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ORIGINAL ARTICLE

Pulmonary Functions and Exercise Tolerance before and after Device Closure of Atrial Septal Defect: Determinants and Outcome

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ABSTRACT

Background: Secundum atrial septal defects (ASDs) are the most common congenital heart diseases and its closure affords changes in the function of the pulmonary activities.
Our study aimed to demonstrate that the closure ASD not only improves cardiac function but also results in symptomatic relief by improving functional class by improving exercise tolerance and pulmonary functions.
Methods: This is a prospective study was conducted on 100 patients underwent device closure of secundum ASD. Investigations included NT-pro-brain natriuretic peptide levels (NT-pro-BNP), electrocardiography, chest X-ray, transthoracic echocardiogram, spirometry, and 6-min walk test, before and 3 months after the procedure.
Results: All patients were classified according to significant symptomatic improvement into group I (not improved) and group II (improved). Regards NYHA classification, pulmonary hypertension, tricuspid regurgitation and NT-pro-BNP, there was statistically significant lower values both pre-closure and post-closure in the improved group ($p<0.001$). There was statistical significant difference in pulmonary functions (spirometry and 6-minute walk test) in ASD patients before and 3 months after ASD closure in both groups as all parameters ($FEF_{25\text{-}75}$, FVC, and FEV1 and 6-minute walk test) as they were statistically significant higher values in the improved group both pre-closure and post-closure. The significant predictors was age < 48, ASD size ≤35, pulmonary hypertension (mild/moderate), $FEF_{75\text{-}25}$ ≥61, FVC≥67, FEV 1%≥64 and 6-MWTD ≥325
Conclusion: Transcatheter ASD device closure leads to significant improvement in the heart dimensions especially right-sided dimensions and functional class by improving exercise tolerance and pulmonary functions.
keywords: ASD; NYHA ; 6-minute walk test; spirometry

INTRODUCTION

Atrial septal defects constitute around 25-30% of recent diagnoses of congenital heart defects in adults. The left-to-right shunt through the inter-atrial septal defect will lead to chronic overload of the right heart. If it is not treated, it may lead to atrial arrhythmias, right heart failure, pulmonary hypertension, systemic embolism, atrioventricular valve regurgitation [1]. The transcatheter closure of atrial septal defect has been increasingly used in recent years with high success rates and with complication rates that compare rather favorably with surgical repair even in terms of a residual shunt and normalization of right ventricular dimensions [2]. The cases with the atrial septal defect are commonly asymptomatic early in life. Yet, there is some physical under-development with increased tendency to have infection in the respiratory system in adults. The symptoms of the cardiopulmonary system and its complications take place in older patients in spite of the considerable volume overloading. Plenty of adults with atrial septal defect do not grumble about restricted exercise capacity [3]. In spite of such extraordinary outcomes, the available information about the improvement of cardiopulmonary function after elective percutaneous closure of the atrial septal defect is limited and sometimes contradictory. Moreover, the mechanisms of physiopathology that intervene in determining cardiopulmonary function improvement after transcatheter occlusion remain to be identified. So, this study aimed to demonstrate that the closure of atrial septal defect (ASD) improves cardiac function and leads to the symptomatic alleviation through the improvement of the functional class by means of improving exercise tolerance and pulmonary functions. Also, to look for the factors which lead to enhanced exercise tolerance, after the trans-catheter closure of the atrial septal defect.

