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ORIGINAL ARTICLE

Transcatheter Atrial Septal Defect Closure Before Versus After Adulthood

Mohamed S. Hafez*, Mohamed I. Abdelrahman El-sayed, Maiy H. El Sayed

Department of Cardiovascular Medicine, Ain Shams University Hospitals, Cairo, Egypt

Abstract

Objectives: **To evaluate the long-term outcome of patients who underwent percutaneous transcatheter closure of secundum atrial septal defects during teenage life versus adulthood.**

Methods: **The study included 100 patients with secundum type ASD who were treated by transcatheter closure of their defects 2–5 years before enrollment. The study population was subdivided into 2 equal groups: group 1 who underwent transcatheter closure during teenage life (13–19 years) and group 2 who underwent transcatheter closure after the age of 30 years. The two groups were compared according to resting 12 lead ECG, 24-h Holter ECG and transthoracic echocardiographic findings (Right ventricular size and functions, right atrial size, etc.)**

Results: **The study population showed female predominance. The average follow up period was similar in both groups. Adult patients had more frequent right bundle branch block morphology in their resting 12 lead ECG than teenagers (69% versus 45% respectively, $p < 0.01$). The incidence of arrhythmias encountered in Holter ECG was also significantly higher in the adult group. Premature atrial contractions (PAC) were present in 10 patients (20%) in adult group while 3 patients (6%) had PACs in teenagers' group with $p < 0.01$. The mean PAC burden was also higher in the adult group (9% versus 1.3%, $p < 0.001$). Paroxysmal AF lasting more than 30 seconds was found in 6 patients (12%) in the adult group while 1 patient in teenagers developed AF, $p < 0.01$. Regarding transthoracic echocardiography, adult patients showed significantly larger RV diameter, indexed RA area, indexed LA volume and more LV diastolic dysfunction. RV systolic functions were better in the teenage group as measured by 2D echocardiography. Adult patients with higher age, bigger defect size and device size had more abnormal ECG and echocardiographic findings.**

Conclusion: **Early *trans*-catheter closure of secundum ASD during teenage life yields better right ventricular systolic function, better right ventricular size and less incidence of atrial arrhythmia.**

Keywords: Atrial septal defects, Transcatheter device closure, Early intervention

1. Introduction

Atrial septal defects (ASDs) are one of the most common types of acyanotic congenital heart diseases, comprising 6–10% all congenital heart defects. They represent the most common congenital heart disease diagnosed during adulthood [1].

According to the latest guidelines of adult congenital heart disease, ASD closure should be done when there is evidence of right ventricular volume overload after confirmation that pulmonary vascular resistance (PVR) is less than 5 Wood units. If the PVR is higher, fenestrated closure may be considered. ASD closure is contraindicated in the case of Eisenmenger syndrome [2].

Regarding secundum ASDs, the defect is considered for closure once diagnosed, given that the defect is hemodynamically significant and persists

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* Corresponding author.
E-mail address: Dr.mohammadsaber@yahoo.com (M.S. Hafez).

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beyond the age of four years. The most common treatment modality in the majority of cases is transcatheter device closure [3].

Complications of untreated ASD include right ventricular dilatation and failure, atrial arrhythmias, pulmonary hypertension, paradoxical thromboembolism and rarely infective endocarditis [4].

Although the routine practice is ASD closure as early as possible, yet the exact benefits of early transcatheter ASD device closure are not really known. The aim of this study was to evaluate the long-term outcome of patients who underwent percutaneous transcatheter closure of secundum atrial septal defects during teenage life versus those who underwent closure in adult life.

Abbreviations

ASD	atrial septal defect
AF	Atrial fibrillation
PAP	pulmonary artery pressure
PVR	pulmonary vascular resistance
RVSP	right ventricular systolic pressure
LV	left ventricle
BSA	body surface area
PAC	premature atrial contractions
RA	Right atrium
FAC	Fractional area change

2. Materials and methods

This retrospective study was conducted in Ain Shams University hospital in the period between January 2021 and January 2022. The study design was approved by the ethical committee of Cardiology department, faculty of medicine, Ain Shams University and was in accordance with the declaration of Helsinki updated on 2008. All patients gave informed written consent. The study included 100 consecutive patients who previously underwent transcatheter ASD device closure 2–5 years before enrollment. All patients had hemodynamically significant defects with signs of right ventricular overload at time of closure and Qp/Qs more than 1.5. Patients who had associated congenital heart defects, concomitant coronary artery disease or those who underwent ASD surgical closure were excluded.

