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CARDIOLOGY
Research Article

Transcatheter Closure of Atrial Septal Defect Preserves Right Ventricular Function

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Received: July 14, 2015; **Published:** September 03, 2015

Abstract

Aim: To investigate the intermediate and short-term effects of transcatheter secundumatrial septal defect (ASD) closure on cardiac remodeling in children and adult patients.

Methods: 50 patients with secundum ASD referred for possible transcatheter device closure were subjected to history taking; proper physical examination; electrocardiographic assessment and transthoracic echocardiographic examination and were evaluated before the ASD closure, 1 day, 3m and 6m after closure.

Results: At the 6 month follow up electrocardiographic parameters of remodeling improved so P dispersion decreased from 49.73 ± 9.01to 30.53 ± 5.08 ms (p = 0.004), QT dispersion decreased from 67.6 ± 5.31 to 51.13 ± 5.73 ms (p = 0.003), QRS duration decreased from 134.4 ± 4.97 to 116.20 ± 3.47 ms(p = 0.002) , PR interval decreased from 188.87 ± 6.06 to 168.00 ± 6.16 ms (p = 0.002).At the end of follow-up period of 6 month, RVEDD had decreased from 25.67 ± 5.50 mm to 17.80± 2.7 mm (p = 0.001), and the LVEDD had increased from 33.17 ± 6.44 to 37.53 ± 5.15 mm (p = 0.002), Mean PAP decreased from 16.97 ± 3.37 to 9.22 ± 1.37 mmHg (p = 0.000), RVSP decreased from 30.77 ± 4.69 to 18.8 ± 2.11 mmHg. After 6m 93.3% of the patients had normal RV size.

Conclusion: Transcatheter ASD device closure leads to significant improvement in right sided chambers dimension and function and can reverse electrical and mechanical changes in atrial and ventricular myocardium in children and adults in short and intermediate term follow up.

Keywords: *Transcatheter; Astium premium; Tachyarrhythmia; Secundum; Electrocardiographic; Interatrial septum*

Introduction

Atrial septal defect (ASD) is the second most common congenital lesion in adults (behind bicuspid aortic valves). They represent approximately 7% of all cardiac anomalies [1]. These defects are often undetected until adulthood due to the lack of prominent clinical symptoms initially. If untreated, an ASD can eventually result in right ventricular (RV) heart failure, pulmonary hypertension, atrial arrhythmias, or paradoxical embolization and ischemic cerebral events.

Often, atrial tachyarrhythmias may coexist or precede symptoms. The incidence of arrhythmias increases with age as well as an increase in pulmonary pressures [2]. However, it is still unclear whether atrial arrhythmias improve with the closure of the defect, although some trials have shown that atrial flutter may improve with atrial septal defect (ASD) closure as opposed to atrial fibrillation, which usually remains unchanged following closure [2]. As a result, the development of an atrial tachyarrhythmia alone does not constitute an immediate need for ASD closure.

Recently, the definition of "significant ASD" has been changed. Nowadays significant ASD, according to the ESC Guidelines, is defined as shunt with signs of right ventricular volume overload despite the Qp : Qs ratio [3]. Patients with significant shunt (signs of right ventricle volume overload) and pulmonary vascular resistance < 5 Wood units should undergo ASD closure regardless of symptoms. But the closure of the ASD in patients with insignificant shunt with Qp : Qs ratio less than 1.5 and lack of pulmonary overload and hypertension is controversial.

Historically, ASDs have been closed surgically. More recently, these procedures have been accomplished with minimally invasive surgical techniques as well as a percutaneous transcatheter technique. The latter technique has been increasing in popularity due to the avoidance of cardiac surgery and the associated risks.

ASD repair with the transcatheter technique has been shown to have a high closure rate [4]. Unfortunately, anatomy of the defect often limits their use. Currently, transcatheter closure is limited to secundum-type defects which are less than 36 mm in size.

Patients with severe fixed pulmonary hypertension may actually do worsen with ASD closure due to the need for partial right-to-left shunting of blood to decrease right-sided pressures [5]. Early diagnosis and follow-up of ASDs offers the best opportunity to avoid late complications from pulmonary hypertension, heart failure, arrhythmia, and stroke.

Aim of the work: This study aimed to investigate the intermediate and short-term effects of transcatheter secundum ASD (at the site of fossa ovalis in the middle of the interatrial septum, astium premium at the lower part of the septum was excluded) closure on cardiac remodeling in children and adults.

Patients and Methods: The study included 50 patients who were referred to National Heart Institute – Cardiology Department for the possibility of elective percutaneous closure of their Secundum ASD in period from April 2014 to April 2015.

Inclusion criteria

1- Secundum ASD with a left-to-right shunt
2- ASD diameter equal to or less than 36 mm
3- Presence of 4mm or more septal rims.
4- Increased right ventricular volume load (QP/QS ratio > 1.5 and/ or RV dilation.