METHODS

This is an observational cohort study which included 100 patients who were subjected to transcatheter ASD closure with the Amplatzer septal occluder (ASO; AGA Medical Corporation, Golden Valley, MN, USA) in the cardiology department of Zagazig University and National Heart Institute during the period from June 2016 to June 2019. The inclusion criteria were: patients with ASD equal to or less than 38 mm, their diagnosis was proved by either transthoracic echocardiography or trans-esophageal echocardiography. Exclusion criteria: ASD >38mm, concomitant congenital heart disease, and pulmonary hypertension did not fit for percutaneous closure, those patients who unable to perform an exercise test. Informed written consent was obtained from the patients after the explanation of the study and approval of the Ethical Committee of Zagazig Faculty of Medicine. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans

Study procedures: All participants were subjected to the following 48 hours preoperative and 3 months postoperative: Full history and physical examination with emphasis on the New York heart association (NYHA) dyspnea class and palpitation were recorded. Echocardiography Transoesophageal echocardiography (TEE) was customarily carried out in all patients examined for transcatheter closure to assess ASD morphology to preclude further lesions like an atypical pulmonary venous connection. A comprehensive trans-thoracic echocardiogram (TTE), including M-mode, two-dimensional, continuous-wave, pulsed-wave, and colour doppler echocardiography, was carried out prior to the intervention and at every follow-up visit. The right ventricular size was determined by taking the transverse diameter in the apical four-chamber view. The pulmonary artery pressure (PAP) was measured from the tricuspid regurgitate velocity [4]. The shunt ratio (Qp: Qs) was attained through the assessment of the velocity time integrals as well as the cross-sectional areas at the corresponding sites in the pulmonary artery and the left ventricular outflow tract [5].

Catheter intervention: All methods were performed under general anesthesia with endotracheal intubations and guided by fluoroscopy and TEE. After the hemodynamic estimation, all patients went through balloon sizing of the defect. The ASO was selected 2–4 mm larger than the stretched diameter. Aspirin therapy (100 mg/day) was administered at least 2 days before and sustained for at least 6 months after the intervention. Intravenous heparin was applied intra-procedure. The patients were subjected to examinations 48 hours preoperative and 3 months postoperative along with clinical examination, TTE, and electrocardiography. Special care was practiced to study the functional status and to attain information with regard to any complications or developed symptom. Trans-esophageal echocardiography was only executed on manifestation (suspected residual shunt 6 months post-interventionally, suspicion of embolism).

NT- pro Brain Natriuretic Peptide were measured 48 hours preoperative and 3 months by electrochemiluscent immunoassay by Elecsys–2010 system (Roche Diagnostics) using two polyclonal antibodies directed at the NT pro-BNP molecule **[**6].**Pulmonary function tests:** All subjects gone through pulmonary function testing (PFT) including spirometer 48 hours prior to ASD closure and 3 months after closure were carried out as reported by the American Thoracic Society and European Respiratory Society child criteria **[**7-8**]** by using (ZAN100 USB spirometer, n Spire Health GmbH, Oberthulba, Germany). Spirometry was performed at the standing patient. Rest was permitted after each recurrent test. At least three trials were carried out by every patient. The curve with the largest forced vital capacity (FVC) and forced expired volume in 1 sec (FEV1) was selected as the preferred trial. The FVC, FEV1, FEV1 to FVC ratio (FEV1/FVC), peak expiratory flow (PEF), and mean forced expiratory flow during the middle half of the FVC (FEF25–75) were taken. The ASD patients at baseline and 3 months after percutaneous transcatheter ASD closure were assorted to normal [forced vital capacity (FVC) and forced expired volume in 1 s (FEV1) > 80% of the predicted value with normal FEV1/FVC], obstructive (FEV1/FVC< 80%), or restrictive (FVC< 80% of the predicted value with normal FEV1/FVC).**The 6MWT**: was performed 48 hours prior to ASD closure and 3 months following the closure as explained by the guidelines of the American Thoracic Society **[9].** It was carried out indoors on a long, flat, straight, and hard surface. This test assesses the length in meters which a patient can quickly arrive at without help in 6 min. The abnormal functional capacity was defined as a 6MWT distance of less than 350 m. Supplemental oxygen was not provided to any patient during the 6MWT. Echocardiography data was used as the basic data for the further ASD evaluation

STATISTICAL ANALYSIS

The accumulated data were analyzed using SPSS program. The quantitative parameters were displayed as a mean ± standard deviation (mean ± SD) or median (minimum–maximum). The qualitative parameters were displayed in numbers and percentages. The quantitative parameters were tested using the Shapiro–Wilk normality test. Unpaired tests, Mann–Whitney U tests, and Pearson chi-square analysis were employed to contrast group means. Repeated and measured one-way analysis of variance (ANOVA) was employed to compare the PFT data of baseline and 3 months after the procedure. The differences at $P<0.05$ were considered statistically significant. Univariable and multivariable logistic regression analysis was run to detect the significant predictors of improvement.

