a left-to-right shunt with subsequent right ventricle (RV) volume overload, increased pulmonary flow and overloading of the pulmonary circulation. Thus, the most frequent clinical syndromes encountered in ASD patients are supraventricular arrhythmias, right heart failure and, in a small proportion of patients, different degrees of pulmonary arterial hypertension. Also, the pathophysiology of pre-tricuspid shunts impacts the left heart due to volume unloading and adverse ventricular–ventricular interaction.[2] Surgical or percutaneous closure of ASD is associated with reverse right heart remodelling, improved functional class and exercise capacity, irrespective of age.[3] Even if earlier studies have reported optimal long-term outcomes and normal survival only in younger adults (less than 25 years of age) who underwent ASD closure,[4] more recent data showed that mid to longer term survival is excellent irrespective of age, gender and mode of closure, and similar to matched general population.[5]

In the present study we aimed to assess the short and mid-term outcomes of ASD closure in terms of hemodynamic response, cardiac remodelling and clinical data in a population of adult patients with ostium secundum ASD eligible for percutaneous closure within the National Program for percutaneous procedures in adults with congenital heart disease in a single centre.

METHODS

Patients

Patients with ostium secundum ASD referred to our institution from November 1st 2017 to September 30th 2021 were assessed for percutaneous closure within the National Program for percutaneous procedures in adults with congenital heart disease. A total of 66 patients were assessed for the percutaneous procedure. Of the 66 patients, 2 had too small defects with no indication for closure, 4 had too large defects (> 36 mm) and were referred for surgery, 2 had associated PAH with PVR >3 Wood units and the closure was deferred, and PAH-specific treatment was initiated, 10 underwent percutaneous closure in a different centre, 4 chose surgery, 5 are still waiting for the procedure and 39 underwent percutaneous closure. The procedure was successful in 38 patients; in 1 patient the procedure was aborted due to the instability of the device (the defect's rims were too soft) and 1 patient lacked complete pre-procedure transthoracic echocardiography and was excluded from this study. Written informed consent of the patients was obtained as part of our institutional filing system, and consent regarding the use of collected information for research purposes was signed by all patients.

Indications for ASD closure were the presence of shunt related symptoms and/or echocardiographic signs of right ventricle (RV) volume overload.[6] Patients with significant LV systolic and/or diastolic dysfunction underwent a complete hemodynamic assessment with invasive measurement of PAP and measurement of LV end-diastolic pressure and LA pressure. No patient had a LA pressure more than 10 mmHg.

All patients underwent a clinical and echocardiographic evaluation; demographics, biological data (e.g. BNP levels, haemoglobin level and platelets number) were collected. A transoesophageal echocardiography (TOE) was performed in all patients in order to assess the feasibility of percutaneous closure: ostium secundum ASD, no anomalous pulmonary venous drainage, ASD size <36 mm, all atrial septal rims >5 mm except for the aortic rim.

Transthoracic echocardiography

A transthoracic echocardiography was performed a day prior to the percutaneous closure. Two dimensional echocardiography-derived parameters of RV size (RV basal diameter from RV-focused apical 4C view, RV end-diastolic and end-systolic area) and function (TAPSE, TDI-derived lateral tricuspid annulus S wave velocity, fractional area change), RA size (RA midlateral diameter and end-systolic area), PA size (PA transversal diameter at end-diastole) and estimated pressure (systolic PA pressure using the peak velocity of the tricuspid regurgitation jet, mean PA pressure using the peak velocity of the pulmonary regurgitation jet and the size and respiratory variations of the inferior vena cava), left chambers size (LV end-diastolic and end-systolic diameter, LA antero-posterior diameter and volume, LV systolic (TDI-derived lateral and septal mitral annulus S wave velocity) and diastolic function (E and A waves of the mitral flow, TDE, E/e' ratio) were obtained as recommended by current guidelines.[7,8] Whenever the acoustic window was appropriate, 2D speckle-tracking echocardiography was used to assess RV longitudinal strain as an average value of 6-segments from the RV-focused apical 4C view.