The study population was divided into two equal groups: group 1: Transcatheter closure occurred during teenage period (13–19 years) and group 2: Transcatheter closure occurred during adulthood (above 30 years). All the procedures were previously done under general anesthesia with transesophageal echocardiographic and fluoroscopic guidance.

Proper detailed history taking was carried out for all patients with emphasis on residual symptoms like palpitations, dyspnea with New York Heart association (NYHA) class, chest pain and exercise tolerance. Regarding adult group, special emphasis was done on risk factors of coronary artery disease, e.g. hypertension, diabetes mellitus. Full clinical examination was carried out including general examination for weight, height and body surface area and cardiac examination. We recorded the defect size measured by transesophageal echocardiography, invasive pulmonary artery pressure (PAP), size and type of device used, and any periprocedural complications.

Resting electrocardiogram (ECG) recording was performed in all patients at the time of examination. Holter ECG monitoring for 24 hours (Schiller medilog AR) was done for all patients to assess the rate, rhythm, pauses, tachyarrhythmias, bradyarrhythmias, etc. Burden of atrial ectopics was recorded as a percentage of the total number of beats in the whole day. Paroxysms of atrial fibrillation (AF) were defined as the presence of periods of irregular rhythm with absence of persistent P wave for more than 30 seconds [5].

Transthoracic echocardiography was performed for every patient using a GE E95 Echocardiography machine with an S3 probe with frequency range from 5 to 1 Megahertz according to Body Surface area. The ASD closure device was visualized in different views (subcostal, apical 4 chambers, parasternal short axis and RV inflow) to assess size, location, relation to adjacent structure and any residual shunt using color Doppler. RV basal diameter was measured at end-diastole in the RV-focused view. RV systolic function was measured by Fractional area change (FAC) method in apical four chamber view. RV FAC $\geq$30% in males, or $\geq$35% in females, was considered normal. Right atrial (RA) area was measured at the end of ventricular systole in apical 4-chamber view. Degree of tricuspid and pulmonary valve regurgitation were recorded, from which right ventricular systolic pressure (RVSP) and mean PAP were calculated. Left ventricular (LV) ejection fraction was measured by Simpsons' method in apical four and apical two chamber views. Left atrial volume was calculated by area-length method in apical two-chamber and four-chamber views. Measured values were indexed to body surface area (BSA). Mitral E/A ratio was obtained by measuring peak E-wave velocity and A-wave velocity at apical four-chamber with color flow imaging for optimal alignment of PW Doppler with blood flow between

mitral leaflet tips. Tissue Doppler was used to assess LV diastolic function by measurement of medial and lateral mitral annular tissue velocities (e' velocity) then calculating the average E/e' ratio [6].

3. Statistical analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. Quantitative data were presented as mean, standard deviation and range; all data were parametric. Qualitative variables were presented as number and percentages. Comparison between groups regarding qualitative data was done using Chi-square test and/or Fisher exact test when the expected count in any cell was less than 5. The comparison between two independent groups with quantitative data and parametric distribution was done using independent *t*-test. Spearman correlation coefficients were used to assess the correlation between two quantitative parameters in the same group. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as following: P-value > 0.05: non-significant, P-value < 0.05: significant, P-value < 0.01: highly significant.

4. Results

The mean age of the patients was 35.17 ± 13.41 years. The study population showed female predominance. The mean follow up period was similar in both teenage and adult groups. All demographic data are shown in Table 1. Among the adult patients, 5 patients (10%) were hypertensive, 4 patients (8%) were diabetic and 3 patients (6%) had both.

