Long Term Follow up of Biatrial Function after Transcatheter Closure of Atrial Septal Defect

Original Article

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ABSTRACT

Background: Atrial septal defect (ASD) is a prevalent congenital cardiac anomaly with significant long-term complications if untreated, including atrial fibrillation (AF) and pulmonary hypertension. Device closure is a preferred treatment option with well-documented benefits for right ventricular remodelling, but its impact on long-term biatrial function remains underexplored.
Aim of the Work: This study aims to evaluate long-term biatrial function in patients undergoing transcatheter ASD closure.
Methods: This prospective case-control study included 40 patients who underwent transcatheter ASD closure at least three years prior and 40 age- and sex-matched healthy controls. Comprehensive echocardiographic evaluation, including 2D speckle tracking echocardiography (STE), was performed to assess right and left atrial strain (reservoir, conduit, and contractile) and volumetric indices.
Results: Compared to controls, patients demonstrated significantly reduced right atrial (RA) Reservoir Strain (RS) (32.75 ± 9.36% vs. 43.05 ± 12.05%, $P < 0.001$), Cond S (17.55 ± 7.67% vs. 23.85 ± 5.72%, $P < 0.001$), and Cont S (13.38 ± 5.87% vs. 16.73 ± 5.20%, $P = 0.008$). Left atrial (LA) Cont S was also reduced (16.28 ± 4.84% vs. 18.58 ± 5.32%, $P = 0.047$). Patients who underwent closure before age 15 had better biatrial function, with strain values approximating those of controls (e.g., RA RS: 38.35 ± 7.98% vs. 43.05 ± 12.05%, $P = 0.032$).
Conclusions: Early ASD closure (<15 years) preserves atrial function, with near-normal strain values, while later closure is associated with significant long-term impairment, particularly in RA.

Key Words: Atrial septal defect, atrial strain, biatrial function, 2D speckle tracking echocardiography, transcatheter closure.

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INTRODUCTION

Atrial septal defect (ASD) is among the most common congenital cardiac anomalies, with a prevalence of 2.5 per 1,000 live births. It accounts for approximately 10–15% of all congenital heart diseases [1]. ASD may manifest clinically during early childhood or remain asymptomatic until adulthood. If left untreated, chronic right ventricular (RV) volume overload caused by left-to-right shunting can eventually lead to significant complications, including pulmonary hypertension and Eisenmenger syndrome[2]. Patients who do not undergo ASD closure are at a higher risk for adverse long-term outcomes, such as atrial arrhythmias, reduced functional capacity, and progressive pulmonary hypertension [3].

Device closure has become the preferred treatment option for secundum ASDs in up to 80% of cases due to its established safety and efficacy, with a very low rate of serious complications (<1%) [4]. Outcomes are most favourable when ASD closure is performed before the age of 25, significantly reducing the risk of long-term sequelae. However, closure after the age of 40 does not appear to reduce the incidence of atrial tachyarrhythmias, though symptomatic improvement, along with reductions in pulmonary artery pressure and RV dimensions, has been observed across all age groups [5].

While multiple studies have demonstrated improvements in ventricular function and reverse remodelling following ASD device closure, there is limited data on its impact on biatrial function and remodelling[6,7]. Left atrial (LA) enlargement, for instance, is a well-established marker of adverse cardiovascular outcomes, including atrial fibrillation (AF), heart failure (HF), and all-cause mortality. Additionally, a decline in LA functional indices has been identified as an independent predictor of

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HF hospitalizations and mortality in patients with coronary artery disease, HF with reduced ejection fraction (HFrEF), and AF [8].

Atrial function has traditionally been assessed using atrial volumes and myocardial strain analysis, often employing speckle tracking techniques. However, standardized reference values for atrial strain remain lacking, despite recent efforts to establish meta-analyses in this area. Interest in the post-treatment changes in LA function following ASD closure has grown. Most studies are constrained to short-term follow-up periods. Consequently, the long-term trajectory of atrial functional changes—whether they persist, improve, or deteriorate—remains uncertain [9].

Therefore, this study aims to assess long-term right and LA function at least three years post-ASD device closure and identify predictors of atrial function.

PATIENTS AND METHODS

Study Design and Population

This cross-sectional case-control study included 40 patients who underwent percutaneous ASD device closure (all ASD devices used were Lifetch) more than three years prior and were followed up at the congenital heart disease clinic at the Faculty of Medicine, Ain Shams University. A sex- and age-matched control group of 40 healthy individuals were also included.

ETHICAL COMMITTEE

The study was conducted from January 2023 to August 2023, with ethical approval from the Ain Shams University ethical committee (Approval no.: MS104/2023). Written informed consent was obtained from all participants, ensuring privacy and confidentiality.

Patients with associated congenital anomalies, valvular heart disease, left ventricular dysfunction, coronary artery disease, cardiomyopathy, or pericardial diseases were excluded.

Baseline Patient Assessment

At baseline, all patients underwent comprehensive evaluation, including detailed history taking to document demographic data (age, sex), cardiovascular risk factors (smoking, hypertension, diabetes, family history of cardiovascular disease), and cardiac history with a focus on new symptoms such as dyspnea, palpitations, or fever, indicative of potential complications like residual defects, AF, or infective endocarditis. A full clinical examination was performed alongside cardiac evaluation (auscultation for murmurs or a loud second heart sound).

Conventional 2D Echocardiography

Echocardiographic studies were performed using a Vivid E95 cardiac ultrasound system (GE Healthcare) equipped with a multifrequency transducer (3–8 MHz). Transthoracic Echocardiography (TTE) was conducted for all patients using standard four windows (parasternal, apical, subcostal, and suprasternal) and various modalities, including M-Mode, 2D mode, color Doppler, continuous and pulsed wave Doppler, and tissue Doppler imaging. All examinations were ECG-gated and performed by a single cardiologist.