A similar echocardiography study was performed at follow-up (at 1, 3 months, 1 year after the procedure and yearly afterwards). Due to the Covid 19 pandemic during the last 2 years this follow-up schedule was not possible. For this reason, the last follow-up data were used in the present analysis.

A control group of 33 age- and gender-matched healthy volunteers was analysed in order to assess the right and left heart remodelling and function in ASD patients.

Percutaneous ASD closure procedure

Percutaneous closure of the ASD was performed under general anaesthesia using fluoroscopic and 3D-TOE guidance. Prior to the ASD closure, re-measurement of defect size and rims was performed from all the dedicated views in 2D and 3D-derived 2D images (Fig. 3) using the VIVID E95 ultrasound machine (GE, Horten, Norway). The largest ASD diameter was considered and device size was established by adding 4-8 mm to the largest ASD diameter. Balloon-sizing was performed only in 2 cases with floppy rims; this technique, which could have overestimated the ASD size, was not necessary in the other cases due to a good assessment of the ASD diameter by TOE. The deployment of the device was both fluoroscopic and TEE-guided. Percutaneous ASD closure was performed using Cocoon and Lifetech Cera devices. Post-interventional treatment included 100 mg/day of aspirin and 75 mg/day of clopidogrel for 3 months, followed by aspirin monotherapy for up to 5 years.

Statistical analysis

Continuous variables are displayed as mean and standard deviation. The paired-samples t test was used to compare paired continous data. Categorical data are presented as n (%) and differences were compared using Fisher's exact test. Two-sided p value <0.05 was considered statistically significant. Data were analyzed using IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA).

RESULTS

Baseline characteristics of the study group

The study population included 37 adult patients of whom 29 (78.4%) were women. At the time of percutaneous ASD closure, the patients had a mean age of 43.5 ± 14.4 years (range 19 - 68 years). The most frequent symptom was fatigue (28 patients, 75.7%) with 27 patients (73%) in NYHA functional class II and 1 patient (2.7%) in NYHA class III. Nine patients (24.3%) were asymptomatic or exhibited fatigue only at intense exertion (Table 1). Eight patients had a history of supraventricular arrhythmias (7 patients had atrial fibrillation and 1 patient atrial flutter) and 1 patient had persistent atrial fibrillation at the time of ASD closure. Among other comorbidities, 3 patients

Table 1. Baseline demographic, clinical and biological characteristics of the study group (37 adult patients who underwent percutaneous ASD closure

Parameter	Value
Age (years)	43.5 ± 14.4
Gender F/M (n, %)	29/8 (78.4/21.6)
Body mass index (kg/m^2)	26.3 ± 5.2
Body surface area (m^2)	1.78 ± 0.17
Symptoms at presentation (n, %)	28 (75.7%)
Supraventricular arrythmias	9 (24.3%)
NYHA class 0/I/II/III (n, %)	3/6/27/1 (8.1/16.2/73/2.7)
Systolic blood pressure (mmHg)	117 ± 12
Diastolic blood pressure (mmHg)	74 ± 10
Heart rate (bpm)	73 ± 10
Resting O_2 saturation in room air (%)	97 ± 1
BNP levels (pg/ml)	55.7 ± 48.4
Haemoglobin (g/dl)	13.7 ± 1.1

Values are expressed as mean ± standard deviation.
ASD, atrial septal defect; BNP, brain natriuretic peptide; F, female; M, male; NYHA, New York Heart Association; O_2, oxygen.

(8.1%) had coronary artery disease, 1 of the 3 had also moderate aortic stenosis and 1 patient (2.7%) had a history of stroke.