Regarding transcatheter intervention details, ASD size measured by transesophageal echocardiography ranged from 6 mm to 33 mm with a mean ± SD 14.32 ± 6.02 mm. Defect size was larger in adult group (ranged from 9 to 33 mm with a mean ± SD 15.57 ± 6.57 mm) than teenagers (ranged from 6 to 22 mm with a mean ± SD 13.06 ± 5.18 mm). The device size ranged from 9 to 36 mm with a mean ± SD 17.15 ± 6.50 mm. Similarly, device size used was larger in adult group (ranged from 11 to 36 mm with a mean ± SD 18.26 ± 7.00 mm) than teenagers (ranged from 9 to 25 mm with a mean ± SD 16.04 ± 5.81mm). The differences between both groups regarding defect size and device size were statistically non-significant. Invasive mean PAP ranged from 15 to 25 mmHg with a mean ± SD 18.70 ± 2.08 mmHg and showed no significant difference between both groups. No significant difference between the two groups was noted regarding type of the device used. No major peri-procedural complications were recorded.

Atrial fibrillation was present in two adult patients in the resting 12 lead ECG, the rest of the study population had normal sinus rhythm. Adult patients had more frequent right bundle branch block morphology in their resting ECG than teenagers (69% versus 45% respectively, p < 0.01). The incidence of arrhythmias encountered in Holter ECG was also significantly higher in the adult group. Premature atrial contractions (PAC) were present in 10 patients (20%) in adult group while 3 patients (6%) had PACs in teenage group with p < 0.01. The mean PAC burden was also higher in the adult group (9% versus 1.3%, p < 0.001). Paroxysmal AF lasting more than 30 seconds was found in 6 patients (12%) in the adult group while 1 patient in teenagers, p < 0.01. No patients showed supraventricular tachycardia. No other brady or tachyarrhythmias were detected.

Regarding transthoracic echocardiography, adult patients showed significantly larger RV diameter, indexed RA area, indexed LA volume and more LV diastolic dysfunction. RV systolic functions were better in the teenage group as measured by FAC (Table 2).

The adult group was further classified into two groups according to Holter findings, RV basal

Table 1. Demographic data of the study population.

Demographic data		Teenagers group	Adults group	P-value
		No. = 50	No. = 50	
Age at time of study (years)	Mean ± SD	18.5 ± 2.3	37.9 ± 3.6	<0.001
Follow up period (years)	Mean ± SD	2.8 ± 0.7	2.7 ± 0.6	0.675
Sex	Female	28 (56.0%)	31 (62.0%)	0.542
	Male	22 (44.0%)	19 (38.0%)	
Weight (kg)	Mean ± SD	57.80 ± 7.40	84.02 ± 8.06	<0.001
Height (cm)	Mean ± SD	159.72 ± 7.06	172.24 ± 5.31	<0.001
Body Surface Area (m^2)	Mean ± SD	1.60 ± 0.13	2.00 ± 0.10	<0.001

Table 2. Comparison between echocardiographic data in both groups.

2D Echo		Teenagers group	Adults group	P-value
		No. = 50	No. = 50	
RV basal diameter	Normal	48 (96.0%)	38 (76.0%)	0.004
	Dilated	2 (4.0%)	12 (24.0%)	
RV systolic function (%)	Mean ± SD	44.5 ± 3.2	39.6 ± 4.9	0.000
by FAC	Normal	49 (98.0%)	42 (84.0%)	0.001
	Abnormal	1 (2.0%)	8 (16.0%)	
Indexed RA area (cm^2/m^2)	Mean ± SD	9.06 ± 1.18	9.68 ± 1.60	0.030
	Range	7–11	7–14	
Mitral E/A ratio	Mean ± SD	1.45 ± 0.17	1.06 ± 0.20	0.000
Average E/e'	Mean ± SD	4.94 ± 1.13	5.43 ± 1.24	0.041
RVSP (mmHg)	Mean ± SD	23.54 ± 2.21	24.44 ± 3.41	0.0120
Mean PA pressure (mmHg)	Mean ± SD	13.34	14.78	0.219
Degree of tricuspid regurgitation	Mild	47 (94.0%)	48 (96.0%)	0.646
	Trivial	3 (6.0%)	2 (4.0%)	
Degree of pulmonary regurgitation	Mild	3 (6.0%)	3 (6.0%)	1.000
	Trivial	47 (94.0%)	47 (94.0%)	
LV EF (%)	Mean ± SD	62.64 ± 3.95	65.44 ± 6.16	0.8
	Range	55–74	55–74	
Indexed LA volume (ml/m^2)	Mean ± SD	24.08 ± 2.78	36.94 ± 3.40	0.000
	Range	19–29	30–46	

diameter and RV systolic functions to assess the factors affecting these findings. Age, ASD size, device size and LA volume were significantly higher in patients with arrhythmia during Holter monitoring. Similarly, age, defect size and device size were higher in patients with dilated RV and in those with impaired RV systolic functions.