Exclusion criteria

1-Sinus venosus and primum ASD types
2- ASD > 36 mm or < 4 mm
3- Absence of an indication or contraindication of ASD closure as (QP/QS < 1.5 mm or pulmonary vascular resistance > 8 woods.
4- Non sinus rhythm at time of ECG recording
5- Use of antiarrythmic drugs

Patients included in the study were subjected to the following

1- History taking and clinical examination

Thorough history taking and physical examination with emphasis on the New York heart association (NYHA) class, signs of pulmonary hypertension (accentuated second heart sound) and signs of RV volume overload.

2-Twelve lead surface electrocardiogram

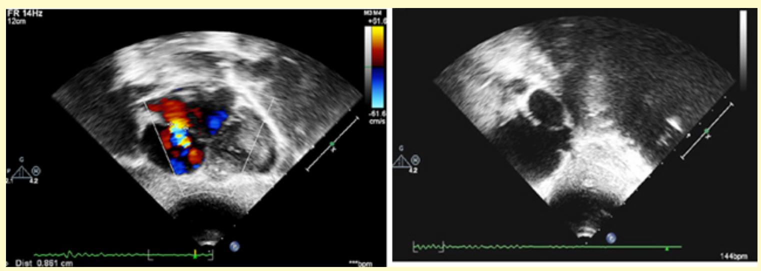
A standard 12- lead electrocardiogram (ECG) was recorded at a rate of 50 mm/s (to show all ECG criteria and small P waves) and a calibration of 1 mV/cm for all the patients as a baseline before the procedure and during the follow up period. The P wave, PR interval, and QRS and QT dispersion times were measured.

3-Trans thoracic Echocardiography

All patients underwent full echocardiographic study using general electric Vivid 5 echocardiography machine using 3.5-5 MHz phased array transducers for children and 2.5 MHz phased array transducers for adult patients. In agitated infants and children, sedation with chloral hydrate (50 mg per kilogram) 15 minutes prior to the study was done.

A-Sequential analysis: to determine the situs, AV and ventriculoarterial (VA) connections, great vessel relation and abnormalities, state of cardiac valves, venous connections.

B-The interatrial septum: The atrial septum was visualized from multiple aspects in order to assess the size, shape, number and location of the defect as well as its relationship to adjacent structures. Particular care was taken to assess the relationship of the defect to the superior and inferior vena cava, the pulmonary veins and the coronary sinus (figure 1).



(a) *(b)*

Figure 1: *(a): Subcostal 4 chamber view and (b): Subcostal sagittal view*

C- Left atrial dimensions (LAD) and right atrial dimensions (RAD): Apical four chamber view: left and right atria were measured in this view in two dimensions both transverse and longitudinal axis. [6] Figure 2.

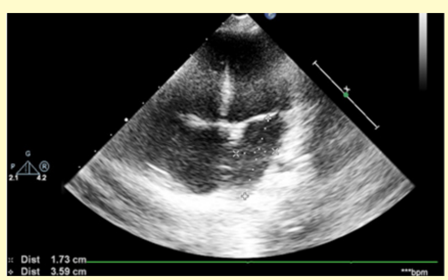


Figure 2: *Apical 4 chamber view with measurement of the LAD in both horizontal and vertical dimensions.*

D- Tricuspid valve and right ventricular systolic pressure (RVSP)

1. Apical 4 chamber view: The tricuspid valve was examined regarding mobility of the leaflets and presence of tricuspid regurgitation.
2. If TR was present, a continuous wave Doppler was applied to the TR jet after being properly aligned to determine the TR velocity and hence the right ventricular systolic pressure was calculated according to the modified Bernoulli equation which states right ventricular systolic pressure (RVSP) = (TR velocity) 2 + P (RA) where TR velocity is the maximal velocity of the TR jet (in meters per second) and PRA is an estimate of right atrial pressure [6]

3. Parasternal long axis view (RV inflow): the tricuspid valve was re-assessed using this view and the RVSP was calculated again and the maximum value obtained from two views was taken. [6]
4. Tricuspid annular plane systolic excursion (TAPSE): by placing the M-mode cursor through the lateral annulus of the tricuspid valve and record and Measure the maximum excursion. Normally value < 16 mm indicates right ventricular systolic dysfunction.
5. In Parasternal long axis view (RV outflow): the pulmonary valve was examined and If pulmonary regurgitation (PR) was present, a continuous wave Doppler was applied to the PR jet after being properly aligned to determine the PR peak velocity and hence the Mean pulmonary artery pressure (PAP) was calculated according to the modified Bernoli equation where
6. MPAP = 4 (Peak PR velocity)2 + RAP
7. Parasternal short axis (at level of the aortic valve): the pulmonary valve was re-examined and the PR was re-measured if present for the mean PAP to be calculated according to the modified Bernoulli's equation and the maximum value obtained from the two views was taken. [7].
8. E- Right ventricular dimensions and size: The right ventricular end diastolic dimension (RVEDD) was evaluated using the following:
9. In the parasternal short-axis view M mode was applied and the RVEDD was measured and categorized accordingly into normal, mildly, moderately and severely dilated right ventricle (Reference values RV diameter 1.8-3.4 cm by M-mode) [6].
10. F- Left ventricular dimensions and systolic function:
11. Parasternal short axis view M mode was applied and the left ventricular (LV dimensions) were measured including left ventricular end diastolic dimension (LVEDD normal values 3.9-5.3 in Women and 4.2-5.9 in Men) and ejection fraction was obtained by a cut through the tip of papillary muscles [6].