RESULTS

After 3 months of follow up, improvement occurred , means significant symptomatic improvement assessed by NYHA class as well as regression of right-sided dimensions, PAP as well as the progress in functional state involving spirometry in the form of FEF 25-75, FVC and FEV1 and 6-minute walk test in the form of both 6 min walk distance and oxygen saturation

So, we classified them according to the improvement to Group I (Not improved); it included 20 cases only (20%) and Group II (Improved); 80 cases (80%).

Collectively; the age ranging from 15 years old to 68 years old with a mean of 39.00±15.5 years old. We had 64 females (64%). Only 12 cases had chronic AF (12%). The size of ASDs ranged from 12mm to 38mm with a mean of 30.8±7.5mm. Qp/Qs ranged from 1.8 to 3.3 with a mean of 2.6 ± 0.34. Only 4 cases out of the 100 cases got complications in the form of TIA (4%). No other complications happened. Considering socioeconomic and basic data, there was a statistically significant difference between both groups with regard to the age, where the younger age was associated with significant improvement. Also, a statistically significant difference existed between both groups with regard to basal NYHA status, the high class associated with non-significant improvement.

Regarding Echocardiographic parameters before the closure of ASD

Statistical significant differences existed in the right ventricle (RVDD in PSLA, RV inlet), RV\LV diastolic ratio, and RVSP between both groups as it was lower in Group II (improved group). Statistically significant differences were detected in PWD on TV (D.T), DTI on TV (A wave), TAPSE, TR degree, and PWD on MV (E, D.T) between both groups as it was higher in Group II (improved group)**.**

Regarding Echocardiographic parameters 3 months post-closure Statistically significant decrease was detected in RVDD in PSLA, RV inlet in Group II. The increase in D.T and A wave in Group II were found to be significant as well. The decrease in RV volume, RV\LV diastolic ratio and RVSP in Group II showed a statistical significance. The increase in TAPSE in the improved group also displayed a significant difference. There was a statistically significant difference in TR degree between both groups as sever degree associated with no improvement. There was statistically significant increase in PWD on MV (E wave, D.T) in improved groups **[Table 1].**

Regarding Pre and post-NT-pro-BNP pre-closure and 3 months post-closure

Both groups had a significant difference with regard to NT-pro BNP as it was significantly lower in improved one both pre-closure and post-closure**.**

Regarding Spirometry and 6-MWT before and 3 months after device closure There was a statistically significant difference in pulmonary function parameters (FEF_{25-75}, FVC and FEV1) in ASD patients before and 3 months after percutaneous transcatheter ASD closure in the improved group as all parameters were increased. While there was no statistically significant difference in pulmonary function parameters in not improved groups. Also, there was statistical a significant difference between both groups preclosure and 3 months after closure regarding FEF_{25-75}, FVC, and FEV1 as they were statistically higher in the improved group.

There was a statistically significant difference in both 6 min walk distance and oxygen saturation (pre-closure and post-closure) as they were higher in the improved group. In the improved group there was statistically significant difference regarding pre-closure and post-closure 6 min walk test and oxygen saturation as they were higher post-closure while there was no statistically significant difference in the not improved group, **[Table 2].**

Regarding pulmonary function patterns in ASD patients before and 3 months after device closure Both groups showed significant difference regarding both pre-closure and post-closure pulmonary function patterns as normal and restrictive patterns was statistically higher in the improved group, while no statistical significant difference existed between pre-closure and post-closure in the not improved group, **[Table 3].**