In 2D mode, the apical four-chamber and subcostal views were used to confirm atrial and ventricular anatomy and exclude atrioventricular or ventriculoarterial discordance. For patients with ASD, particular attention was given to visualizing the ASD, ruling out device-related complications, and identifying residual shunts. Global LV function and regional wall motion were assessed to exclude LV systolic dysfunction and possible coronary artery disease.

M-Mode echocardiography was utilized to measure left ventricular dimensions, fractional shortening, ejection fraction, aortic root, and LA dimensions. Images were obtained with the interventricular septum (IVS) and LV posterior wall aligned parallel, and the IVS and anterior aortic wall positioned horizontally. Tricuspid annular plane systolic excursion (TAPSE) was measured in the apical four-chamber view by placing an M-mode cursor parallel to the RV free wall and measuring the distance between maximal diastolic backwards and systolic forward excursions.

Color Doppler was employed in the subcostal view to evaluate the interatrial septum for residual shunting or sinus venosus defects. In the apical four-chamber and parasternal views, it was used to exclude valvular abnormalities or ventricular septal defects. Diastolic function was assessed using pulsed wave Doppler echocardiography. Mitral inflow velocities were recorded from the apical four-chamber view with the sample volume positioned at the tips of the mitral and tricuspid valve leaflets. Early diastolic inflow velocity (E), atrial contraction velocity (A), and the E/A ratio were measured. Pulsed wave tissue Doppler imaging was used to assess velocities at the lateral mitral annulus and the IVS.

Volumetric analysis of RA and LA

Right and LA volumes (maximal, minimal, and pre-A volumes) were measured using the modified Simpson's method in the apical four-chamber and two-chamber views. Maximal LA volume was assessed at end-systole, on the frame just before the mitral valve opening, by tracing the inner border of the LA, excluding the area under the mitral valve annulus, the LA appendage, and pulmonary vein inlets. Minimal and pre-A LA volumes were measured similarly at end-diastole and just before the A wave, respectively.

2D STE

Right and LA walls were assessed using the 2D-STE technique with the Echo Pac software. The atrial strain was measured at end-expiration over at least three successive cardiac cycles, with R-to-R gating, at a frame rate of 40–80 frames per second. LA strain was analyzed in the apical four- and two-chamber views by identifying the lateral, septal, anterior, and inferior walls, and LA roof. RA strain was evaluated in the apical four-chamber view, identifying the septal, lateral walls, and RA roof. Measurements were taken at maximal atrial volume, just before mitral or tricuspid valve opening. (Figure 1)

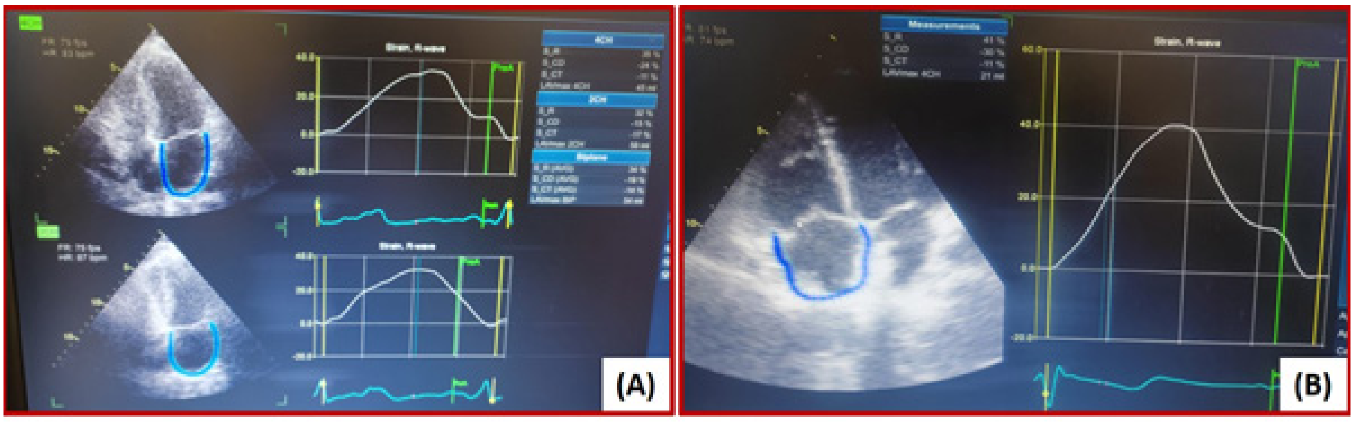

Fig. 1: 2D STE of (A) Left atrial strain curve, (B) Right atrial curve.

The septal wall was included in the analysis based on evidence suggesting that 2D STE can distinguish true atrial deformation from passive motion, unaffected by global heart motion or adjacent segment tethering [10, 11]. Manual tracing of the epicardial and endocardial borders was performed to outline the region of interest and strain curves were generated for both atria. Reservoir, conduit, and contractile strains were subsequently calculated.

Statistical analysis

Data analysis was performed using SPSS software (version 23.0, SPSS Inc., Chicago, Illinois, USA). Quantitative data were presented as mean ± standard deviation (SD) and range for parametric distributions, and as median with interquartile range (IQR) for non-parametric distributions, while qualitative variables were summarized as numbers and percentages. Normality was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Statistical analyses included the independent-samples t-test for comparing two means, the Chi-square test for qualitative data, and Fisher's exact test when any cell's expected count was <5. Statistical significance was defined as $P < 0.05$, with $P < 0.001$ considered highly significant.