4-Transoesophageal echocardiography: Most of the patients had full transesophageal echocardiographic examination under general anesthesia in the cath. Lab before starting the procedure and during the procedure for assessment of the atrial septal defect and rims.

5-Atrial septal defect transcatheter device closure: Informed consent was obtained from each patient or patient's parents before the procedure. The procedure was performed under both echocardiographic and fluoroscopic guidance.

TEE or TTE was used to document complete occlusion of the defect, both prior to and following release of the device from the delivery cable. If device position was not certain or questionable after all these maneuvers, the device was recaptured entirely or partly and repositioned following similar steps. Once device position was verified, the device was released by counter clockwise rotation of the delivery cable using a pin vice. There was often a notable change in the angle of the device as it was released from the slight tension of the delivery cable and it self-centers within the ASD and aligns with the interatrial septum.

Post catheterization Care: Patients received a dose of an appropriate antibiotic during the catheterization procedure and two further doses at 8-hour intervals post-catheterization. Patients were also asked to take endocarditis prophylaxis when necessary for 6 months after the procedure, as well as aspirin 5 mg/Kg daily in children for 6 months and the adult patients were kept on both aspirin 75- 150 mg and clopidogrel for 6months.

Follow up evaluation: All patients were evaluated by ECG and echocardiography 24hours, 3 months and 6 months after the procedure.

Criteria of success

1. No residual shunts
2. No encroachment upon nearby structure
3. Decrease in pulmonary artery pressures
4. Improvement in cardiac remodeling

Statistical Analysis: All data were collected, tabulated and statistically analyzed using the PC computer. The data were entered to the Statistical Package for Social Science Program (SPSS) version 20. The quantitative data were presented as mean and SD for the parametric data and as median and interquartile ranges (IQR) for the non parametric data while the qualitative data was presented as a number and percentage. Chi square test was used to compare between two groups with qualitative data. While, paired sample t-test was used to compare between two paired groups with quantitative data.

The Confidence Interval (CI) was set to be a 95% and the probability (p-value) was considered significant at the following levels:

1. P > 0.05: Considered non statistical significant.
2. P < 0.05: Considered a statistically significant.
3. P < 0.01: Considered a highly statistically significant. [8]

Results

This study included 50 patients undergoing ASD transcatheter device closure in National Heart Institute hospital in the period from April 2014 to April 2015.

Patient characteristics: The study included 27 males (54%) and 23 females (46%) with age ranging from 2.5 to 49 years (mean 6 years). The weight of our patients ranged from 10 to 125 kg with mean 32.60 ± 27.28. The body surface area (BSA) of our patients ranged from 0.6-2.3 with mean 1.02 ± 0.48

The ASD diameter using TTE ranged from 7to 35 mm (mean 16.13 ± 6.51 mm) and using TEE ranged from 10 to 36 mm (mean 18.67 ± 6.63 mm)

The aortic rim ranged from 2 to 10 mm (mean 4.95 ± 2.06 mm), the mitral rim ranged from 4 to 15 mm (mean 9.50 ± 2.71 mm), the SVC rim ranged from 5 to 15 mm (mean 10.60 ± 2.65 mm), the IVC rim ranged from 6 to 19 mm (mean 10.43 ± 3.09 mm) , the pulmonary vein rim ranged from 5 to 14 mm (mean 10.3±2.58 mm).

Twenty patients (40%) underwent ASD closure under TTE guidance while 30 patients (90%) underwent ASD closure under TEE guidance. TEE guidance decreased the fluoro time.

Electrocardiographic remodeling after ASD closure: All ECG parameters representing the electrical remodeling showed statistically significant improvement after 24h of ASD closure except for QT minimum and P minimum (table 1) after 3m all parameters showed statistically significant improvement compared to before ASD closure and 24h after closure except for QT minimum (table 2, 3) and at 6m of follow up all parameters showed statistically significant improvement (table 4).

1-Comparison between the ECG parameters before closure with those 24 hours after closure: It showed a highly significant reduction in the values of P maximum (p = 0.001), P dispersion (p = 0.001), QT maximum (p = 0.001), QT dispersion (p = 0.001), QRS interval (p = 0.001) and the PR interval (p = 0.001), while there was no significant reduction in the P minimum (p = 0.072) and the QT minimum (p = 0.145) (table 1).

2-Comparison between the ECG parameters before closure with that3month after closure: There was statistically significant improvement in the values of P maximum (p = 0.001), P minimum (p = 0.004), P dispersion (p = 0.001), QT maximum (p = 0.001), QT dispersion (p = 0.001), QRS interval (p = 0.003) and the PR interval (p = 0.002) while there was no statistically significant reduction in the QT minimum (p = 0.237) (table 2).