All factors found to be significantly correlated with pulmonary artery pressure post-closure, were entered the stepwise multiple linear regression model to detect the significant predictors of post-closure outcome and it was found that age < 48 and NYHA I, II were the significant predictors among socio-demographic and basic clinical characters. Also size ≤35, pulmonary hypertension (mild/moderate), RVDD ≤45.5, RV inlet ≤54.5, E velocity TV≥ 90.7, D.T (ms) TV ≥197.5, E velocity MV ≥81.5, D.T (ms) MV ≥188.3, RV\LV diastolic ratio≤0.96, TAPSE≥15.5, the grade of TR (mild/moderate) and pre TN-BNP were the significant predictors among factors related to Echo findings. FEF $_{75\text{-}25}$ ≥61, FVC≥67, FEV 1%≥64, 6-MWTD ≥325, oxygen saturation (%) ≥ 90.5 were the significant predictors among spirometry and 6 mint walk test **[Table 4,5,6,7].**

Table [1]: Comparison between both groups regarding Echocardiographic parameters 3 months post-closure**.**

Variable		**Group 1 (n=20)**		**Group 11 (n=80)**		**Z_{MWU} test**	**(p)**
		Median	**IQR**	**Median**	**IQR**		
RVDD in PSLA (mm)		45.2	44-46	36.0	31-39	6.98	<0.001 (HS)
RV inlet (mm)		52.9	49-55	47.0	45-50	3.48	<0.001 (HS)
PWD on TV	**E velocity**	88.9	88-91	89.6	87.1-92.8	1.55	0.12
	D.T (ms)	193.4	189-197	197.0	191.5-200.8	3.01	0.003 (S)
DTI on TV (cm/s)	**S wave**	14.2	13.4-15.2	14.0	12.9-15.1	0.22	0.82
	E wave	10.2	9.2-10.3	10.1	8.7-11.3	0.29	0.77
	A wave	12.8	12.3-12.9	13.0	12.3-14.1	2.21	0.027 (S)
RA volume (ml)		99.8	89-101	84.0	80-88	3.32	0.001 (HS)
RV\LV diastolic ratio		0.95	0.8-0.9	0.7	0.6-0.8	5.84	<0.001 (HS
RVSP mmHg		65	60.8-65	35	27-37.7	7.1	<0.001 (HS
TAPSE mm		14.6	15-15.5	24	23-25	7.0	<0.001 (HS
TR	**Mild**	0	0.0	56	70.0	**Fisher's exact test 89.8**	**<0.001 (HS)**
	Moderate	0	0.0	24	30.0		
	Severe	20	100.0	0	0.0		
PWD on MV	**E velocity**	81.7	80.3-83.1	85.8	82.7-87.8	3.56	<0.001 (HS)
	D.T (ms)	190	185-193	194.0	191-204.8	3.99	<0.001 (HS)
DTI on MV (cm/s)	**S wave**	9.6	9.3-9.6	9.35	8.8-9.82	1.11	0.27
	E wave	7.9	7.9-8.8	8.5	7.83-8.95	0.903	0.37
	A wave	11.2	11.1-11.3	11.1	10.9-11.5	1.33	0.18

RVDD in PSLA: Right ventricular diastolic dimension in parasternal long axis. **RV inlet**: Right ventricular inlet in apical view. **PWD on TV**: Pulsed wave doppler on the tricuspid valve. **DTI on TV:** Doppler tissue imaging on the tricuspid valve. **RA:** Right atrium. **IQR**: interquartile range **LVDD** Left ventricular diastolic dimension **PWD on MV**: Pulsed wave doppler on mitral valve DTI **on TV:** Doppler tissue imaging on mitral valve RV**\LV diastolic ratio:** Right ventricular / Left ventricular diastolic ratio. **TAPSE:** Trans Annular Plain Systolic Excursion **ASD:** atrial septal defect

Table [2]: Comparison between both groups regarding Spirometry and 6-MWT before and 3 months after.