Considering the associated congenital heart defects, 2 patients (5.4%) had an associated valvular pulmonary stenosis (one moderate and one severe) and 1 patient (2.7%) had an aneurysm of the atrial septum. One patient had two ASDs (22/14 mm and 9/7 mm); we chose to close the largest defect with a 26 mm device, the residual shunt through the smallest defect being haemodynamically nonsignificant.

The mean value of the BNP levels was mildly increased: 55.7 ± 48.4 pg/ml (range 10-189.5 pg/ml).

Baseline echocardiographic parameters of the study group

Table 2 displays the main echocardiographic parameters of the 37 patients included in the present study compared with the healthy controls, showing the right and left heart remodelling in the presence of ASD.

The ASD patients had a significant dilation of the RV (higher basal diameter, end-systolic and end-diastolic area) and RA (higher mid-lateral diameter, end-systolic area) compared to controls. The parameters of RV longitudinal and radial function had higher values in ASD patients, but statistical significance was only reached for TAPSE (25.9 ± 3.8 mm vs 24.0 ± 2.8 mm, p = 0.023) and RV fractional area change (51 ± 5% vs 47 ± 6%, p = 0.009). The RA was also significantly dilated in ASD patients. Moreover, the pulmonary artery (PA) trunk transversal diameter was increased in ASD patients compared to healthy volunteers (27.6 ± 5.1 mm vs 18.6 ± 2.7 mm, p <0.001) and the estimated pulmonary artery pressures (PAP) were also significantly higher in the ASD group (systolic PAP 37 ± 7 mmHg vs 23 ± 4 mmHg, p <0.001; mean PAP 23 ± 7 vs 16 ± 2 mmHg, p = 0.007).

The LV diastolic diameter was significantly smaller in ASD patients compared to healthy volunteers (42.7 ± 3.7 mm vs 46.7 ± 4.5 mm, p <0.001) while the end-systolic diameter was similar in both groups. The LV systolic function was normal in ASD patients, while parameters of LV diastolic function (septal and lateral e', E/e' ratio) were mildly impaired in ASD patients (Table 2). The LA was significantly dilated in ASD patients (Table 2).

The maximum ASD diameter assessed using TOE was 9 to 30 mm with a mean of 19.2 ± 4.6 mm. Device size ranged from 12 to 34 mm, with a mean of 24.3 ± 4.8 mm. No intraprocedural complications occurred.

The ASD size significantly correlated with RV dimensions (RV basal diameter, RV systolic and diastolic area), RA size (RA mid-lateral diameter and RA end-systolic area) and with PA trunk transversal diameter (Table 3) but not with LV or LA size. Also, ASD size did not impact RV function parameters or estimated systolic PAP (Table 3).

Follow-up data in the ASD group

At least 1 follow-up visit data was available in 23 patients and the mean follow-up was 12 ± 8 months (range 1-27 months). The functional class significantly improved after ASD closure, but BNP levels remained similar between baseline and the last follow-up visit (Table 4).

Four patients presented with supraventricular arrythmias after ASD closure, all of them with a history of atrial fibrillation/atrial flutter prior to the percutaneous closure: 1 patient with preprocedural persistent atrial fibrillation underwent successful electrical cardioversion to sinus rhythm after ASD closure; 1 patient with a history of paroxysmal atrial fibrillation presented in the first month after the procedure with an episode of atrial flutter that required electrical cardioversion; 1 patient with a history of paroxysmal atrial flutter developed atrial fibrillation one year after ASD closure that was chemically converted to sinus rhythm. No other early or mid-term complications were noticed during follow-up.