3-Comparison between the ECG parameters 24 hours after closure with that 3month after closure: It was observed that there was highly significant reduction in the values of P maximum (p = 0.001), P minimum (p = 0.002), P dispersion (p = 0.001), QT maximum (p = 0.001), QT dispersion (p = 0.002), QRS interval (p = 0.001) and the PR interval (p = 0.001) while there was no statistically significant reduction in the QT minimum (p = 0.6684).

ECG	Before			After 24 hours			Paired t-test	
	range	Mean	SD	Range	Mean	SD	t-test	p-value
P max	129-158	140.20	6.04	119-140	130.67	5.40	13.896	0.001
P min	76-114	90.47	9.44	75-112	89.10	8.96	1.865	0.072
P dispersion	26-69	49.73	9.01	26-69	41.43	7.65	9.400	0.001
PR interval	174-200	188.87	6.06	170-193	182.73	5.80	11.547	0.001
QRS duration	122-141	134.40	4.97	119-136	127.87	4.44	9.642	0.001
QT max	596-662	619.07	15.73	591-645	613.43	11.87	6.232	0.001
QT min	530-589	551.47	13.93	531-580	550.50	12.00	1.497	0.145
QT dispersion	59-75	67.60	5.31	51-69	62.60	4.68	7.266	0.001

Table 1: *Comparison between ECG results before and 24h after the procedure.*

ECG	Before			After 3 month			Paired t-test	
	range	Mean	SD	Range	Mean	SD	t-test	p-value
P max	129-158	140.20	6.04	102-124	113.20	5.93	42.814	0.001
P min	76-114	90.47	9.44	73-91	80.57	4.46	7.573	0.004
P dispersion	26-69	49.73	9.01	24-44	32.13	6.00	11.687	0.001
PR interval	174-200	188.87	6.06	166-191	174.27	6.76	12.498	0.002
QRS duration	122-141	134.40	4.97	113-128	119.87	4.12	16.373	0.003
QT max	596-662	619.07	15.73	588-641	605.27	13.57	13.906	0.001
QT min	530-589	551.47	13.93	532-581	550.17	13.00	1.209	0.237
QT dispersion	59-75	67.60	5.31	48-67	55.00	4.76	16.803	0.001

Table 2: *Comparison between ECG results before and 3 month after procedure.*

ECG	24 hours after			3 month after			Paired t-test	
	range	Mean	SD	Range	Mean	SD	t-test	p-value
P max	119-140	130.67	5.40	102-124	113.20	5.93	29.672	0.001
P min	75-112	89.10	8.96	73-91	80.57	4.46	6.723	0.002
P dispersion	26-57	41.43	7.65	24-44	32.13	6.00	7.183	0.001
PR interval	170-193	182.73	5.80	166-191	174.27	6.76	10.772	0.001
QRS duration	119-136	127.87	4.44	113-128	119.87	4.12	12.073	0.001
QT max	591-645	613.43	11.87	588-641	605.27	13.57	11.353	0.001
QT min	531-580	550.50	12.00	532-581	550.17	13.00	0.433	0.668
QT dispersion	51-69	62.60	4.68	48-67	55.00	4.76	11.305	0.002

Table 3: *ECG parameters 24 hours and 3 month after closure.*

4-Comparison between the ECG parameters 3month after closure with that 6month after closure: It was observed that there was significant reduction in the values of P maximum (p = 0.004), P minimum (p = 0.004), P dispersion (p = 0.004), QT maximum (p = 0.002), QT dispersion (p =0.003), QRS interval (p = 0.002) and the PR interval (p = 0.002) with also statistically significant reduction in the QT minimum (p = 0.004) (Table 4).

ECG	3 month			6 months			t-test	p-value
	Range	Mean	SD	Range	Mean	SD		
P max	102-124	114.87	5.25	102-122	110.67	5.19	11.846	0.004
P min	73-91	81.27	4.79	71-89	79.13	4.94	5.264	0.004
P disp	24-44	33.60	5.55	24-42	30.53	5.08	10.213	0.004
PR	166-191	174.40	6.92	160-182	168.00	6.16	14.379	0.002
QRS	113-128	119.33	3.90	110-123	116.20	3.47	10.783	0.002
QT max	588-641	604.33	12.54	582-637	598.67	13.28	17.000	0.002
QT min	532-581	549.20	12.90	530-575	547.13	12.20	5.998	0.004
QT disp	48-67	54.93	5.13	42-65	51.13	5.73	14.511	0.003

Table 4: *ECG parameters 3m and 6 month after closure.*

Echocardiographic remodeling after ASD closure

All echocardiographic parameters of remodeling were improved after 24h including those of the right sided chambers dimension and function , left sided chambers dimension and function and pulmonary artery pressure (table 5) and also after 3m of follow up (table 6,7) and at 6m (table 8,9).

1- Comparison between the echocardiographic parameters measured before and those measured 24 hours after device closure: There was a highly significant difference in all parameters; the LVEF (p = 0.000), LVEDD (p = 0.000), LAD1 (p = 0.002), LAD2 (p = 0.002), TAPSE showed a significant increase while the RVEDD (p = 0.001), RAD1 (p = 0.001), RAD2 (p = 0.001), RVSP (p = 0.000), and mean PAP (p = 0.001) showed a significant decrease (Table 5).

