The Outcomes of Transcatheter Closure of Secundum Atrial Septal Defects on Cardiac Remodeling by Electrocardiography and Holter Study in Pediatric Population

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ABSTRACT
Background: A significant atrial septal defect leads to atrial interstitial fibrosis, arrythmia and right ventricle remodelling.
Objective: This study aimed to investigate the outcomes of transcatheter closure of secundum atrial septal defects on cardiac remodelling by electrocardiography and Holter study in pediatric population
Patients and Methods This prospective observational study was conducted on 69 patients (35 males and 34 females), aged from 1.5 to 16 years, diagnosed with secundum ASD who were referred for elective transcatheter secundum ASD device closure at Department of Pediatrics, Faculty of Medicine, Sohag University Hospitals, between April 2022 and June 2023.
Results: There was a significant reduction in all ECG parameters including HR, PR interval, QRS duration, QRS Axis and QTc interval immediately, one day post-procedure, after 1 month, 6 months and after 1year compared to pre-transcatheter (P value<0.05). Sinus tachycardia, prolonged QTC duration, prolonged PR interval, prolonged QRS duration and rt axis deviation were insignificantly different between males and females pre transcatheter, post transcatheter ASD closure. Heart rate variability indices (Pnn50, RMS-SD, SDNN, SDANN and tri) were significantly higher one day post transcatheter, also after one month, after 6 months and after one year compared to the baseline values pre-closure (P value 0.05).
Conclusions: It could be concluded that transcatheter ASD device closure leads immediately to a significant improvement in electrical reverse remodelling parameters. Holter ECG study is considered a beneficial tool to evaluate cardiac autonomic functions and the influence of transcatheter closure of ASD on cardiac autonomic function and magnitude of arrhythmia.
Keywords: Atrial Septal Defects, Holter, ECG Changes, Transcatheter Closure.

INTRODUCTION

Ten percent of congenital cardiac anomalies are atrial septal defects (ASD) [1]. ASD can be identified as a single abnormality, in conjunction with additional cardiac anomalies, or in conjunction with other syndromes, which are occasionally connected to well-known characteristics [2].

Despite its high success rate, low mortality, and favorable long-term results, surgical repair is linked to thoracotomy scars, pain, and morbidity [3]. For this reason, TCC of the ASD has emerged as a viable alternative to surgery in recent years [4].

Over the past ten years, the majority of patients' surgical ASD repair has been replaced with ASD device closure as the accepted procedure for treating secundum ASD [5, 6]. Right chamber enlargement and cardiac arrhythmias are well-known long-term effects of ASD [7]. Many writers thus advocate for ASD closure before to maturity [8, 9].

The traditional ECG characteristics that signify a severe ASD include a longer PR interval, a prolonged QRS duration, and a right axis deviation of the QRS [10].

Since cardiac incisions, cardiopulmonary bypass, and sutures on the right atrium and interatrial septum are not present, percutaneous ASD closure is the best option for researching changes in right ventricle (RV) dimensions and their effects on ECG [11].

This study aimed to investigate the outcome of transcatheter closure of secundum atrial septal defects on cardiac remodelling by electrocardiography and Holter study in pediatric population.

We studied the cardiac electrical remodelling and heart rate variability by 12 lead electrocardiography (ECG) and Holter examination immediately at one day, one months, 6 and 12 months after TCC of secundum ASD in a group of paediatric population.

PATIENTS AND METHODS

This prospective observational study included a total of 69 patients (35 males and 34 females), aged from 1.5 to 16 years, diagnosed with secundum ASD who were referred for elective transcatheter secundum ASD device closure at Department of Pediatrics, Faculty of Medicine, Sohag University Hospitals, between April 2022 and June 2023.

Inclusion criteria: Children diagnosed with solitary Secundum ASD with enough rims appeared favorable for device closure by transthoracic echocardiography (TTE), which was confirmed by transesophageal echocardiogram at the time of the surgery.