RESULTS

The study included 80 participants divided equally into two groups: 40 patients who underwent percutaneous ASD device closure and were followed up at the congenital heart disease clinic, and 40 healthy individuals matched by the same inclusion and exclusion criteria.

There were no statistically significant differences between the two groups in baseline characteristics, including age ($P = 0.979$), gender distribution ($P = 0.823$), weight ($P = 0.988$), height ($P = 0.557$), and body surface area (BSA; $P = 0.849$). Similarly, vital data such as heart rate ($P = 0.238$), systolic blood pressure ($P = 0.640$), and diastolic blood pressure ($P = 0.324$) showed no significant differences. (Table 1)

Table 1: Comparison between patients group and control group according to Baseline characteristics.

Baseline characteristics	Patients Group (*n*=40)	Control Group (*n*=40)	*P-value*
Age (years)			
Mean±SD	22.50±6.17	22.58±7.82	0.979
Range	4-53	4-48	
Gender			
Male	22 (55.0%)	21 (52.5%)	0.823
Female	18 (45.0%)	19 (47.5%)	
Weight			
Mean±SD	60.80±29.79	60.70±27.13	0.988
Range	15-125	15-124	
Height			
Mean±SD	152.95±24.50	156.20±24.84	0.557
Range	101-190	99-190	
BSA			
Mean±SD	1.56±0.51	1.58±0.48	0.849
Range	0.64-2.38	0.64-2.38	

BSA: Body Surface area; *n*: number of patients; SD: standard deviation.

Among the patient group, the mean age at closure was 14.35 ± 5.05 years, with 57.5% of patients undergoing closure before the age of 15. AF was present in 5% of patients, while 95% had no history of AF. The mean duration since closure was 8.15 ± 2.61 years, ranging from 3 to 26 years. (Table 2)

Table 2: Age at closure, AF and Years after closure distribution among study group.

	Patients Group (*n*=40)
Age at closure "years"	
Mean±SD	14.35±5.05
Range	1-48
Age at closure Group	
<15 years	23 (57.5%)
≥15 years	17 (42.5%)
AF	
No	38 (95.0%)
Yes	2 (5.0%)
Years after closure	
Mean±SD	8.15±2.61
Range	3-26

n: number of patients; SD: standard deviation.

The echocardiographic parameters revealed significant differences between the groups, with higher Mitral E velocity (P = 0.041) and E/e' ratio (P < 0.001) in the patient group. Other parameters, including Left ventricular ejection fraction (LVEF), Left Ventricular End-Diastolic Diameter (LVEDD), Left ventricular end systolic diameter (LVESD), Mitral A velocity, E/A ratio, and TAPSE, showed no statistically significant differences (P > 0.05). (Table 3)

Table 3: Echocardiographic parameters among the studied groups.

Echo parameters	Patients (*n*=40)	Controls (*n*=40)	*P-value*
LVEF			
Mean±SD	61.35±4.74	61.43±5.35	0.947
Range	54-72	53-74	
LVEDD			
Mean±SD	46.03±5.65	47.60±5.46	0.209
Range	35-59	38-59	
LVESD			
Mean±SD	29.03±5.40	30.05±5.22	0.391
Range	20-40	21-40	
Mitral E vel			
Mean±SD	0.89±0.18	0.80±0.18	0.041
Range	0.56-1.3	0.54-1.43	
Mitral A vel			
Mean±SD	0.79±0.24	0.86±0.15	0.099
Range	0-1.1	0.59-1.2	
E/A			
Mean±SD	1.02±0.30	0.92±0.12	0.057
Range	0-1.9	0.75-1.36	
E/e'			
Mean±SD	7.76±1.52	6.59±1.36	<0.001
Range	4.65-11.3	4.4-9.7	
TAPSE			
Mean±SD	20.80±3.86	22.08±4.07	0.155
Range	14-28	16-30	

Significant *P-value* <0.05; LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end systolic diameter; LVEDD: Left ventricular end diastolic diameter; TAPSE: Tricuspid annular plane systolic excursion.

There were significant differences in RA function parameters between the groups, with lower RA Reservoir Strain (RS) ($P < 0.001$), RA Cond S ($P < 0.001$), and RA Cont S ($P = 0.008$) observed in the patient group. LA function showed a significant reduction in LA Cont S in the patient group ($P = 0.047$). Other left and right atrial parameters, including LA and RA maximal, minimal, and pre-A volumes (and their indexed values), as well as Left Atrial Emptying Fraction (LAEF) and Right Atrial Emptying Fraction (RAEF), did not differ significantly between the groups ($P > 0.05$). (Table 4)

Table 4: LA and RA function between the studied groups.

	Patients (*n*=40)	Controls (*n*=40)	*P-value*
	LA Function		
LA maximal volume			
Mean±SD	36.95±10.68	40.18±11.70	0.202
Range	19-56	19-67	
LA maximal volume (I)			
Mean±SD	24.10±4.51	25.80±6.63	0.184
Range	16-31	16-42	
LA minimal volume			
Mean±SD	14.53±5.11	14.30±4.43	0.834
Range	7-31	7-25	
LA minimal volume (I)			
Mean±SD	9.63±2.80	9.18±2.73	0.468
Range	5-16	5-15	
LA pre-A volume			
Mean±SD	21.58±5.68	23.50±6.64	0.168
Range	11-35	12-38	
LA pre-A volume (I)			
Mean±SD	14.48±3.22	15.23±3.18	0.298
Range	9-22	8-21	
LA RS			
Mean±SD	34.85±8.99	36.73±10.12	0.384
Range	22-54	18-60	
LA Cond S			
Mean±SD	19.03±6.70	18.13±6.44	0.542
Range	10-34	10-38	
LA Cont S			
Mean±SD	16.28±4.84	18.58±5.32	0.047
Range	9-27	7-29	
LAEF			
Mean±SD	60.60±7.44	63.63±8.05	0.085
Range	42-75	49-79	
	RA Function		
RA maximal volume			
Mean±SD	37.48±9.82	39.50±10.73	0.381
Range	22-55	23-66	
RA maximal volume (I)			
Mean±SD	25.10±4.88	25.80±6.43	0.585
Range	16-34	15-42	
RA minimal volume			
Mean±SD	15.13±5.24	14.73±4.54	0.716
Range	6-28	6-24	
RA minimal volume (I)			
Mean±SD	10.08±2.90	9.38±2.98	0.290
Range	5-17	4-16	
RA pre-A volume			
Mean±SD	22.25±6.51	22.65±6.47	0.784
Range	12-36	13-37	