ECHO	Before			24 hours after			Paired t-test	
	Range	Mean	SD	Range	Mean	SD	t-test	p-value
LV EF	60-76	66.80	4.22	67-80	72.93	3.41	-10.489	0.000
LV EDD (mm)	24-49	33.17	6.44	26-51	35.03	6.48	-5.361	0.000
RV EDD (mm)	15-40	25.67	5.50	15-29	21.20	4.72	7.613	0.001
LAD1	18-38	25.57	5.86	20-40	27.93	5.76	-5.572	0.002
LAD2	25-47	35.73	6.73	25-48	37.70	6.35	-5.410	0.002
RAD1	17-50	33.00	6.82	22-42	29.30	6.10	5.798	0.001
RAD2 (mm)	27-50	39.07	5.59	25-45	36.47	5.80	3.928	0.001
Mean PAP (mmHg)	14-22	16.97	3.37	9-20	13.33	3.20	9.091	0.001
RVSP (mmHg)	23-40	30.77	4.69	20-33	24.70	3.35	11.275	0.000
TAPSE (mm)	15-18	16.44	3.30	17-20	18.55	3.60	9.08	0.001

Table 5: *Echocardiographic results before and 24 hours after device closure.*
Left ventricle ejection fraction(LVEF); left ventricle end-diastolic dimension (LVEDD); right ventricle end-diastolic dimension(RVEDD); horizontal left atrial dimension (LAD1); vertical left atrial dimension (LAD2);horizontal right atrial dimension (RAD1); vertical right atrial dimenmsion (RAD2); right ventricle systolivpressutre (RVSP); mean pulmonary artery preasure (PAP), tricuspid annulus plane systolic excursion (TAPSE).

2-Comparison between the echocardiographic parameters measured before and those measured 3 month after device closure: There was a highly significant difference in all parameters; the LVEF (p = 0.000), LVEDD (p = 0.001), LAD1 (p = 0.001), LAD2 (p = 0.001) and RV function by TAPSE (p = 0.000) showed a significant increase while the RVEDD (p = 0.000), RAD1 (p = 0.000), RAD2 (p = 0.000), RVSP (p = 0.000) and mean PAP (p = 0.000) showed a significant decrease (Table 6).

ECHO	Before			3 month after			Paired t-test	
	Range	Mean	SD	Range	Mean	SD	t-test	p-value
LVEF	60-76	66.80	4.22	70-82	75.77	2.93	-14.809	0.000
LV EDD (mm)	24-49	33.17	6.44	28-52	36.70	5.91	-8.253	0.001
RV EDD (mm)	15-40	25.67	5.50	15-28	19.43	3.66	10.922	0.000
LAD1	18-38	25.57	5.86	21-43	29.93	5.32	-7.824	0.001
LAD2	25-47	35.73	6.73	29-48	39.60	5.52	-7.136	0.001
RAD1	17-50	33.00	6.82	17-38	26.67	4.80	9.023	0.000
RAD2 (mm)	27-50	39.07	5.59	28-45	34.70	5.13	7.037	0.000
Mean PAP (mmHg)	14-22	16.97	3.37	8-16	10.43	2.34	13.379	0.000
RVSP (mmHg)	23-40	30.77	4.69	15-25	21.27	2.41	13.616	0.000
TAPSE	15-18	16.44	3,30	19-24	20.21	2.46	11.543	0.000

Table 6: *Echocardiographic results before and 3 month after procedure.*
Left ventricle ejection fraction(LVEF); left ventricle end-diastolic dimension (LVEDD); right ventricle end-diastolic dimension(RVEDD); horizontal left atrial dimension (LAD1); vertical left atrial dimension (LAD2); horizontal right atrial dimension (RAD1); vertical right atrial dimension (RAD2); right ventricle systolicpressutre (RVSP); mean pulmonary artery pressure (PAP), tricuspid annulus plane systolic excursion (TAPSE).

3-Comparison between the echocardiographic parameters measured 24h and those measured 3 month after device closure: It showed a highly significant increase in LVEF (p = 0.000), LVEDD (p = 0.000), LAD1 (p = 0.001), LAD2 (p = 0.001)and RV function by TAPSE (p = 0.000) , while the RVEDD (p = 0.002), RAD1 (p = 0.000), RAD2 (p = 0.000), RVSP (p = 0.000), mean PAP (p = 0.000) showed a significant decrease (Table 7).

4-Comparison between the echocardiographic parameters measured 3 month and those measured 6 month after device closure: It showed a significant difference in all parameters; LVEDD (p = 0.001), LAD1 (p = 0.001), LAD 2(p = 0.004) ,TAPSE (p = 0.000) showed a significant increase while the RVEDD (p = 0.001), RAD1 (p = 0.004), RAD2 (p = 0.002), RVSP (p = 0.000), mean PAP (p = 0.000) showed a significant decrease, while the LVEF (p = 0.014) showed no statistically different changes (Table8).

