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Effect of Atrial Septal Defect Closure on Right Atrial Function in Adults; A Prospective Comparative Controlled Study

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Abstract

Background: Atrial septal defects (ASDs) account for approximately 10% of all congenital heart defects. The closure of ASD with significant left-to-right shunt results in improved functional capacity and improves arrhythmias. ASD closure in adult patients has certain risks, it may result in pulmonary edema and heart failure.

Objectives: The study aimed to assess right atrial (RA) function by speckle-tracking echocardiography (STE) in adult patients with ostium secundum ASD, before and 3 months after transcatheter or surgical closure.

Material and methods: A prospective comparative controlled study involved 40 ASD adult patients and 20 healthy age-matched individuals, to study and compare the RA function in patients diagnosed with ostium secundum ASD, before and 3 months after closure.

Results: There was a significant difference between the mean RA volume index (RAVI) in the case group which was significantly higher than the mean RAVI in the control group (p-value <0.001). The mean tricuspid E/e' ratio in the case group was significantly lower than the mean tricuspid E/e' ratio in the control group (p-value 0.003). The mean RAS-r was statistically significantly lower in the ASD group than the mean RAS-r in the control group (p-value 0.001). The mean RAS-ct was significantly lower in the ASD group than the mean RAS-ct in the control group (p-value <0.001). RAS-ct increased significantly after ASD closure (p-value <0.05). RAS-r increased significantly in the catheter group than in the surgical group after closure (P-value <0.001).

Conclusions: Reduced right atrial (RA) mechanical function assessed by speckle tracking echocardiography due to long-standing ASD in adults. Improved RA contractile function after ASD closure. Also, the RA geometrical reverse remodeling was evident at 3 months following ASD closure. Finally, In the catheter-treated patients, RA function improvement was greater than in the surgically treated patients.
Keywords: ASD, Congenital Heart Defects, Closure, Trans-catheter, Atrium, Speckle Tracking.

Abbreviations: **ASD**: atrial septal defect, **EF**: ejection fraction, **LV**: left ventricle, **RA**: right atrium, **RAScd:** right atrial conduit strain; **RASct**: right atrial contractile strain. **RASr:** right atrial reservoir strain, **RAVI**: right atrial volume index, **RV**: right ventricle, **TAPSE**: tricuspid annular plane systolic excursion.

Introduction

Atrial septal defects (ASDs) are a relatively common type of congenital heart defect, accounting for approximately 10% of all such anomalies [1]. However, in the adult population, ASDs comprise a more significant proportion, accounting for 30%-40% of congenital heart diseases (CHD) [1].

Patients with ASDs often remain asymptomatic until later in life, when they may present with palpitations, decreased exercise tolerance, and arrhythmias in adulthood [2,3]. The closure of ASDs with significant left-to-right shunts has been associated with improved functional capacity and a reduction in the incidence of arrhythmias, which can become more responsive to treatment [4].

Nevertheless, the closure of ASDs in adult patients is not without its risks. Specifically, it may result in the development of pulmonary edema, heart failure, and in some cases, even mortality [4]. This is due to an abrupt elevation in left ventricular preload following ASD closure in patients with a non-compliant left ventricle (LV), which may be secondary to the mechanical response to chronic right ventricular (RV) volume overload, leading to compression of the LV, abnormal diastolic-systolic relations of the interventricular septum, and chronic LV underfilling with increased left atrial (LA) pressure, resulting in "masked LV restriction." Additionally, comorbid conditions such as systemic hypertension, coronary heart disease, or age-related LV diastolic dysfunction may also contribute to these complications [4].

Transcatheter closure of isolated secundum ASDs has become an established mode of treatment in adult patients [5]. Speckle tracking echocardiography (STE) is a novel, angle-independent technique that allows for a more comprehensive assessment of atrial mechanics, including strain and strain rate parameters, providing a detailed evaluation of right atrial (RA) function compared to conventional echocardiographic measures [6,7].

The RA is the most under-evaluated heart chamber in clinical practice. [8] Thus, we aimed to assess RA function by speckle-tracking echocardiography in adult patients with ostium secundum ASD, before and 3 months after closure, using either transcatheter or surgical techniques.