RA pre-A volume (I)			
Mean±SD	14.95±3.95	14.58±3.82	0.667
Range	8-25	7-23	
RA RS			
Mean±SD	32.75±9.36	43.05±12.05	< 0.001
Range	19-59	27-75	
RA Cond S			
Mean±SD	17.55±7.67	23.85±5.72	< 0.001
Range	6-33	13-36	
RA Cont S			
Mean±SD	13.38±5.87	16.73±5.20	0.008
Range	5-26	10-32	
RAEF			
Mean±SD	60.28±7.45	62.60±8.17	0.188
Range	47-79	45-78	

LA: Left atrium; RA: Right atrium; RS: Reservoir strain; Cond S: Conduit strain; Cont S: Contractile strain; LAEF: Left atrial emptying fraction; RAEF: Right atrial emptying fraction; Vol: Volume; Vol (I): Indexed volume. Data are presented as mean ± standard deviation (SD) and range. $P < 0.05$ indicates statistical significance.

Subgroup analysis revealed significant differences based on age at closure. Patients with closure before 15 years had higher LA RS ($P < 0.001$), LA Cond S ($P = 0.002$), and LA Cont S ($P = 0.002$) compared to those with closure at 15 years or older. For RA function, younger patients exhibited lower RA vol max ($P < 0.001$), RA vol min ($P < 0.001$), RA vol pre-A ($P < 0.001$), and higher RA RS ($P < 0.001$), RA Cond S ($P < 0.001$), and RA Cont S ($P < 0.001$). Additionally, RA VOL MAX (I) was significantly higher in the younger group ($P = 0.049$). Other parameters, including LA maximal, minimal, and pre-A volumes (indexed), LAEF, RA VOL MIN (I), RA VOL PRE A (I), and RAEF, showed no statistically significant differences ($P > 0.05$). (Table 5)

Table 5: Subgroup analysis according to age at closure in the patients group with LA and RA function.

	Age at closure Group		
	<15 years (*n*=23)	≥15 years (*n*=17)	*p-value*
	Mean ±SD	Mean ±SD	
LA Function			
LA maximal volume (I)	24.91 ±4.58	23 ±4.3	0.188
LA minimal volume (I)	9.91 ±2.87	9.24 ±2.73	0.456
LA pre-A volume (I)	15.13 ±3.55	13.59 ±2.55	0.136
LA RS	39.13 ±8.72	29.06 ±5.52	<0.001
LA Cond S	21.74 ±6.17	15.35 ±5.68	0.002
LA Cont S	18.26 ±4.83	13.59 ±3.43	0.002
LAEF	60.61 ±6.62	60.59 ±8.65	0.993
RA Function			
RA vol max	32.61 ±8.54	44.06 ±7.39	<0.001
RA VOL MAX (I)	26.39 ±5.19	23.35 ±3.92	0.049
RA vol min	12.7 ±4.47	18.41 ±4.43	<0.001
RA VOL MIN (I)	10.35 ±3.27	9.71 ±2.37	0.497
RA vol pre A	19.09 ±5.32	26.53 ±5.52	<0.001
RA VOL PRE A (I)	15.78 ±4.55	13.82 ±2.7	0.123
RA RS	38.35 ±7.98	25.18 ±4.45	<0.001
RA Cond S	22.74 ±5.72	10.53 ±2.7	<0.001
RA Cont S	17.39 ±4.08	7.94 ±2.56	<0.001
RAEF	62.04 ±7.56	57.88 ±6.79	0.081

RS: Reservoir strain; Cond S: Conduit strain; Cont S: Contractile strain; LAEF: Left atrial ejection fraction; RAEF: Right atrial ejection fraction. $P < 0.05$ indicates statistical significance.

The analysis revealed significant gender differences in right atrial function. Male patients had higher RA RS ($P = 0.032$), RA Cond S ($P = 0.018$), and RA Cont S ($P = 0.004$) compared to females. No statistically significant differences were observed between males and females in any of the LA function parameters or other right atrial parameters ($P > 0.05$). (Table 6)

Table 6: Subgroup analysis according to gender in the patients group with LA and RA function.