Variable		**Group I (n=20)**		**Group II (n=80)**		**St."t"test**	**P**
		Mean	**±SD**	**Mean**	**±SD**		
FEF $_{25\text{–}75}$	**Pre-closure**	55.4	3.53	77.05	10.01	9.49	<0.001 (HS)
	Post-closure	56.1	4.27	81.8	9.32	11.99	<0.001 (HS)

Variable		Group I (n=20)		Group II (n=80)		St."t"test	P
		Mean	±SD	Mean	±SD		
Paired "t" test (P value)		1.33(0.199,NS)		24.0 (<0.001,HS)			
FVC	Pre-closure	57.6	5.13	85.4	12.27	9.88	<0.001 (HS)
	Post-closure	58.1	4.81	87.9	11.53	10.8	<0.001 (HS)
Paired "t" test (P value)		0.70 (0.49,NS)		12.9 (<0.001,HS)			
FEV 1%	Pre-closure	56.4	5.13	83.6	10.69	11.05	<0.001 (HS)
	Post-closure	57.0	4.0	86.8	9.51	13.35	<0.001 (HS)
Paired "t" test (P value)		1.31 (0.21,NS)		14.1 (<0.001,HS)			
FEV1\FVC	Pre-closure	81.0	11.12	83.0	7.92	0.95	0.35
	Post-closure	81.2	10.01	84.2	7.85	1.47	0.14
Paired "t" test (P value)		0.55 (0.59)		3.5 (<0.001,HS)			
6-MWTD	Pre-closure	264.0	±47.5	432.3	±148.3	4.99	<0.001 (HS)
	Post-closure	267.9	±44.8	538.0	±125.7	9.43	<0.001 (HS)
Paired "t" test (P value)		0.97 (0.34,NS)		24.9 (<0.001,HS)			
Oxygen saturation (%)	Pre-closure	89.6	±1.04	93.3	±1.39	11.2	<0.001 (HS)
	Post-closure	90.7	±1.57	95.8	±0.91	14.3	<0.001 (HS)
Paired "t" test (P value)		2.08 (0.052,NS)		24.1 (<0.001,HS)			

$FEF_{25–75}$: Forced expiratory flow between 25% and 75% of vital capacity. **FVC:** Forced vital capacity**FEV1:** forced expired volume in1 sec**FEV1/FVC:** FEV1 to FVC ratio

Table [3]:comparison between both groups regarding pulmonary function patterns in ASD patients before and 3 months after closure

Variable		Group 1 (n=20)		Group 11 (n=80)		Fisher's exact test	P
		No.	%	No.	%		
Pulmonary function pre-closure	Normal	4	20.0	44	55.0	**48.4**	**<0.001 (HS)**
	Obstructive	16	80.0	4	5.0		
	Restrictive	0	0.0	32	40.0		
Pulmonary function post-closure	Normal	4	20.0	60	75.0	**63.4**	**<0.001 (HS)**
	Obstructive	16	80.0	0	0.0		
	Restrictive	0	0.0	20	25.0		
P value of Mc-Nemer's test		1.0 (NS)		>0.001 (HS)			

Table [4]: Correlation between post-closure pulmonary artery pressure and pre-closure Spirometry and 6-min walk test in all cases

Variables		Post closure pulmonary artery pressure	
		All patients (n=100)	
		Rho	P
pre-closure spirometry (determinants)	FEF $_{25-75}$	-0.827	<0.001 (HS)
	FVC	-0.805	<0.001 (HS)
	FEV 1%	-0.787	<0.001 (HS)
	FEV 1\FVC	-0.226	<0.001 (HS)
Pre-closure 6-min walk test (determinants)	6-min walk test distance (6MWTD)	-0.886	<0.001 (HS)
	Oxygen saturation (%)	-0.832	<0.001 (HS)

Table [5]: Univariable and multivariable logistic regression analysis for the predictors of improvement according to factors related to socio-demographic and basic clinical characters