Table 2. Baseline echocardiographic parameters of the study group (37 adult patients who underwent percutaneous ASD closure) compared to a control group of 33 healthy volunteers

Parameter	ASD patients (n = 37)	Healthy controls (n = 33)	p value
Age (years)	43.5 ± 14.4	39.9 ± 11.1	0.25
Gender F/M (n, %)	29/8	21/12	0.14
RV basal diameter (mm)	42.4 ± 5.8	30.4 ± 2.8	**<0.001**
RV end-diastolic area (cm²/m²)	14.7 ± 3.0	8.6 ± 1.3	**<0.001**
RV end-systolic area (cm²/m²)	7.1 ± 1.6	4.5 ± 0.9	**<0.001**
Fractional area change (%)	51 ± 5	47 ± 6	**0.009**
TAPSE (mm)	25.9 ± 3.8	24.0 ± 2.8	**0.023**
RV free wall S-wave (cm/s)	14.0 ± 2.4	13.5 ± 1.9	0.41
RV global longitudinal strain (%)	-24.9 ± 2.9	-23.3 ± 2.7	0.057
RA mid-lateral diameter (mm)	46.0 ± 5.9	34.9 ± 3.3	**<0.001**
RA end-systolic area (cm²/m²)	20.7 ± 4.6	13.4 ± 2.3	**<0.001**
Tricuspid regurgitation grade mild/moderate/severe (n, %)	28/9/0 (75.7/24.3/0)	33/0/0 (100/0/0)	**0.004**
Pulmonary artery trunk (mm)	27.6 ± 5.1	18.6 ± 2.7	**<0.001**
Systolic PAP (mmHg)	37 ± 7	23 ± 4	**<0.001**
Mean PAP (mmHg)	23 ± 7	16 ± 2	**0.007**
Cardiac index (l/min/m²)	2.51 ± 0.38	2.48 ± 0.66	0.77
LV end-diastolic diameter (mm)	42.7 ± 3.7	46.7 ± 4.5	**<0.001**
LV end-systolic diameter (mm)	27.6 ± 4.3	28.9 ± 3.6	0.17
LV ejection fraction (%)	60 ± 4	61 ± 4	0.42
Septal S wave (cm/s)	7.8 ± 1.4	8.2 ± 1.2	0.32
Lateral S wave (cm/s)	10.2 ± 2.3	9.4 ± 1.5	0.13
E wave (cm/s)	71.1 ± 17.8	76.6 ± 15.4	0.20
A wave (cm/s)	62.9 ± 18.8	58.8 ± 13.9	0.33
E/A ratio	1.2 ± 0.4	1.4 ± 0.5	0.16
EDT (ms)	182 ± 30	180 ± 22	0.83
Septal e' (cm/s)	9.4 ± 2.1	11.3 ± 2.3	**0.005**
Lateral e' (cm/s)	11.2 ± 2.6	14.6 ± 2.6	**<0.001**
Average E/e'	7.8 ± 3.2	6.0 ± 1.4	**0.021**
LA antero-posterior diameter (mm)	39.5 ± 7.2	32.2 ± 3.5	**<0.001**
LA volume (ml/m²)	37.8 ± 13.1	26.9 ± 6.2	0.001
ASD maximum diameter (mm)	19.2 ± 4.6	-	-
Device size (mm)	24.3 ± 4.8	-	-

Values are expressed as mean ± standard deviation.
ASD, atrial septal defect; EDT, E-wave deceleration time; LA, left atrium; LV, left ventricle; PAP, pulmonary artery pressure; RA, right atrium; RV, right ventricle; PAP, pulmonary artery pressure; TAPSE tricuspid annulus plane systolic excursion.

The echocardiographic data showed a significant decrease in RV and RA size after the ASD closure (Table 4). The RV longitudinal function parameters (TAPSE, RV free wall S-wave) decreased after ASD closure. Also, at the follow-up visit, the PA trunk diameter (24.4 ± 5.0 mm vs 27.7 ± 5.8 mm) and the systolic PAP (29 ± 5 mmHg vs 39 ± 8 mmHg) were significantly lower (p <0.001) compared with the pre-procedural values. The LV end-diastolic diameter increased after ASD closure (45.6 ± 2.8 mm vs 42.8 ± 2.9 mm, p <0.001), while the increase in LV end-systolic diameter did not reach statistical significance (Table 4).