	Male (n=22)	Female (n=18)	*P-value*
	Mean ±SD	Mean ±SD	
LA Function			
LA maximal volume	35.41 ±11.12	38.83 ±10.11	0.319
LA maximal volume (I)	23.86 ±4.8	24.39 ±4.24	0.719
LA minimal volume	14.18 ±5.46	14.94 ±4.77	0.645
LA minima volume (I)	9.68 ±3.03	9.56 ±2.57	0.889
LA pre-A volume	20.59 ±5.75	22.78 ±5.5	0.23
LA pre-A volume (I)	14.32 ±3.67	14.67 ±2.66	0.738
LA RS	35.41 ±9.52	34.17 ±8.52	0.669
LA Cond S	19.32 ±6.85	18.67 ±6.7	0.764
LA Cont S	16.59 ±4.8	15.89 ±5	0.654
LAEF	60.14 ±7.92	61.17 ±7.01	0.669
RA Function			
RA vol max	36.09 ±10.29	39.17 ±9.21	0.331
RA VOL MAX (I)	24.95 ±5.35	25.28 ±4.38	0.838
RA vol min	14.77 ±5.42	15.56 ±5.15	0.645
RA VOL MIN (I)	10.14 ±2.93	10 ±2.95	0.885
RA vol pre A	21.55 ±6.72	23.11 ±6.32	0.456
RA VOL PRE A (I)	15 ±4.06	14.89 ±3.94	0.931
RA RS	35.59 ±9.43	29.28 ±8.22	0.032
RA Cond S	20.09 ±7.36	14.44 ±7.03	0.018
RA Cont S	15.73 ±5.82	10.5 ±4.6	0.004
RAEF	60.32 ±6.39	60.22 ±8.78	0.968

RS: Reservoir strain; Cond S: Conduit strain; Cont S: Contractile strain; LAEF: Left atrial ejection fraction; RAEF: Right atrial ejection fraction. $P < 0.05$ indicates statistical significance.

Significant correlations were observed between LA function and various parameters. LA Max Vol ($r = 0.725$, $P < 0.001$), LA Min Vol ($r = 0.607$, $P < 0.001$), and LA Pre-A Vol ($r = 0.733$, $P < 0.001$) showed strong positive correlations with age, while LAEF was not significantly correlated ($P = 0.84$). Closure age also showed significant positive correlations with LA Max Vol ($r = 0.605$, $P<0.001$) and LA Pre-A Vol ($r = 0.624$, $P < 0.001$). Among echocardiographic parameters, LVEDD was significantly correlated with LA Max Vol ($r = 0.376$, $P = 0.016$), LA Min Vol ($r = -0.616$, $P < 0.001$), and LA Pre-A Vol ($r = 0.286$, $P = 0.073$). LVESD showed significant positive correlations with LA Max Vol ($r = 0.501$, $P = 0.001$) and LA Pre-A Vol ($r = 0.434$, $P = 0.005$). There were no significant correlations with parameters such as Mitral A velocity, Mitral E velocity, and E/A ratio across most LA function parameters ($P > 0.05$). Additionally, years after closure exhibited weaker correlations with most LA function parameters ($P > 0.05$) except LA Max Vol ($P = 0.009$) and LA Pre-A Vol ($P = 0.013$). (Table 7)

Table 7: Correlation between left atrial function and other parameters in patients group.

		LA Cond S	LA Cont S	LA RS	LA Max Vol	LA Max Vol (I)	LA Min Vol	LA Min Vol (I)	LA Pre-A Vol	LA Pre-A Vol (I)	LAEF
Age	r	-0.145	-0.004	-0.116	0.725	-0.405	0.607	-0.256	0.733	-0.431	0.032
	P-value	0.370	0.978	0.4774	<0.001	0.009	<0.001	0.111	<0.001	0.005	0.84
Closure age	r	-0.122	-0.046	-0.119	0.605	-0.247	0.532	-0.140	0.624	-0.278	-0.001
	P-value	0.452	0.777	0.465	<0.001	0.124	<0.001	0.3890	<0.001	0.082	0.99
E/A	r	-0.113	-0.030	-0.193	-0.184	0.276	0.030	0.353	-0.128	0.283	-0.337
	P-value	0.486	0.852	0.232	0.255	0.084	0.852	0.025	0.430	0.076	0.03
E/e'	r	-0.135	0.171	0.051	0.251	-0.129	0.311	0.025	0.369	-0.016	-0.205
	P-value	0.406	0.292	0.754	0.118	0.426	0.051	0.880	0.019	0.921	0.205
LVEDD	r	-0.056	0.207	0.002	0.376	-0.534	0.079	-0.616	0.286	-0.620	0.413
	P-value	0.733	0.200	0.992	0.016	<0.001	0.627	<0.001	0.073	<0.001	0.008
LVEF	r	-0.156	-0.303	-0.297	-0.089	0.118	-0.094	0.142	-0.113	0.153	-0.076
	P-value	0.335	0.057	0.062	0.583	0.467	0.563	0.380	0.487	0.346	0.63
LVESD	r	-0.216	0.176	-0.191	0.501	-0.540	0.329	-0.445	0.434	-0.599	0.181
	P-value	0.180	0.276	0.238	0.001	<0.001	0.038	0.004	0.005	<0.001	0.264
Mitral A velocity	r	0.089	-0.003	0.058	-0.081	0.025	-0.120	-0.021	-0.073	0.076	0.075
	P-value	0.586	0.985	0.722	0.620	0.878	0.461	0.899	0.654	0.641	0.646
Mitral E velocity	r	-0.151	-0.040	-0.083	-0.077	0.179	0.110	0.372	0.039	0.282	-0.386
	P-value	0.352	0.807	0.609	0.636	0.269	0.5	0.018	0.810	0.078	0.014
Years after closure	r	-0.080	0.090	-0.017	0.407	-0.427	0.284	-0.304	0.387	-0.420	0.079
	P-value	0.622	0.582	0.918	0.009	0.006	0.075	0.056	0.013	0.007	0.628

LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic diameter; LVEDD: Left ventricular end-diastolic diameter; RS: Reservoir strain; Cond S: Conduit strain; Cont S: Contractile strain; LAEF: Left atrial ejection fraction. r: correlation coefficient.