5-Comparison between the Quantitative RV measurements before closure with that 24 hours after closure: Before closure 8 patients had normal RV (16%), 30patients had mildly dilated RV (60%) and 12 patients had moderately dilated RV (24%), 24 hours after closure 31 patients had normal RV (62%) and 13 had mildly dilated RV (26%) and 6 patients had moderately dilated RV (12%). The number of normal patients had significantly increased after 24 hours and number of patients who had mild and moderate RV dilatation significantly decreased (P value = 0.001) (table 9)

6-Comparison between the Quantitative RV measurement 24h and 3 month after closure: Three month after closure 45 patients had normal RV (90%) and 5 had mildly dilated RV (10%) and there were no patients having moderately dilated RV (P value = 0.105). By comparing RV size 24 hours and 3 month after closure; there was no statistically significant difference. (Table 10)

ECHO	After 24 hours			After 3 month			Paired t-test	
	Range	Mean	SD	Range	Mean	SD	t-test	p-value
LV EF	67-80	72.93	3.41	70-82	75.77	2.93	-8.268	0.000
LV EDD (mm)	26-51	35.03	6.48	28-52	36.70	5.91	-5.053	0.000
RV EDD (mm)	15-29	21.20	4.72	15-28	19.43	3.66	5.452	0.002
LAD1	20-40	27.93	5.76	21-43	29.93	5.32	-6.361	0.001
LAD2	25-48	37.70	6.35	29-48	39.60	5.52	-4.725	0.001
RAD1	22-42	29.30	6.10	17-38	26.67	4.80	7.244	0.000
RAD2 (mm)	25-45	36.47	5.80	28-45	34.70	5.13	5.176	0.000
Mean PAP (mmHg)	9-20	13.33	3.20	8-16	10.43	2.34	8.204	0.000
RVSP (mmHg)	20-33	24.70	3.35	15-25	21.27	2.41	9.961	0.000
TAPSE	17-20	18.55	3.60	19-24	20,21	2.46	11.543	0,000

Table 7: *Echocardiographic results 24h and 3 month after procedure.*
Left ventricle ejection fraction (LVEF); left ventricle end-diastolic dimension (LVEDD);right ventricle end-diastolic dimension (RVEDD); horizontal left atrial dimension (LAD1); vertical left atrial dimension (LAD2); horizontal right atrial dimension (RAD1); vertical right atrial dimension(RAD2); right ventricle systolicpressure (RVSP); mean pulmonary artery pressure (PAP), tricuspid annulus plane systolic excursion (TAPSE).

Echo		3 month			6 months		T	p-value
	Range	Mean	SD	Range	Mean	SD		
LVEF	70-82	74.40	2.38	71-78	75.33	2.26	-2.824	0.014
LVEDD	28-52	36.13	6.23	30-50	37.53	5.15	-3.862	0.001
RVEDD	15-28	19.87	4.03	15-24	17.80	2.70	4.800	0.001
LAD1	21-43	28.73	5.13	28-43	32.13	3.82	-7.462	0.001
LAD2	29-48	38.67	6.26	33-49	39.87	5.22	-2.316	0.004
RAD1	21-38	26.87	4.63	21-36	25.33	4.24	5.996	0.004
RAD2	28-45	34.47	4.88	27-40	32.53	4.67	16.358	0.002
PAP	8-16	11.00	2.62	7-12	9.20	1.37	4.583	0.000
RVSP	15-25	21.87	2.85	14-22	18.80	2.11	10.800	0.000
TAPSE	19-24	20.21	2.46	20-29	24.64	4.22	9.765	0,000

Table 8: *Echocardiographic results 3m and 6 month after procedure.*
left ventricle ejection fraction(LVEF); left ventricle end-diastolic dimension (LVEDD); right ventricle end-diastolic dimension(RVEDD); horizontal left atrial dimension (LAD1); vertical left atrial dimension (LAD2); horizontal right atrial dimension (RAD1); vertical right atrial dimension (RAD2); right ventricle systolicpressure (RVSP); mean pulmonary artery pressure (PAP (tricuspid annulus plane systolic excursion (TAPSE).

RV	Before		24 hours after		Chi-square	
	No.	%	No.	%	X2	P-value
Normal	8	16%	31	62%	13.613	0.001
Mild	30	60.00%	13	26%		
Moderate	12	24%	6	12%		
Total	50	100.00%	50	100.00%		

Table 9: *Quantitative RV measurement before closure with that 24 hours after closure.*

RV	After 24 hours		After 3 month		Chi-square	
	No.	%	No.	%	X2	P-value
Normal	39	78%	45	90%	4.51	0.105
Mild	8	16%	5	10%		
Moderate	3	6%	0	0.00%		
Total	50	100.00%	50	100.00%		

Table 10: *Quantitative RV measurement 24h and 3m after closure.*

7-Comparison between the Quantitative RV measurements 3 month after closure with that 6 month after closure: By comparing the RV size in the patients who had completed the 6 month period post device closure and underwent the six month follow up, at 3 month 46 patients (92%) of the 50 patients had normal RV while 4 patients (8%) of the 50 patients had mildly dilated RV while at 6 month 49 patients had normal RV (98%) and 1 had mildly dilated RV (2%) and there were no patients having moderately dilated right ventricle. (P value = 0.142). By comparing RV size 3 month and 6 month after closure; there was no statistically significant difference.