The ASD patients were divided into two groups according to their age: less than 60 and more or equal to 60 years. The frequency of supraventricular arrhythmias was similar in both groups, but patients

Table 3. Correlations of ASD size in the ASD population

Parameter	r	p
BNP levels (pg/ml)	0.19	0.37
RV basal diameter (mm)	0.38	**0.019**
RV end-diastolic area (cm^2/m^2)	0.59	**0.003**
RV end-systolic area (cm^2/m^2)	0.57	**0.005**
Fractional area change (%)	-0.05	0.82
TAPSE (mm)	0.17	0.33
RV free wall S-wave (cm/s)	0.08	0.66
RV global longitudinal strain (%)	-0.13	0.60
RA mid-lateral diameter (mm)	0.35	**0.040**
RA end-systolic area (cm^2/m^2)	0.45	**0.021**
Pulmonary artery trunk (mm)	0.42	**0.031**
Systolic PAP (mmHg)	0.29	0.10
Cardiac index ($l/min/m^2$)	0.25	0.18
LV end-diastolic diameter (mm)	-0.22	0.18
LV end-systolic diameter (mm)	-0.14	0.42
LA antero-posterior diameter (mm)	0.28	0.11
LA volume (ml/m^2)	0.20	0.34

ASD, atrial septal defect; BNP, brain natriuretic peptide; EDT, E-wave deceleration time; LA, left atrium; LV, left ventricle; NYHA, New York Heart Association; PAP, pulmonary artery pressure; RA, right atrium; RV, right ventricle; TAPSE tricuspid annulus plane systolic excursion.

older than 60 years were more functionally impaired (Table 5).There were no differences in baseline (pre-procedural) biological or echocardiographic parameters between the two subgroups of ASD patients, except for the baseline estimated systolic PAP which was higher in patients over 60 years (44.4 ± 5.9 mmHg vs 35.7 ± 6.6 mmHg, p = 0.01) and for the LA dimensions (LA antero-posterior diameter and LA volume) which were higher in older patients (Table 5). Despite these differences, reverse remodelling of the right chambers was similar in both groups: the decrease in RV, RA and PA size was similar in patients younger and older than 60 years (Table 5) but the decrease in estimated systolic PAP was higher in older patients (16.3 ± 4.3 mmHg decrease in patients over 60 years vs 7.5 ± 5.6 mmHg in patients below 60 years, p = 0.01). The BNP value at the last follow-up visit was higher in ASD patients older than 60 years (40.2 ± 8.9 pg/ml vs 23.8 ± 11.2 pg/ml) even if the change in LA volume was not significantly different in the two groups (-1.5 ± 5.5 ml/m^2 in patients older than 60 years vs 2.5 ± 7.4 ml/m^2, p = 0.39).

Table 4. Effect of ASD closure on clinical, biological, and echocardiographic parameters in the patients from the study group who had at least a 1-month follow-up visit (23 from the 37 adult patients who underwent percutaneous ASD closure)