Significant correlations were observed between RA function and several parameters. RA Max Vol (r = 0.707, P < 0.001), RA Min Vol (r = 0.614, P < 0.001), and RA Pre-A Vol (r = 0.608, P < 0.001) showed strong positive correlations with age, while RA Max Vol (I) and RA Pre-A Vol (I) were negatively correlated with age (P < 0.001 and P = 0.008, respectively). Age at closure significantly correlated positively with RA Max Vol (r = 0.583, P=0.001) and RA Pre-A Vol (r = 0.487, P = 0.001), while RA Max Vol (I) and RA Pre-A Vol (I) were negatively correlated (P =0.02 and P = 0.01, respectively). Among echocardiographic parameters, LVEDD and LVESD correlated positively with RA Max Vol (P = 0.012 and P< 0.001, respectively), and negatively with RA Max Vol (I) and RA Pre-A Vol (I) (P < 0.001). LVEF exhibited a significant positive correlation with RA Cond S (r =0.401, P = 0.010). Similarly, years after closure correlated significantly with RA Max Vol (P < 0.001) and RA Pre-A Vol (P = 0.014), while other RA metrics showed weaker or no correlations (P > 0.05). (Table 8)

Table 8: Correlation between right atrial function and other parameters in patients group.

		RA Cond S	RA Cont S	RA RS	RA Max Vol	RA Max Vol (I)	RA Min Vol	RA Min Vol (I)	RA Pre-A Vol	RA Pre-A Vol (I)	RAEF
Age	r	-0.045	-0.120	-0.040	0.707	-0.522	0.614	-0.282	0.608	-0.510	0.312
	P-value	0.782	0.462	0.808	<0.001	<0.001	<0.001	0.077	<0.001	0.008	0.05
Age at closure	r	0.000	-0.192	-0.061	0.583	-0.367	0.480	-0.211	0.487	-0.401	0.226
	P-value	0.998	0.234	0.706	0.001	0.02	0.001	0.191	0.001	0.01	0.16
E/A	r	0.150	0.127	0.198	-0.121	0.393	0.046	0.430	-0.032	0.371	0.124
	P-value	0.355	0.434	0.221	0.456	0.012	0.778	0.005	0.846	0.018	0.4
E/e'	r	0.109	0.091	0.231	0.270	-0.120	0.244	-0.014	0.270	-0.077	0.064
	P-value	0.501	0.577	0.151	0.091	0.459	0.129	0.929	0.092	0.634	0.696
LVEDD	r	0.037	0.094	0.065	0.392	-0.572	0.257	-0.504	0.301	-0.537	0.027
	P-value	0.822	0.562	0.691	0.012	<0.001	0.108	<0.001	0.059	<0.001	0.86
LVEF	r	0.401	0.221	0.307	-0.093	0.160	0.016	0.244	0.010	0.257	0.038
	P-value	0.010	0.170	0.054	0.569	0.322	0.923	0.129	0.950	0.109	0.816
LVESD	r	0.085	0.135	0.053	0.504	-0.642	0.498	-0.355	0.458	-0.529	0.279
	P-value	0.602	0.405	0.746	<0.001	<0.001	0.001	0.024	0.003	<0.001	0.08
Mitral A velocity	r	-0.117	-0.136	-0.099	-0.111	0.000	-0.105	-0.026	-0.072	0.039	0.075
	P-value	0.472	0.402	0.544	0.495	0.999	0.518	0.875	0.659	0.809	0.643
Mitral E velocity	r	-0.056	0.101	0.149	-0.043	0.200	-0.004	0.223	0.068	0.334	0.318
	P-value	0.729	0.535	0.360	0.794	0.217	0.980	0.166	0.676	0.035	0.04
Years after closure	r	-0.108	0.134	0.039	0.413	-0.443	0.414	-0.212	0.385	-0.341	0.249
	P-value	0.506	0.409	0.809	<0.001	0.004	0.007	0.189	0.014	0.031	0.12

LVEF: Left ventricular ejection fraction; LVESD: Left ventricular end-systolic diameter; LVEDD: Left ventricular end-diastolic diameter; RS: Reservoir strain; Cond S: Conduit strain; Cont S: Contractile strain; RAEF: Right atrial ejection fraction. r: correlation coefficient.

DISCUSSION

Several studies have shown improvement in ventricular function and reverse remodeling after ASD device closure[12, 13], yet there is insufficient data about its effect on biatrial function and remodeling.

Our interest in atrial function comes from the growing evidence about the role of both left and right atrial function in predicting the risk of adverse cardiac events. LA enlargement is associated with adverse cardiovascular outcomes such as development of AF. A decrease in the LA function index is an independent predictor of all-cause mortality or HF hospitalization in patients with coronary artery disease, HFrEF, and AF [14-17]. Most studies highlighted the role of left-sided valvular heart disease and LA enlargement on AF development but Antonio ***Vitarelli et al.*** [18] showed that preexisting RA dilatation and dyssynchrony before ASD closure was significantly associated with the development of AF independent of LA function. RA volumetric indices and deformation parameters (time to peak strain) were the strongest parameters associated with the risk of AF.

Interest in changes in LA function after ASD treatment has increased recently, and the results of the few studies that have been reported have been inconsistent. Some possible reasons for these discrepancies include differences in the timing of evaluation of LA function after ASD treatment and differences in methods used for evaluation [8]. ***Seo et al.*** [8] showed that LA strain demonstrated reduced LA reservoir, conduit, and contraction function in ASD patients treated with device closure compared with healthy controls after 1 to 3 years of the procedure while there was no difference in atrial volumes between the two groups. All patients in this study were diagnosed after the age of 20 years old.

Hajizeinali et al. [19] studied RA and LA function in patients who underwent device closure and compared them to patients who underwent surgical closure and healthy controls. The main finding was that the 2D STE-derived parameters of the LA reservoir function (peak systolic strain and peak systolic strain rate) and conduit function (early diastolic strain and early diastolic strain rate) were more likely to be abnormal in the device closure group than in the control group. While in the RA, only the contractile strain was abnormal in the device closure group compared to a control group, the reservoir, conduit, and contractile strain were significantly reduced in the surgical closure group compared to a control group.