Exclusion criteria: (1) Patients with primum type ASD or sinus venosus, (2) Patients with insufficient rims.

Transcatheter closure of secundum ASD:
Under general anesthesia and with the use of TEE (Trans-oesophageal echocardiography) or TTE

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guidance, percutaneous transcatheter ASD closure was carried out on patients whose anatomical features and rims were suitable. Each patient received 100 IU/kg of heparin. Prophylaxis against infective endocarditis was given in form of a combination of Cefotaxime and Unasyn according to the child weight. The procedure was done without using balloon sizing. The diameter of defect was measured in three views of TTE or TEE and the largest diameter was obtained and adding 20% more to achieve the appropriate device diameter. Many techniques were used to deploy the device in large defects like, left upper pulmonary vein (LUPV) deployment technique, right upper pulmonary vein (RUPV) deployment technique or Balloon assisted method.
The procedures used in the surgery were the Amplatzer septal occluder (ASO), the Occlutech septal occluder (OSO), and the Life-Tech cera septal occluder.

Electrocardiography study:

Prior to catheterization, every patient had sinus rhythm, and all were not using antiarrhythmic drugs, except for a male child who experienced recurrent SVT episodes that were managed with medical treatment. All patients underwent 12 leads ECG (Fukuda Denshi CardiMax ECG device model FCP-7101 with a 25mm/s paper speed, gain 10 mm/mV) pre-closure and the day after the procedure then repeated at 1, 6 and 12 months respectively.

By creating descriptive reports and identifying the following characteristics, twelve-lead surface ECGs were acquired and computerized values were examined: QRS axis, heart rate (HR). The QT interval was measured from the beginning of the QRS complex to the end of the T wave, which was defined by the return of the terminal T wave to the isoelectric TP baseline. The PR interval duration in lead II was measured from the initial deflection of the P wave to the initial deflection of the QRS complex.

Furthermore, the width of the QRS duration was measured from the initial deflection of the QRS complex to where the terminal deflection crosses the baseline, taken in any chest lead where the deflection was severe enough to allow for an accurate assessment [expressed in milliseconds]. Bazett's algorithm was then used to adjust the QT interval for heart rate. Every ECG paper was interpreted using particular centile charts for age-based normal ECG wave and interval values [12]. Any aberrant rhythms (heart block, ectopic, supraventricular, or ventricular tachycardia) were checked on the ECG.

Holter Study:

Prior to the surgery, a 6-channel Holter ECG (Mortara H3+Holter ECG) was taken. The day following the procedure, it was repeated at one, six, and twelve meters. Heart rate variability metrics (standard deviation of the IBI of normal sinus beats (SDNN), standard deviation of 5-minute average NN intervals (SDANN), root mean square of successive differences (RMS-SD), Tri, and Pnn50%) were assessed for the recordings.

Ethical approval:
This study was ethically approved by Ethical Committee of Sohag University Hospital in Egypt. Written informed consent of the participants' parents was obtained. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical analysis

SPSS version 26.0 was used for the statistical analysis. The paired T-test was used to compare the two measurements and give the quantitative data as mean± SD. The X2-test or Fisher's exact test, as applicable, was used to analyze the qualitative variables, which were expressed as frequency and percentage (%). Statistical significance was defined as a two-tailed P value < 0.05.

RESULTS

The participants' average age was 6.3 ± 4.14 years, and the majority were female 35 (50.72%). Successful closure of secundum ASD was achieved in 98.5% of patients (Table 1).

Table (1): Demographics and ASD data.

N=69	
Age (year)	6.3 ± 4.14
Weight (Kg)	18.7± 10.6
Sex Male Female	 34 (49.28%) 35 (50.72%)
ASD diameter by TTE, mm	12.83 ± 4.48
ASD diameter by TEE, mm	15.32± 5.62
Device diameter, mm	19.2 4± 7.13
Pulmonary pressure (mmHg).	21.43± 5.62
Qp/Qs	1.76± 0.82
Procedure time (min)	40 ± 15
Fluoroscopy time (min)	7 ± 4.36

The current study revealed a significant reduction in HR, PR interval duration, QRS axis, QRS duration and QTc interval measurements post catheter, after 1 month, 6 months and after 1year compared to pre transcatheter (P value<0.001, 0.009, <0.001, <0.001, 0.002, and <0.001 respectively) (Table 2).