Parameter	Pre-procedure	Last follow-up	p value
NYHA class 0/I/II/III (n)	3/3/16/1	7/2/14/0	0.005
BNP levels (pg/ml)	46.4 ± 41.3	27.7 ± 13.2	0.11
RV basal diameter (mm)	42.1 ± 5.8	32.0 ± 3.2	**<0.001**
RV end-diastolic area (cm^2/m^2)	15.7 ± 3.6	9.5 ± 2.0	**0.001**
RV end-systolic area (cm^2/m^2)	7.6 ± 1.6	4.8 ± 1.3	**0.001**
Fractional area change (%)	51 ± 4	50 ± 4	0.45
TAPSE (mm)	25.5 ± 4.1	23.4 ± 2.6	**0.025**
RV free wall S-wave (cm/s)	13.8 ± 2.4	12.6 ± 1.4	**0.029**
RV global longitudinal strain (%)	-24.5 ± 3.4	-23 ± 4.0	0.48
RA mid-lateral diameter (mm)	45.3 ± 5.8	32.0 ± 3.2	**<0.001**
RA end-systolic area (cm^2/m^2)	21.1 ± 5.0	16.4 ± 3.8	**<0.001**
Tricuspid regurgitation grade mild/moderate/severe (n, %)	20/3/0	23/0/0	-
Pulmonary artery trunk (mm)	27.7 ± 5.8	24.4 ± 5.0	**<0.001**
Systolic PAP (mmHg)	39 ± 8	29 ± 5	**<0.001**
Cardiac index ($l/min/m^2$)	2.55 ± 0.38	2.59 ± 0.48	0.79
LV end-diastolic diameter (mm)	42.8 ± 2.9	45.6 ± 2.8	**<0.001**
LV end-systolic diameter (mm)	27.6 ± 4.2	29.1 ± 4.0	0.066
LV ejection fraction (%)	61 ± 3	60 ± 1	0.27
Septal S wave (cm/s)	7.9 ± 1.4	7.4 ± 1.0	0.065
Lateral S wave (cm/s)	10.0 ± 2.3	8.3 ± 1.3	**0.005**
E wave (cm/s)	72.2 ± 20.5	78.1 ± 19.9	0.13
A wave (cm/s)	67.6 ± 18.8	62.3 ± 19.2	0.21

E/A ratio	1.1 ± 0.5	1.4 ± 0.6	0.15
EDT (ms)	185 ± 26	203 ± 36	**0.019**
Septal e' (cm/s)	9.2 ± 2.2	8.9 ± 2.9	0.67
Lateral e' (cm/s)	10.5 ± 2.7	10.3 ± 3.5	0.79
Average E/e'	8.4 ± 3.5	10.4 ± 5.3	0.21
LA antero-posterior diameter (mm)	41.2 ± 8.5	40.4 ± 4.6	0.64
LA volume (ml/m²)	39.1 ± 14.2	40.9 ± 13.5	0.31

Values are expressed as mean ± standard deviation.
ASD, atrial septal defect; BNP, brain natriuretic peptide; EDT, E-wave deceleration time; LA, left atrium; LV, left ventricle; NYHA, New York Heart Association; PAP, pulmonary artery pressure; RA, right atrium; RV, right ventricle; PAP, pulmonary artery pressure; TAPSE tricuspid annulus plane systolic excursion.

Table 5. Differences in clinical, biological, and echocardiographic parameters in the 37 patients who underwent percutaneous ASD closure according to the patient's age at the time of the procedure