37 patients underwent closure using Amplatzer device (74%) and 13 patients underwent closure using Occultech device (26%). Amplatzer device size used ranged from 12-36 mm while occlutech device size used ranged from 12-34 mm. The study showed a highly statistically significant linear correlation between ASD size by TTE (r = 0.937) and TEE (r = 0.966) (p = 0.000)

All the patients studied had successful ASD device closure, after 24 hours only 2 patients had trivial residual shunting (6.6%) which disappeared after 3 month.

Discussion

ASDs account for 5–10% of all congenital heart defects. These defects should be closed when diagnosed during childhood or adulthood because they lead to right atrial and ventricular volume load, arrhythmias and paradoxical embolism [9].

Transcatheter closure of ASD has become an important alternative to surgical repair in the management of patients with secundum-type ASD [10]. As a result of ASD closure, the right heart is protected from volume load, leading to reduction in both pulmonary artery pressure and right heart cavity dimensions. Thus, significant symptomatic improvement with decrease in arrhythmic events was observed in these patients [11].

The current study evaluated the effect of trans-catheter closure of secundum ASD in adults and children on the electric and echocardiographic remodeling in intermediate and short- term follow-up for 6 month.

This study included 50 patients that underwent trans-catheter ASD device closure (27 males and 23 females) in National Heart Institute in the period from April 2014 to April 2015 with age range from 2- 65 years and median 6 years. All patients had successful device closure (100%) with 2 patients having a residual trivial shunt after 24 hours (6.6%) that disappeared after 3 month of device closure (p = 0.313).

In the current study the ASD diameter by TTE ranged from 7-35 mm (mean 16.13 ± 6.51 mm) and by TEE from 10-36 mm (mean 18.67 ± 6.63 mm) where the ASD size ranged from 8-33 mm (mean 18.78 ± 6.38 mm). 37 patients underwent closure using Amplatzer device (74%) and 13 patients underwent closure using Occultech device (26%) and Amplatzer device size used ranged from (12-36 mm) while occlutech device size used ranged from (12-34 mm). The study showed a highly statistically significant linear correlation between ASD size by TTE (r = 0.937) and TEE (r = 0.966) (p = 0.000)

Electrical remodeling

Comparing the ECG parameters measured before closure and those after 24h, 3m and 6m of closure in the present study showed a highly significant reduction in the values of P maximum, P dispersion, QT maximum, QT dispersion, QRS interval and the PR interval while significant reduction in the P minimum appeared at 3m but QT minimum didn't show significant change during follow up.

As a noninvasive marker, P-wave dispersion is especially useful in predicting atrial arrhythmias [28]. Arrhythmias, particularly atrial fibrillation and flutter, are significant causes of morbidity among patients with ASD.

A few studies evaluating ECG variables among patients with secundum-type ASD have demonstrated an increase in P-wave dispersion [29]. After comparing 62 patients with Secundum-type ASD and 47 healthy individuals it was reported that P maximum, P minimum, and P dispersion times were prolonged for patients with Secundum-type ASD due to mechanical and electrical changes in the atrial myocardium.

The reasons for the increase in P-wave duration in patients with ASD may be increased atrial stretch, atrial dilation or atrial conduction disturbance it was also demonstrated a reduction in P dispersion after surgical ASD closure.

Mehmet., *et al*. [12] was the first to demonstrate statistically significant reductions in P maximum and P dispersion after transcatheter closure of ASD. Trans-catheter ASD closure can reverse electrical and mechanical changes in the atrial myocardium and result

It is known that QT dispersion increases the risk of cardiac events and arrhythmia. In previous studies, QT dispersion increased in various cardiac diseases such as arrhythmia, myocardial infarction, heart failure, and cardiomyopathy [31].

However, to date, the relationship of QT dispersion and arrhythmias is not clear. It was demonstrated an early decrease in QRS duration after surgical ASD closure [32] and a significant decrease in QT dispersion after trans-catheter ASD closure [33]. These mechano-electrical changes reflect better intra-atrial and intra-ventricular conduction properties after volume unloading of both right heart chambers and can potentially decrease the substrate for late atrial arrhythmias.

In our study; we showed highly statistically significant reduction in QT maximum and QT dispersion values. But no significant reduction in the QT minimum value in the 3 month follow up that maybe related to changes in the intra ventricular conduction properties but at the 6 month follow up period there was a significant reduction in the QT minimum to a mean of 547.13 ± 12.2 (p = 0.004).

Only a few reports in the literature relate to the prevalence of cardiac arrhythmias after ASD closure, and these reports are somewhat conflicting [34]. Reductions in right heart volume overload and improvements in right atrium and ventricular diameters after percutaneous ASD closure decrease the prevalence of cardiac arrhythmias [35].

However, some studies demonstrated that increased prevalence of atrial arrhythmias due to unknown causes after surgical ASD closure [34] suggesting that older age and mean PAP are risk factors for persistent atrial arrhythmias and the development of new atrial arrhythmias after surgical ASD closure.