Table (2): ECG parameters of the studied patients

	Pre transcatheter	Post transcatheter	After 1 month	After 6 months	After 1 year
HR (beats/min)	116.6 ± 21.26	105.9 ± 17.48	98.5 ± 18.1	94 ± 16.69	90.3 ± 14.69
P value compared to pre		**<0.001***	**<0.001***	**<0.001***	**<0.001***
PR interval (ms	138.9 ± 22.34	131.5 ± 23.27	123.9 ± 23.27	121.1 ± 29.54	116.8 ± 26.7
P value compared to pre		**0.009***	**<0.001***	**<0.001***	**<0.001***
QRS (ms)	89.8 ± 11.35	85.4 ± 12.33	82.4 ± 14.44	78 ± 14.16	74.6 ± 14.89
P value compared to pre		**<0.001***	**<0.001***	**<0.001***	**<0.001***
Axis	69.5 ± 29.64	62.4 ± 30.3	54.2 ± 33.53	48.6 ± 31.99	45.9 ± 32.83
P value compared to pre		**0.002***	**<0.001***	**<0.001***	**<0.001***
QTc (ms)	436 ± 20.6	425.9 ± 23.04	416.8 ± 20.3	410.7 ± 19.89	404.9 ± 21.78
P value compared to pre		**<0.001***	**<0.001***	**<0.001***	**<0.001***

HR: heart rate, *: significant. QRS: depolarization of ventricles, QTc: axis and interval reflect ventricular repolarization, and its prolongation.

Abnormalities found in ECG were sinus tachycardia, prolonged QRS duration were due to right bundle branch block in most cases, one case with left anterior fascicular block and one case with Wolf Parkinson White syndrome, prolonged PR interval duration (first degree heart block), prolonged QTC interval duration and Rt axis deviation which were insignificantly different between males and females pre transcatheter, post transcatheter, after 1month, after 6 months and after 1 year. Left axis was found in 1 (2.94%) male after 1month, after 6months and after 1year associated with left anterior fascicular block (Table 3).

Table (3): ECG findings in the studied patients pre and post transcatheter closure

		Pre transcatheter	Post transcatheter	After 1 month	After 6 months	After 1 year
Prolonged PR interval						
Males (n=34)		5 (14.71%)	4 (11.76%)	4(11.76%)	4 (11.76%)	3 (8.82%)
Females (n=35)		3 (8.57%)	2 (5.71%)	1 (2.86%)	1 (2.86%)	1 (2.86%)
P value between males and females		0.477	0.428	0.198	0.198	0.356
Sinus Tachycardia						
Males (n=34)		5 (14.7%)	3(8.82%)	0(0%)	0 (0%)	0(0%)
Females (n=35)		5(14.3%)	3(8.58%)	2(5.72%)	1(2.86%)	1(2.86%)
P value between males and females		0.492	0.492	0.239	0.239	0.053
Prolonged QRS duration						
Males (n=34)		10(29.41%)	11 (32.35%)	12 (35.29%)	11(32.35%)	9(26.47%)
Females (n=35)		9 (25.71%)	6 (17.14%)	6 (17.14%)	6 (17.14%)	4(11.43%)
P value between males and females		0.731	0.142	0.086	0.142	0.133
		Pre transcatheter	**Post transcatheter**	**After 1 month**	**After 6 months**	**After 1 year**
Axis deviation						
Males (n=34)	**Normal**	30(88.2%)	30(88.2%)	32(94%)	32(94%)	32(94%)
	Right	4 (11.76%)	4 (11.76%)	1(2.94%)	1 (2.94%)	1(2.94%)
	Left	0(0%)	0(0%)	1 (2.94%)	1 (2.94%)	1 2.94%)
Females (n=35)	**Normal**	32(91.4%)	33(94.28%)	34(97.1%)	34(97.1%)	34(97.1%)
	Right	3 (8.58%)	2(5.72%)	1 (2.86%)	1 (2.86%)	1(2.86%)
	Left	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
P value between normal axis		--	1.00	1.00	0.492	0.239
P value between right axis		0.356	0.239	0.492	0.492	0.492
P value between left axis		--	--	1.00	1.00	1.00
Prolonged QTC duration						
Males (n=34)		3 (8.82%)	2 (5.88%)	1 (2.94%)	1 (2.94%)	3 (8.82%)
Females (n=35)		9(25.71%)	5 (14.29%)	4(11.43%)	(14.29%)	2(5.71%)
P value between males and females		1.00	0.428	0.356	0.198	0.673