Variable	Univariate logistic regression				Multivariate logistic regression			
	β	Crude OR	95%CI	P	B	Adjusted OR	95%CI	P
Age (<48ys)	2.77	16	4.7-54.4	<0.001 (HS)	2.98	19.7	4.3-89.2	**<0.001 (HS)**
Sex (F)	0.214	1.2	0.45-3.4	0.67	----	----	----	----
Smoking (no)	0.44	1.5	0.56-4.2	0.39	----	----	----	----
HTN (no)	1.25	3.5	1.27-9.65	0.012 (S)	0.35	1.4	0.34-5.9	0.62
DM (No)	0.214	1.2	0.45-3.4	0.67	----	----	----	----
Paroxysmal AF	0.0	1.0	0.29-3.4	1.0	----	----	----	----
NYHA (1,2)*	21.8	----	----	**<0.001 (HS)**	----	----	----	----

Table [6]: Univariable and multivariable logistic regression analysis for the predictors of improvement according to Echo findings

Variable	Univariate logistic regression				Multivariate logistic regression			
	B	Crude OR	95%CI	P	B	Adjusted OR	95%CI	P
Size ≤35	2.42	11.2	3.3-37.4	<0.001 (HS)	2.31	10.2	2.96-34.7	<0.001 (HS)
Pulmonary hypertension (mild/mod)	21.8	----	---	<0.001 (HS)	----	----	----	----
RVDD ≤45.5	2.06	7.85	2.4-25.8	0.001 (HS)	2.52	12.5	2.5-61.6	0.002 (S)
RV inlet ≤54.5	1.7	5.7	1.7-18.6	0.004 (S)	1.46	4.3	1.2-15.0	0.022 (S)
E velocity TV≥ 90.7	1.03	2.78	1.02-7.6	0.046 (S)	0.58	1.81	0.74-13.4	0.41
D.T (ms) TV ≥197.5	1.25	3.5	1.3-9.6	0.015 (S)	1.68	5.3	1.2-23.4	0.021(S)
S wave TV ≥13.9	-0.205	0.82	0.3-2.2	0.68	----	----	----	-----
E wave TV≥9.35	0.214	1.23	0.45-3.4	0.67	----	----	----	-----
A wave TV≥13.05	0.81	2.25	0.83-6.1	0.11	----	----	----	-----
RA volume ≤107	0.61	1.83	0.68-4.9	0.23	----	----	----	-----
LVDD ≤43.5	0.27	1.3	0.48-3.5	0.6	----	----	----	-----
E velocity MV ≥81.5	2.23	9.3	2.8-30.8	<0.001 (HS)	2.08	8.0	1.9-34.3	0.005 (S)

Variable	Univariate logistic regression				Multivariate logistic regression			
	B	Crude OR	95%CI	P	B	Adjusted OR	95%CI	P
D.T (ms) MV ≥188.3	1.5	4.5	1.6-12.5	0.004 (S)	0.23	1.3	0.34-4.7	0.72
S wave MV ≥9.25	0.98	2.66	0.81-8.7	0.104	----	----	----	-----
E wave MV≥8.0	0.81	2.25	0.83-6.1	0.11	----	----	----	-----
A wave MV ≥11.1	0.12	1.14	0.6-5.9	0.87	----	----	----	-----
LA volume ≤77	0.81	2.25	0.83-6.1	0.11	----	----	----	-----
RV\LV diastolic ratio of ≤0.96	1.53	4.65	1.4-15.1	0.011 (S)	1.36	3.9	1.09-13.9	0.036(S)
QP\QS≤2.65	0.21	1.22	0.45-3.3	0.69	----	----	----	-----
TAPSE≥15.5	22.2	---	----	<0.001 (HS)	----	----	----	----
Grade of TR (mild/mod)	22.8	----	---	<0.001 (HS)	----	----	----	----
NT Pro BNP	2.09	8.1	1.77-37.4	0.007 (S)	1.98	7.4	1.2-23.9	0.01 (S)

Table [7]: Univariable and multivariable logistic regression analysis for the predictors of improvement according to spirometry and 6 mint walk test.