In 2014, ***Aslan et al.*** [20] found that LA reservoir function wasn't changed, conduit function was improved, and contractile function deteriorated, right and LA electromechanical delays were not changed in the early post-procedural period but were decreased in midterm follow up which may reflect the decreased risk of AF owing to favorable remodeling and RA unloading after defect closure.

Regarding the impact of age at the time of ASD closure, a study by ***Michael Humenberger et al.*** [5], showed that transcatheter ASD closure can be safely and successfully performed in adults at any age. Regression of RV size and PAP as well as symptomatic improvement can be expected across all age groups. However, the best outcome is achieved in patients with less functional impairment and less elevated PAP. Considering the continuous increase in symptoms, RV remodelling, and PAP with increasing age, ASD closure is recommended irrespective of symptoms early after diagnosis even in adults of advanced age.

Previous data showed that RA and RV volumes are reduced following the procedure, but some structural and electrical remodeling may persist despite regression in RA and RV volumes and symptomatic improvement. This is evident in a study by ***Vitarelli et al.*** [18] which showed those with dilated RA compared to controls carried a higher risk for AF. RA stretch and dyssynchrony caused by left-to-right shunt promotes changes in atrial refractoriness and ionic currents (electrical remodeling), as well as tissue remodeling due to atrial fibrosis (structural remodeling), which generates a favorable substrate for AF initiation.

Most studies were bound by a certain time after the procedure as 6 months or 1 year follow-up. It is unknown whether the changes in atrial indices persist, improve, or deteriorate in the long term. So, in our study, we evaluated both RA and LA volumetric indices and deformation patterns in patients who underwent the procedure for at least 3 years.

In our study, we compared a group that underwent ASD device closure more than 3 years ago with a sex and age-matched control group. After three years of follow-up post-procedure, we found no difference in LA reservoir and conduit function in the patients group compared to healthy controls. Mean values of LA reservoir and conduit strain were 34.85±8.99 and 19.03±6.70 respectively in ASD patients compared to 36.73±10.12 and 18.13±6.44 respectively in the control group with *p-value* (P=0.384) for RS and (P=0.542) for conduit strain. Only LA contractile strain was significantly reduced in patients group with mean of 16.28±4.84 compared to 18.58±5.32 in the control group with *p-value* (p=0.047).

While the RA strain values showed more impairment than LA in patients group, All RA strain values were significantly reduced in patients group compared to control group not only contractile strain as in LA. There was a statistically significant difference according to RA RS, RA conduit strain and RA contractile strain. RA RS was significantly lower in patients group with mean 32.75±9.36 compared to mean value of 43.05±12.05 in control group with *p-value* (p=0.000). RA conduit strain and contractile strain are also significantly lower in patients group compared to control group with mean values of 17.55±7.67 and 13.38±5.87 in patients group compared to 23.85±5.72 and 16.73±5.20 in control group with *p-value* (p=0.000) and (p=0.008) respectively.

Humenberger et al. [5] highlighted the role of age at closure in the final outcomes in ASD patients. A subgroup analysis according to age at closure was done, we compared LA strain values between patients who underwent ASD device closure less than 15 years and those who underwent closure more than 15 years old; we found a significant difference in all LA strain values between the two groups. Mean LA strain values in patients underwent closure at age less than 15 years old compared to those who underwent closure more than 15 years old were 39.13±8.72, 21.74±6.17 and 18.26±4.83 versus 29.06±5.52, 15.35±5.68 and 13.59±3.43 with *p-value* (P<0.05) for reservoir, conduit and contractile strain respectively.

Similar results were obtained when comparing RA strain values between the two groups. Mean RA strain values were significantly higher in patients underwent closure less than 15 years old (38.35±7.98, 22.74±5.72, 17.39±4.08) vs (25.18±4.45, 10.53±2.70, 7.94±2.56) for reservoir, conduit and contractile strain respectively, with *p-value*(0.000) in all of them.

The subgroup analysis showed that patients who underwent closure less than 15 years old had strain values close to control group. Mean LA RS was 39.13±8.72 in patients group (<15 years) versus 36.73±10.12 in control group. Mean LA conduit strain was 21.74±6.17 in patients group (<15 years) versus 18.13±6.44 in control group. Mean LA contractile strain was 18.26±4.83 in patients group (<15 years) versus 18.58±5.32 in control group.

While in patients aged more than or equal to 15 years at time of ASD closure we found the following, Mean LA RS was 29.06±5.52 in patients group (>15 years) versus 36.73±10.12 in control group. Mean LA conduit strain was 15.35±5.68 in patients group (>15 years) versus 18.13±6.44 in control group. Mean LA contractile strain was 13.59±3.43 in patients group (>15 years) versus 18.58±5.32 in control group.

Same applies to RA, we also found that patients who underwent closure less than 15 years old had mean RA strain values similar to control group. Mean RA RS was 38.35±7.98 in patients group (<15 years) versus 43.05±12.05 in control group. Mean RA conduit strain was 22.74±5.72 in patients group (<15 years) versus

23.85±5.72 in control group. Mean RA contractile strain was 17.39±4.08 in patients group (<15 years) versus 16.73±5.20 in control group.

While in patients aged more than or equal to 15 years at time of ASD closure we found the following, mean RA RS was 25.18±4.45 in patients group (>15 years) versus 43.05±12.05 in control group. Mean RA conduit strain was 10.53±2.70 in patients group (>15 years) versus 23.85±5.72 in control group. Mean LA contractile strain was 7.94±2.56 in patients group (>15 years) versus 16.73±5.20 in control group.