*: significant. QTC: Corrected QT Interval.

Holter study has revealed the mean heart rate, mean QTC duration and was used to evaluate cardiac autonomic functions and the influence of transcatheter closure of ASD on cardiac autonomic function by determination of heart rate variability. Mean HR was significantly lower after 1 month, 6 months and 1 year compared to pre (P value 0.003, 0.006 and 0.001 respectively) and was insignificantly different between pre and post transcatheter. Mean QTC was significantly lower post transcatheter, after 1month, after 6months and after 1year compared to pre (P value 0.003, 0.002 and <0.001 respectively). Heart rate variability indices (Pnn 50, RMS-SD, SDNN, SDANN and tri) were significantly higher post transcatheter, after 1month, after 6months and after 1year compared to pre transcatheter (P value 0.002 and <0.001 respectively) (Table 4).

Table (4): Holter measurements of the studied patients

	Pre transcatheter	Post transcatheter	After 1 month	After 6 months	After 1 year
Mean HR (beats/min)	105.5 ± 16.99	105.9 ± 16.61	97.9 ±12.86	95.5 ± 11.52	90.9 ± 10.86
P value compared to pre		0.870	**0.003***	**0.006***	**0.001***
Mean QTC (ms)	396.3 ± 14.81	390.9 ± 10.78	388.1±10.55	386.1 ±12.57	381.1 ± 11.08
P value compared to pre		**0.003***	**0.002***	**<0.001***	**<0.001***
pNN50%	2.1 ± 2.33	4.3 ± 3.86	5.7 ± 4.39	6.2 ± 4.55	7.1 ± 4.55
P value compared to pre		**0.007***	**<0.001***	**<0.001***	**<0.001***
RMSSD	26.9 ± 11.52	40.9 ± 14.59	47.3 ±13.24	51.9 ± 10.97	56.3 ± 10.52
P value compared to pre		**0.004***	**<0.001***	**<0.001***	**<0.001***
SDNN	36.2 ± 14.47	56.9 ± 19.85	79.1 ±14.94	94.3 ± 14.43	105.3±14.47
P value compared to pre		**<0.001***	**<0.001***	**<0.001***	**<0.001***
SDANN	37.1 ± 16.24	60.6 ± 25.72	81.5 ± 24.7	94.5 ± 27.97	113.6±26.89
P value compared to pre		**0.003***	**<0.001***	**<0.001***	**<0.001***
Tri	10.1 ± 3.17	13.1 ± 4.56	14.5 ± 3	16.1 ± 2.89	17.6 ± 2.41
P value compared to pre		**0.002***	**<0.001***	**<0.001***	**<0.001***

HR: heart rate. *: significant. QTc: axis and interval reflect ventricular repolarization, and its prolongations RMSSD: root mean square of successive differences, SDNN: standard deviation of the IBI of normal sinus beats, SDANN: standard deviation of 5-minute average NN intervals.