Variable	Univariate logistic regression				Multivariate logistic regression			
	β	Crude OR	95%CI	P	B	Adjusted OR	95%CI	P
FEF $_{75-25}$ ≥61	22.8	----	---	<0.001 (HS)	---	----	----	----
FVC≥67	22.8	----	---	<0.001 (HS)	---	----	----	----
FEV 1%≥64	4.33	76	17.2-336.2	<0.001 (HS)	3.02	15.2	3.4-73.8	<0.001 (HS)
FEV 1\FVC≥85.5	0.61	1.83	0.68-4.9	0.23	---	----	----	----
6-MWTD ≥325	21.7	-----	-----	<0.001 (HS)	---	----	----	----
Oxygen saturation (%)≥90.5	4.33	76	17.2-336.2	<0.001 (HS)	3.02	15.2	3.4-73.8	<0.001 (HS)

DISSCUSION

Regarding NYHA class improvement there was a statistically significant difference existed between both groups with regard to basal NYHA status, the high class associated with non-significant improvement. Also NT-pro BNP was significantly lower in improved one both pre-closure and post-closure**.** Arif et al.[10] and Greenen et al. [11] were in disagreement with our study, as they found NT-proBNP didn't decrease after closure of ASD and explained that by the reversed cardiac remodeling following ASD closure may takes more than 3 months after closure, also cardiac remodeling may not be entirely reversible and the molecular or cellular adaptation may have ended after a certain period. As regard to changes in the right sided echocardiographic parameters (tricuspid regurgitation regression, pulmonary artery pressure decrease, right ventricular end diastolic dimensions decrease, TAPSE improvement and right ventricular/left ventricular diastolic ratio, there was optimistic statistically significant differences in changes pre closure and 3 months after closure in G II but without statistically significant improvement in GI.Jung et al. [12] were in agreement with our results. Also, Takaya et al. [13] found that the patients with severe TR were older and had larger ASD diameter and larger RV end-diastolic diameter with higher RV/LV end-diastolic diameter /ratio than those with mild to moderate TR. Patients with severe/TR were more likely to have the prevalence of pulmonary arterial hypertension post device closure also found there was a significant correlation between the decrease in TR jet area and the decrease in RV end-diastolic diameter (p<0.001), RV/LV end-diastolic diameter ratio (p<0.001) and TV annular diameter post device closure.Same results were seen with **Ozturk et al.[14]** and **Greenen et al. [11]**who confirmed that after ASD device closure found an improvement of multiple echocardiographic parameters such as the RVLS, RVEDD right atrial diameter, RV/LV EDD ratio, left atrial diameter, and PASP in the first month post-procedure period. LVDD and LVSD remained unchanged in the first month post-procedure period. However, LVEF and TAPSE were significantly increased in the first month post-procedure period. Also, **Jung et al. [12]and Arif et al.[10]** were in agreement as they found the reduction of right atrial and ventricle size results in favorable cardiac remodeling and significant improvement in functional class, and they stated that percutaneous closure of large ASD was effective for both anatomic and hemodynamic results. These results were in agreement with **Arif et al.[10]** and **Humenberger et al.[15]**who found significant decrease in right ventricular diameter, right ventricular end-diastolic and RV inlet dimensions as well as right atrial volume and Pulmonary artery pressure 3 months after ASD closure (P < 0.0001). In our study, left ventricular systolic function shows significant improvement in GII before and after closing the ASD as RV volume overload is vanished. In patients with an ASD because shunting of blood into the right heart invariably affects LV filling, (steal phenomenon). Our results support the phenomenon of ventricular interdependence associated with RV volume overload and the "reverse Bernheim's effect" in which the septum bulges into the LV cavity leading to impaired LV filling [**16]**. This was in agreement with **Thilen and Persson [17]** where ASD device closure results in improvement of LV filling and so improvement of LV dimensions and ejection fraction, the improvement in LV function was most marked in the first 6 weeks after ASD closure. Also, **Arif et al.[10]** were in agreement as there was significant improvement in global LV systolic function (mean LV ejection fraction: 65%, 76%, and 82%, pre-closure, at 6 weeks, and at 1 year, respectively. So, this suggests that LV remodeling occurs early and plateaus thereafter and the **i**mprovements in LV function are likely to be a major determinant of the early improvement in NYHA functional class seen after ASD closure. It is of interest that the improvement in LV size and function appears to occur earlier than in the RV. This may suggest that LV remodeling is independent of RV remodeling **[10]**.Regarding functional improvement, there is statistically significant difference in pulmonary function parameters including (FEF $_{25\text{-}75}$, FVC and FEV1) in ASD patients before and after 3 months of percutaneous transcatheter ASD closure between both groups. It was statistically higher in Group I comparing pre-closure and post-closure. These results were in agreement with **Nassif et al. [2]**who found that Post-closure spirometry showed a significant increase in forced vital capacity (FVC) and a decrease in FEV1/FVC ratio, also significant increase in FEV1.In addition, it was in concordant with **Giardini et al. [18]**who explained that the limitation of peripheral airway airflow may be due to increased pulmonary blood flow, engorged capillary network, or abnormalities in the elastic properties of the lung. So, ASD closure corrects right heart and pulmonary arterial volume overload and thereby significantly improves spirometry.This improvement of pulmonary function after device closure explained by the way that left-to-right blood shunting across ASD may induce right heart volume overload. Long term exposure to right heart volume overload may cause right atrium and ventricle dilatations and increase pulmonary blood flow, in turn leading to pulmonary hypertension that induce abnormalities in lung structure and pulmonary vascular changes leading to progressive remodeling of the lung parenchyma and even fibrotic changes**.**