Parameter	Age <60 years (n = 32)	Age ≥60 years (n = 5)	p value
NYHA class 0/I/II/III (n)	3/6/23/0	0/0/4/1	**0.049**
History of supraventricular arrhythmias (n)	6	3	0.081
Baseline BNP levels (pg/ml)	47.5 ± 44.6	88.8 ± 53.9	0.087
Baseline RV basal diameter (mm)	42.1 ± 5.2	44.2 ± 9.6	0.66
Baseline RV end-diastolic area (cm²/m²)	14.7 ± 2.8	15.0 ± 5.0	0.87
Baseline RV end-systolic area (cm²/m²)	7.0 ± 1.6	7.6 ± 2.3	0.61
Baseline fractional area change (%)	52 ± 5	49 ± 2	0.059
Baseline TAPSE (mm)	26.1 ± 3.6	24.8 ± 5.0	0.48
Baseline RV free wall S-wave (cm/s)	14.3 ± 2.5	12.2 ± 0.8	0.10
Baseline RV global longitudinal strain (%)	-25.4 ± 2.8	-21.7 ± 2.0	0.10
Baseline RA mid-lateral diameter (mm)	46.1 ± 6.0	45.4 ± 5.7	0.80
Baseline RA end-systolic area (cm²/m²)	20.0 ± 3.9	24.6 ± 6.8	0.065
Baseline pulmonary artery trunk (mm)	27.4 ± 5.1	29.7 ± 5.1	0.47
Baseline systolic PAP (mmHg)	35.7 ± 6.6	44.4 ± 5.9	**0.01**
Baseline cardiac index (l/min/m²)	2.54 ± 0.38	2.37 ± 0.43	0.43
Baseline LV end-diastolic diameter (mm)	42.5 ± 3.9	43.8 ± 2.8	0.49
Baseline LV end-systolic diameter (mm)	27.5 ± 4.3	28 ± 4.7	0.82
Baseline LA antero-posterior diameter (mm)	37.9 ± 5.7	49 ± 8.5	**0.001**
Baseline LA volume (ml/m²)	34.0 ± 10.1	57.5 ± 8.6	**<0.001**
Δ RV basal diameter (mm)	9.6 ± 4.7	12.8 ± 7.6	0.28
Δ RV end-diastolic area (cm²/m²)	5.6 ± 2.9	8.0 ± 4.4	0.40
Δ RV end-systolic area (cm²/m²)	2.4 ± 1.3	4.0 ± 1.6	0.20
Δ Fractional area change (%)	-3 ± 6	1 ± 6	0.51
Δ TAPSE (mm)	2.3 ± 4.4	1.5 ± 2.1	0.74
Δ RV free wall S-wave (cm/s)	1.8 ± 2.4	-0.9 ± 0.8	**0.04**
Δ RA mid-lateral diameter (mm)	7.5 ± 4.2	10.3 ± 3.5	0.28
Δ RA end-systolic area (cm²/m²)	4.9 ± 2.3	3.8 ± 7.1	0.79
Δ Pulmonary artery trunk (mm)	2.9 ± 2.9	6.5 ± 0.7	0.11
Δ Systolic PAP (mmHg)	7.5 ± 5.6	16.3 ± 4.3	**0.01**
Δ LV end-diastolic diameter (mm)	42.5 ± 3.9	43.8 ± 2.8	0.24
Δ LV end-systolic diameter (mm)	27.5 ± 4.3	28.0 ± 4.7	0.67
End-of-follow-up BNP levels (pg/ml)	23.8 ± 11.2	40.2 ± 8.9	**0.045**
End-of-follow-up systolic PAP (mmHg)	28.7 ± 5.9	30.0 ± 8.9	0.67

Values are expressed as mean ± standard deviation.
ASD, atrial septal defect; BNP, brain natriuretic peptide; LA, left atrium; LV, left ventricle; PAP, pulmonary artery pressure; RA, right atrium; RV, right ventricle; TAPSE tricuspid annulus plane systolic excursion

DISSCUSION

In the present study we showed that percutaneous closure of ostium secundum ASD in adult patients is feasible and associated with a low rate of periprocedural complications and good short and mid-term outcomes in terms of clinical and hemodynamic improvement and favourable cardiac remodelling.

At baseline, the ASD patients, compared with age and gender-matched healthy subjects, exhibited features of RV volume overload: significantly dilated RV with preserved or increased longitudinal function and decreased LV end-diastolic diameter, with preserved LV end-systolic diameter, suggesting the interventricular septum flattening only in diastole. The increased values of TAPSE in ASD patients confirm the previously reported finding that chronic volume-overload accentuates the RV long-axis excursion as compared to normals.[9]

Also, ASD patients presented with dilated PA trunk and increased PAP, as signs of an increased pulmonary flow. Moreover, due to left-to-right shunt with increased pulmonary flow both the RA and the LA were significantly dilated, compared with healthy subjects.

At baseline, before the percutaneous ASD closure, 24% of patients had a history of atrial fibrillation or flutter, a proportion slightly higher compared to the data in the literature,[10] possibly due to the older age at the moment of ASD closure. When considering the two groups of ASD patients, aged more or less than 60 years, there was no significant difference in the frequency of atrial fibrillation or flutter before closure. After closure, four patients experienced a new episode of supraventricular arrhythmia, all of them having a previous history of such an arrythmia, which suggests that the occurrence of the arrythmia was probably not a complication of the procedure but a complication of the prolonged disease.