In another study comparing surgical and trans-catheter methods, reported a higher occurrence of cardiac arrhythmias in the surgical group, although the difference did not reach statistical significance [36].

Wilson., *et al*. [4] documented the presence of arrhythmias (most frequently atrial fibrillation and atrial flutter) in 26 of 211 patients (12%) before trans-catheter ASD closure. During a mean follow up period of 1.8 years, arrhythmias had resolved in 16 patients and new arrhythmias had occurred for 6 patients after ASD closure.

Mehmet., *et al*. [12] assessed arrhythmias over a longer follow-up period (2-years). Before ASD closure, three patients had paroxysmal atrial fibrillation, one patient had supra ventricular tachycardia, and two patients had frequent atrial extra beats. After ASD closure, arrhythmias were eliminated in five patients, and only one patient had ongoing paroxysmal atrial fibrillation that the greatest likelihood of remaining free of arrhythmia A prospective study reported was found in patients without a history of arrhythmia and those younger than 40 years at the time of ASD closure [36].

Atrial arrhythmias also may develop in the late period after ASD closure. In a long-term follow-up study, reported complete atrioventricular block in one patient 4.5 years after ASD closure [36]. Atrial tachyarrhythmias resolved after ASD closure, suggesting that atrial size can play a role in the mechanism of the tachycardia. Therefore, regular follow-up evaluation by Holter ECG is recommended for these patients.

Echocardiographic remodeling

All echocardiographic parameters of remodeling were improved after 24h including those of the right sided chambers dimension and function, left sided chambers dimension and function and pulmonary artery pressure and also after 3m of follow up and after 6m.

Our results are in agreement with Edmundo., *et al*. [13] who studied 120 patients with hemodynamically significant ASD closed using Occlutech device in over a period of 3 years follow up, all patients had significant reduction or normalization of the RV size and function by TAPSE without residual shunt.

Also Chien., *et al*. [14] found that right heart volume load is decreased and improvement of RV function by TAPSE after ASD closure using the trans-catheter device closure and so reduction in PAP and right heart cavity dimensions is established. Previous studies have shown a significant cardiac remodeling early after percutaneous ASD closure [15,16].

Du., *et al*. [17] also showed that after trans-catheter closure of the ASD, RV volume overload decreased within 24 hours.

Walker., *et al*. showed that cardiac remodeling occurs quite quickly after ASD device closure [18]. Reduced right atrial and ventricular volumes are apparent within 24 hours, and probably earlier.

Another study showed that the remodeling process appears to continue for at least 1 year and is more advanced in the right ventricle than the right atrium [19]. Furthermore, the magnitude of right atrial remodeling is inversely related to patient age at the time of closure, as demonstrated in another study that reported persistent right atrial dilation in up to 64% of patients who underwent late ASD closure, which in turn was associated with elevation of brain natriuretic peptide levels and right ventricular diastolic dysfunction [20]. All these data clearly argue for early and timely closure of ASDs at the time of diagnosis. Berger., *et al*. found statistically significant reductions in RVEDD, function by TAPSE and systolic PAP.

Another study reported a 30% reduction in the RV EDD/LV EDD ratio (an indicator of cardiac geometry) 6 months after trans-catheter closure of ASD [16]. The improvement of cardiac geometric remodeling after ASD trans-catheter device closure resulted in the increase in LV ejection fraction [21,22].

In a study including 38 patients who underwent successful ASD closure showed a highly statistically significant reduction in RAD (p = 0.004) and RV dimension (p = less than 0.001) in a follow up period of 3-6 months (23) which is agree with our study.

The current study also evaluated RV dimensions quantitatively. Henry., *et al*. investigated RV size quantitatively by subjective TTE assessment. Before closure, 3% of the cohort had a normal RV size, 35% had a mildly dilated RV, 54% had a moderately dilated RV, and 7% had a severely dilated RV. At the last follow-up evaluation, RV had returned to normal for 75%, 19% had persistent mildly dilated RV, 5% had a moderately dilated RV, and 1% had a severely dilated RV [24].

Another study showed that only 29% of patients had persistent RV enlargement 1 year after percutaneous ASD closure. Other report showed that only 33% of the patients had persistent RV enlargement at a 2-year follow up assessment [12]. In agreement with other studies, our study confirmed that the RV generally returns to normal size and function by TAPSE after ASD closure in children and adult patients.

Previous studies [26] have shown that persistent RV enlargement continues in approximately 50–70% of both adults and children after surgical treatment despite elimination of right heart volume load. This situation can be explained by a few mechanisms including myocardial changes due to long-term volume load, functional abnormalities due to cardiopulmonary bypass, and geometric modifications of the heart due to opening of the pericardium

Patel., *et al*. [21] investigated the phenomenon of persistent RV enlargement after surgical ASD closure and showed the importance of early treatment specifically for patients older than 40 years.

Conclusion

Transcatheter ASD device closure leads to significant improvement in the heart cavity dimensions in particular the right sided dimensions and function and can reverse electrical and mechanical changes in the atrial and ventricular myocardium in children and adults in the short and intermediate –term follow up period.

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Volume 2 Issue 1 September 2015