5. Discussion

A previous study compared surgical ASD closure before and after the age of 25 years and concluded that patients who underwent early repair had less RV dilatation, less LA dilatation, lower PAP, lesser degree of tricuspid regurgitation and less incidence of AF. In our study, all these benefits were noticed except for the difference in tricuspid regurgitation and pulmonary artery pressure between both groups. In that study, the adult group had higher mean age than the adult group in our study (52 years versus 37 years respectively). The higher age of patients may be the cause of higher PAP [7].

In the current study, adult patients had significantly higher RV dimensions than teenagers (P = 0.004). A previous study concluded that reverse remodeling of right ventricle began 1 month after transcatheter ASD closure but did not completely get back to normal even after 1 year, a finding that agrees with our study [8].

The RA area corrected to BSA was significantly higher in adults (P = 0.030). RA area corrected to BSA in adults ranged from 7 to 14 cm/m^2 with a mean ± SD 9.68 ± 1.60 cm/m^2 and in teenagers ranged from 7 to 11 cm/m^2 with a mean ± SD 9.06 ± 1.18 cm/m^2 This finding was in line with a previous study conducted on 16 patients who underwent cardiac MRI after transcatheter ASD closure. They stated that indexed RA area started to decrease early after closure in all patients but in some patients with old age it remains higher 2 years after closure. They also demonstrated that the degree of reduction in indexed RA area was related to young age at time of device placement [9].

The association between atrial arrhythmia and ASD is well recognized, and older patients are at the highest risk. In our study, we found that incidence of PACs and AF in adults was higher than teenagers. This finding agreed with Wilson et al. who studied retrospectively 211 patients underwent transcatheter ASD closure and documented occurrence of new arrhythmias for 6 (3%) patients after ASD closure [10].

Our data showed a trend to older age, increased defect size, device size and larger LA dimensions in those who develop arrhythmia. These findings concurred with a previous study who retrospectively collected 159 patients who previously underwent ASD closure with mean age 57 years and median follow-up was 3.6 years (range 6 months–10.9 years). Patients were classified, according to arrhythmia status prior to ASD closure, into Group I, no history of atrial arrhythmia (n = 119, mean age 55.5 years); Group II, paroxysmal atrial arrhythmia (n = 18, mean age 55.7 years); and Group III, persistent atrial fibrillation (n = 22, mean age 65.7 years). After device closure, 7 patients (6%) of Group I developed new

atrial fibrillation. 50% (9/18) of Group II but only 9% (2/22) of Group III were in sinus rhythm on follow-up. i.e. 6% incidence of new atrial arrhythmia after a median follow-up of 2.5 years in patients treated by device. Group III patients were significantly older and had larger left atrial size than Group I and II patients ($P < 0.001$) [11].

6. Conclusion

Patients who underwent transcatheter ASD closure during teenage life showed less abnormal resting ECG, less atrial arrhythmia, less RV dilatation and better RV systolic functions as compared to patients who underwent ASD closure after the age of 30 years.

Study limitation

This study was a single center retrospective study that included a limited number of patients. Assessment of RV size and functions was not done by the recent and more accurate imaging modalities (3D echocardiography and Cardiac MRI).

Author contribution

Conception and design of Study: MSH, MIAE. Literature review: MSH, MIAE, MHE. Acquisition of data: MSH, MIAE. Analysis and interpretation of data: MSH, MHE. Research investigation and analysis: MSH, MHE. Data collection: MIAE. Drafting of manuscript: MSH, MHE. Revising and editing the manuscript critically for important intellectual contents: MSH, MHE. Data preparation and presentation: MSH, MIAE, MHE. Supervision of the research: MHE. Research coordination and management: MHE. Funding for the research: MIAE.

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Conflict of interest

None declared.

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