In the present study there was statistically significant difference in the improved group in both 6-min walk distance and oxygen saturation (pre-closure and post-closure). These results were in agreement with **Supomo et al.[19]**who found that there were significant differences of 6MWT distance between PH and non-PH patients. As there is significant relationship between PH and abnormal functional capacity of the patient, so the increased mPAP and pulmonary vascular resistance (PVR) were significantly correlated with decline in 6MWT distance. These results demonstrated that altered pulmonary hemodynamics have an impact on functional capacity of the adult patients with ASD.Also were in agreement with **Huang et al. [20]**that found that the 6-min walking distance significantly increased by 49.7± 6.3 m at 3 months (short-term) and increased by 75.4± 6.6 m at 23.4 ± 9.7 months (medium-term). **Arif et al.[10]** also found that following ASD closure, a significant improvement in 6MWT distance was observed and stated that transcatheter device closure of ASD in adults over the age of 40 years is not only safe and effective, but also results in symptomatic relief by improving functional class and 6MWT distance with favorable cardiac remodeling.

CONCLUSION

Trans catheter ASD device closure results in significant amelioration in the heart cavity dimensions especially the right-sided dimensions and improving functional class by improving exercise tolerance and pulmonary functions in the short-term follow-up period. The significant predictors of post-closure outcome and it was found that Age < 48 and NYHA I, II were the significant predictors among socio-demographic and basic clinical characters. Also, Size ≤35, Pulmonary hypertension (mild/moderate), RVDD ≤45.5, RV inlet ≤54.5, E velocity TV≥ 90.7, D.T (ms) TV ≥197.5, E velocity MV ≥81.5, D.T (ms) MV ≥188.3, RV\LV diastolic ratio≤0.96, TAPSE≥15.5, Grade of TR (mild/moderate) and PreTN-BNP were the significant predictors among factors related to Echo findings. FEF 75-25 ≥61, FVC≥67, FEV 1%≥64, 6-MWTD ≥325, Oxygen saturation (%) ≥90.5 were the significant predictors among spirometry and 6 mint walk test.

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