Table 5 summarize the relation of deficient rims of ASD with development of arrhythmia in 12 patients, four (33.3%) patients had deficient posterior rim and eight (66.7%) had normal posterior rim. There was a relation between arrhythmia and risk factors (deficient posterior rim) P value (<0.05).

Table (5): Relation between arrhythmia and risk factors (deficient posterior rim) of the studied patients

	Arrhythmia (n=12)	No Arrhythmia (n=57)	P value
Deficient posterior rim	4 (33.3%)	0(75%)	**0.0001***
Sufficient rim	8 (66.7%)	57(100%)	**0.0001***

*: significant.

The present study has showed cardiac arrhythmias in some cases after percutaneous transcatheter ASD closure; one (1.4%) case had non sustained SVT prior catheterization and resolved completely after catheterization. One (1.4%) case had left anterior fascicular block that occur after 1m and persisted at 6,12 months. Two (2.8%) cases had developed complete heart block (CHB) 12 hours after transcatheter closure and persisted for 1 week which has resolved by steroid therapy.

Another female child,7 years old had a large ASD secundum measuring 22 mm by TEE, she underwent ASD closure by Occlutech ASD occlude 27mm after many attempts to stabilize the device using left upper pulmonary technique. She developed complete heart block on the second day. She received steroid 2mg/Kg for one week. The rhythm become alternating between CHB and mobilitz II second degree HB. The child is haemodynamically stable and was observed closely by repeated Holter monitoring and she started regaining more period of normal rhythm. Finally, after 2 months she regained complete normal rhythm and persists for 6 months follow-up.

Eight cases had first degree heart block pre-closure however only 4 cases of them have persisted at one year of Follow up ECG.

DISCUSSION

Classic ECG abnormalities related to a large left-to-right shunt are seen in children with secundum ASD. These abnormalities are predicted to follow dilatation of the right atrium and right ventricle and manifest as PR interval lengthening, QRS duration prolongation, and right axis deviation of the QRS [13, 14]. Several studies had revealed the recovery of the RV and its effect on cardiac remodeling after percutaneous trans catheter ASD closure [15-19]. As shown by **Du *et al.*** [18], the patient's age and the degree of the Lt. to Rt. shunt appear to be related to the pace at which the RV reduces.

Long-term effects of ASD include right chamber hypertrophy and cardiac arrhythmias. Consequently, many studies advocate for ASD closure before adolescence age [8, 9].

We studied cardiac electrical remodelling and heart rate variability by 12 lead surface and ambulatory electrocardiography before closure, one day after, at one, 6 and 12 months after transcatheter closure of ASD in a paediatric population.

Based on this study results, HR measurements were significantly lower post catheter, after 1 month, 6months and after 1year compared to pre transcatheter (P value<0.001). **Özyılmaz *et al.*** [20] noted that HR measurements in transcatheter closure of ASD in children were significantly lower post catheter, after 1 month, 6months and after 1 year compared to pre transcatheter.

Conversely, in contrast to our findings, **Komar *et al.*** [21] noted that heart rate initially increases after 1 month of ASD transcatheter closure then decrease after 6 months and after 1 year.

In the current study, the PR measurements were significantly lower post catheter, after 1 month, 6months and after 1year compared to pre transcatheter (P value 0.009 and <0.001 respectively). **Arafa *et al.*** [22] supported our results as they concluded that there was reduction in PR measurement in ASD transcatheter closure after 1 month, 6months and after 1year compared to pre transcatheter.

Although **Kim and Kil al.** [23] had different results as they stated children's PR interval was unaffected by ASD closure, which may be explained by an electrophysiologic research showing that atrial conduction velocity increased and atrial and atrioventricular node refractory times were decreased following ASD closure.

According to our results, QRS measurements were significantly lower post catheter, after 1 month, 6months and after 1year compared to pre transcatheter (P value<0.001). **Mukundan *et al.*** [24] **and Arafa *et al.***[22] reported that QRS measurements were significantly lower post catheter, after 1 month, 6months and after 1year compared to pre transcatheter.