Both RV and LV systolic function were normal in ASD patients, while LV diastolic function was mildly impaired in ASD population. This finding is explained by the fact that RV dilatation restricts LV size and filling due to both direct (right-to-left septal bulging) and indirect (pericardial constraint) effects.[11]

As expected, ASD size significantly correlated with RV and RA dimensions, but not with the left heart response to an increased pulmonary flow. The PA diameter correlated with ASD size, but systolic PAP did not. This finding suggests that the increase in PAP is not only related to the magnitude of the left-to-right shunt but also to the intrinsic properties of the pulmonary circulation such as different parameters of pulmonary arterial stiffness.

In the present study the mean follow-up was about 1 year after ASD closure. Patients exhibited a significant improvement in functional class but the decrease in BNP levels did not reach statistical significance. The clinical improvement is described after ASD closure irrespective of age[3] and our study confirms this finding. The occurrence of supraventricular arrhythmias is reported more frequently in patients older than 40 years in whom the ASD closure is performed,[10] but in our study the history of atrial fibrillation or flutter was similar in patients younger and older than 60 years. Our findings suggest the clinical benefit of ASD closure in adult patients irrespective of age if there is a definite indication for closure.

At the last follow-up visit, ASD patients showed a significant decrease in RV and RA size, both linear dimensions and areas. This reverse remodelling of the right chambers was shown in previous studies.[11-15] It occurs quickly (within the first 24 hours) after ASD device closure and the remodeling process appears to continue for at least 1 year and is more advanced in the RV than the RA.[16] Moreover, the magnitude of RA remodeling is inversely related to patient age at the time of closure, as shown in a study that reported persistent RA dilation in patients who underwent late ASD closure, which was also associated with an increase in BNP levels and RV diastolic dysfunction.[17]

Furthermore, in our study, as in a previous one,[11] parameters of RV longitudinal function (TAPSE, free RV wall TDI-derived S-wave) also significantly decreased during follow-up in parallel with the decrease in RV volume overload secondary to the ASD closure procedure. The systolic PAP decreased significantly after ASD closure in the present study, as previously described,[11] and a significant decrease in PA trunk transversal diameter was also recorded during follow-up in our study population.

The reverse remodelling of the right chambers – the decrease in RV, RA and PA size – was similar in the two groups of ASD patients, younger and older than 60 years, but the decrease in estimated systolic PAP was higher in older patients. These findings argue for closure of the ASD irrespective of age if there is a clear indication and no concerns related to a significant LV systolic or diastolic dysfunction.

With regards to the left heart, our study showed that LV diastolic diameter increased following ASD closure. This finding is explained by the disappearance of the left-to-right shunt after closing the ASD and by the beneficial effect attributable to decreasing the RV dilatation that previously impaired LV filling due to the interventricular dependence. While LV diastolic diameter increased, the LA size remained unchanged. This finding is similar with that from two previous studies on patients undergoing surgical or percutaneous ASD closure,[18,19] showing that the ventricles appear to have a greater capacity for remodeling than the atria.

Study limitations

The first limitation of our study is the small number of patients with an even smaller proportion of patients in the two groups of age – less than 60 and more than 60 years. Furthermore, the duration of follow-up was relatively reduced and so late complications, such as arrhythmia, may have been underestimated in the study. Also, novel parameters of RV function such as RV global longitudinal strain were not available in all patients during follow-up.

CONCLUSION

In adult patients with ostium secundum ASD, percutaneous closure leads to significant changes in functional class and echocardiographic parameters of right and left heart size and right ventricle function as well as in pulmonary artery size and pressure. The beneficial effects seem to be maintained even in patients older than 60 years, but larger studies are required to confirm this finding.

Compliance with ethics requirements:

The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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