From the available previous data as reported by ***Humenberger et al***[5], ASD closure is recommended in all age groups because its benefit is seen among all age groups but the key point is to determine which type of patients would benefit most from the intervention as this may guide timing of intervention and promote a strategy for screening in the future. Many ASD patients are diagnosed accidentally during adulthood when performing echocardiography for another medical purpose or when symptoms of dyspnea are secondary to pulmonary hypertension develop which is a relatively late stage and such patients benefit less than patients who undergo ASD closure in childhood. Our results favor early intervention as it is associated with better atrial function and may decrease the risk of future arrhythmias.

Our study mainly focused on biatrial function; however, we measured TAPSE as a representative of RV function, we found no significant difference between control group and patients group. Mean TAPSE in patients group was 20.80±3.86 versus 22.08±4.07 in control group with *p-value* (*P*=0.155). However, patients treated under age of 15 years old had higher mean TAPSE value 22.26±3.31 versus 18.82±3.76 in patients treated above 15 years old. On the long term, untreated ASD leads to progressive volume overload on the right side with progressive tricuspid regurgitation and dilatation of the right atrium and ventricle. We showed that earlier closure is associated with better TAPSE, and this is probably due to reverse remodeling at the young age compared to older age group.

Despite the promising findings, this study has several limitations. First, the small sample size may have reduced the statistical power and limited the generalizability of the findings. Second, the lack of preprocedural data on atrial volumes and strain values necessitated comparison with a control group rather than baseline measurements, potentially introducing variability in the interpretation. Additionally, the absence of standardized reference values for atrial volumes and strain posed challenges in contextualizing the results.

CONCLUSION

Early ASD closure (<15 years) is associated with superior long-term biatrial function, with strain values approximating normal levels. In contrast, closure at ≥15 years results in significant impairment, particularly in RA strain parameters, highlighting persistent remodeling. The LA function was largely preserved except for reduced contractile strain in the patient group. Timely intervention is crucial to optimize reverse remodeling and reduce future complications.

CONFLICTS OF INTEREST

No conflicts of interest.

DECLARATION OF CONFLICTING INTERESTS

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CONTRIBUTION

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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المتابعة طويلة المدى لوظيفة الأذينين بعد إغلاق عيب الحاجز الأذيني عبر القسطرة

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المقدمة: يُعد عيب الحاجز الأذيني من التشوهات القلبية الخلقية الشائعة، والتي قد تؤدي إلى مضاعفات خطيرة على المدى الطويل في حال عدم علاجها، مثل الرجفان الأذيني وفرط ضغط الدم الرئوي. يُعتبر الإغلاق بالجهاز عبر القسطرة الخيار العلاجي المفضل، حيث ثبتت فوائده في إعادة تشكيل البطين الأيمن، إلا أن تأثيره على وظيفة الأذينين على المدى الطويل لا يزال غير مدروس بشكل كافٍ.

هدف الدراسة: تقييم وظيفة الأذينين على المدى الطويل لدى المرضى الذين خضعوا لإغلاق عيب الحاجز الأذيني عبر القسطرة.

الطرق: هذه دراسة مستقبلية للحالات والشواهد شملت ٤٠ مريضًا خضعوا لإغلاق عيب الحاجز الأذيني عبر القسطرة منذ ثلاث سنوات على الأقل، بالإضافة إلى ٤٠ شخصًا سليمًا متطابقين في العمر والجنس كمجموعة ضابطة. تم إجراء تقييم شامل بتخطيط صدى القلب، بما في ذلك تخطيط صدى القلب بتقنية تتبع البقع ثنائي الأبعاد، لتحليل الإجهاد الأذيني لكل من الأذين الأيمن والأذين الأيسر من خلال مراحل الخزان، والموصل، والتقلص، إضافة إلى مؤشرات الحجم الأذيني.

النتائج: بالمقارنة مع المجموعة الضابطة، أظهر المرضى انخفاضًا ملحوظًا في كل من معدل الانقباض البطيني الأيمن(٣٢,٧٥ ± ٩,٣٦٪ مقابل ٤٣,٠٥ ± ١٢,٠٥٪، قيمة P أقل من ٠,٠٠١)، ومعدل الانقباض البطيني الأذيني (١٧,٥٥ ± ٧,٦٧٪ مقابل ٢٣,٨٥ ± ٥,٧٢٪، قيمة P أقل من ٠,٠٠١)، ومعدل الانقباض الأذيني (١٣,٣٨ ± ٥,٨٧٪ مقابل ١٦,٧٣ ± ٥,٢٠٪، قيمة P= ٠,٠٠٨) في الأذين الأيمن. كما انخفض أيضًا معدل الانقباض الأذيني في الأذين الأيسر (١٦,٢٨ ± ٤,٨٤٪ مقابل ١٨,٥٨ ± ٥,٣٢٪، قيمة P = ٠,٠٤٧ .)أظهر المرضى الذين خضعوا للإغلاق قبل سن الخامسة عشرة وظيفة أذينية أفضل، مع قيم إجهاد تقارب قيم المجموعة الضابطة(على سبيل المثال، RA RS: ٣٨,٣٥ ± ٧,٩٨٪ مقابل ٤٣,٠٥ ± ١٢,٠٥٪، قيمة *P* = ٠,٠٣٢)

الاستنتاجات: يؤدي الإغلاق المبكر لعيب الحاجز الأذيني (<١٥ عامًا) إلى الحفاظ على الوظيفة الأذينية، مع قيم إجهاد قريبة من المعدل الطبيعي، في حين أن الإغلاق المتأخر يرتبط بتدهور وظيفي طويل الأمد، خصوصًا في الأذين الأيمن.