In current cohort study, there was a significant reduction in axis measurements post catheter closure, after 1 month, 6months and after 1year compared to pre-closure (P value 0.002 and <0.001 respectively). **Dhillon *et al.*** [25] found that Axis measurements were significantly lower post catheter of ASD closure in pediatrics, after 1 month, 6months and after 1year compared to pre transcatheter.

Conversely, **El-Sisi *et al.*** [26] disagreed with the results of our cohort as they stated that no significant axis measurements changes detected in post catheter of ASD closure in pediatrics, after 1 month, 6months and after 1year compared to pre transcatheter.

Our results have displayed that there was a significant reduction in QTc measurements post catheter closure one day, one month, 6 months and after one year compared to pre transcatheter. **Kamphuis *et al.*** [27] observed in post transcatheter closure of ASD that QTc measurements were significantly lower post catheter, after 1 month, 6months and after 1year compared to pre transcatheter.

Our cohort study had revealed some cases that showed arrythmia after transcatheter ASD closure and during follow up ECG.

Similarly, **Hill *et al.*** [28] observed that nine patients (23%) with non-sustained supraventricular tachycardia (SVT), three of whom had short runs of SVT prior to closure.

Further, **Albæk *et al.*** [29] noted that the incidence of Lt. anterior fascicular block was 3.7% in all patients with transcatheter or surgically closed ASD.

In our study, we observed that large ASD that had a deficient posteroinferior rim was the main risk factor for arrhythmias. **Park *et al.*** [30] reported that the difficulty of implanting an ASD device in cases with rim deficiency, which necessitates more manipulation and irritates the atrium, may be the reason for this discovery.

Chung *et al.* [31] noted that certain arrhythmias may arise due to mechanical irritation caused by the device. Atrial tachyarrhythmia that develops suddenly may also be caused by residual shunt and postintervention inflammation.

In our study we reported two patients developed complete heart block (CHB) the 1st case was female, 2.5 years old, 12 kg with large defect 18mm, deficient retroaortic rim, was closed by large device Occlutech occluder 21mm that had required many attempts to obtaining secure position of the device during manipulation. The CHB occurred 1 day after the closure, she received steroid for 1 week that ECG returned normal. **Rohit *et al.*** [32] reported that the inflammation and oedema that the atrial discs create around the AV node has been identified as the source of the conduction blockages that occur following the closure of an ASD device. This is one of the reasons why steroids are empirically administered in these situations. In our case, we could only speculate that the AV node's temporary ischemia and inflammatory oedema caused by the ASD device's mechanical irritation were the causes of complete heart block, and that anti-inflammatory medication helped.

According to our results, Heart rate variability parameters (Pnn50, RMS-SD, SDNN, SDANN and tri) were significantly higher post transcatheter, after 1month, after 6months and after 1year compared to pre (P value 0.002 and <0.001 respectively). Consistent with **Bakari and colleagues** [33] observed that Pnn50, RMS-SD, SDNN, SDANN and tri were significantly higher post transcatheter, after 1month, after 6months and after 1year compared to pre catheter. Following the volume unloading of both right heart chambers, these mechanoelectrical alterations most likely reflect improved intra-atrial and intraventricular conduction characteristics [34].

STUDY LIMITATIONS

Our study's limitations were a limited sample size and mid-term follow-up on transcatheter ASD closure in kids undergoing electrical remodeling. To ascertain when the normalization of the parameters will return to normal levels, a longer follow-up time and a bigger multicenter investigation are needed. The risk factors for occurrence of complete heart block after ASD closure.

CONCLUSIONS

It could be concluded that transcatheter ASD device closure leads immediately to a significant improvement in electrical reverse remodelling parameters. Holter ECG study is considered a beneficial tool to evaluate cardiac autonomic functions and the influence of transcatheter closure of ASD on cardiac autonomic function and magnitude of arrhythmia.

Electrocardiography serves as the standard tool to visualize cardiac electrical activity and the electrical reverse remodelling after TCC as well as potential arrythmias.

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