Material and methods

Ethical considerations:

The study participants who met the established criteria were informed by the authors about the objectives of the investigation, and their participation was solicited only after they had provided verbal consent. All the patients participated in the study voluntarily. The data collection instruments were anonymous, and verbal consent was obtained from the participants to take part in the study. Participants were made aware of their right to decline or withdraw from the study at any point, following the ethical principles outlined in the Helsinki Declaration of 1983. The research protocol was reviewed and approved by the Medical Research Ethics Committee of Kafr Elsheikh University.

Sample size:

An appropriate sampling approach was employed to enroll the participants in this study, 40 ASD patients who met the pre-established inclusion criteria were recruited from the cardiology departments of Kafr Elsheikh University Hospital and the National Heart Institute in Egypt, and 20 healthy age-matched individuals in the control group.

Study Design:

A prospective comparative controlled study has been used to analyze and compare the right atrial function in adult patients with ostium secundum ASD before and 3 months after closure.

Study population and procedure:

The study included 60 patients. The patients were divided into two groups: 40 adults with ostium secundum ASD who were candidates for ASD closure either trans-catheter or surgical and 20 healthy persons in the same age group to be the control one.

ASD patients were recruited before the ASD closure to the outpatient cardiology department of Kafr Elsheikh University Hospitals and National Heart Institute during the patients' visits for regular monitoring and follow-up from November 2021 till December 2023.

The study inclusion criteria for cases were a) adult patients ≥ 40 years old with hemodynamically significant ostium secundum ASD, and b) adequate follow-up. The criteria for exclusion of cases were a) patients with ASD other than secundum type, b) other congenital defects, c) impaired LV systolic function, d) high pulmonary vascular resistance, e) renal impairment, f) patients with allergy to contrast media, and g) patients with poor echo window.

The inclusion criteria of the control group: a) Same age group of patients without any structural or congenital heart diseases.

When selected candidates for the study were determined, an explanation of the study aspects was provided and permission for their participation in the study was obtained. The instruments were self-administered. Each patient's data included: a full clinical evaluation, socio-demographic characteristics (e.g., gender, age, weight, height, and BMI), ECG, echocardiography (conventional trans-thoracic, transesophageal, and RA speckle tracking echocardiography), chest X-ray and laboratory investigations (BUN, serum creatinine, CBC, virology, INR, HbA1c and LDL). All participants were examined before the ASD closure and re-evaluation was done 24 hours, one week, one month, and 3 months after the defect closure.

Data from Conventional Echocardiography:

Based on the recommendations of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI). Using Philips Epic 7C Echocardiography machine equipped with S5-1, X5-1 transthoracic probes, TDI technology, and X7-2t TEE probe. All echocardiographic studies were performed with the subjects in the left lateral decubitus position. Images were stored digitally for offline analysis using dedicated software (PHILIPS Q-Lab cardiac analysis version 15.5).

1) Standard Trans-thoracic echocardiographic study:

LV diameters and wall thickness were measured in the left parasternal long-axis view at the level of the mitral valve tips, ensuring a measurement perpendicular to the long axis of the ventricle. Ejection fraction (EF) was determined using a modified Simpson's method (biplane method) by acquiring apical four-chamber and apical two-chamber views. Color flow and CW Doppler were used to assess cardiac valves. RV dimensions (basal, mid & long axis), and RV systolic function (TAPSE & RV S') were measured.

2) Tissue Doppler Imaging:

PW Doppler over mitral & tricuspid inflow velocities: peak early diastolic velocity (E) wave, peak late diastolic velocity (A) wave, E wave deceleration time (DT) & E/A ratio. Tissue Doppler of lateral, septal mitral & lateral tricuspid annuli.

2D speckle tracking echocardiography:

Speckle tracking is an offline technique that is applied to previously acquired 2D echocardiographic images. Strain results were measured using software on 2D grayscale images of the RA from an RV-focused apical four-chamber view. All images were stored in cine-loop format from three consecutive beats, for tracing the RA region of interest, starting at the tricuspid valve annulus, along the endocardial border of the RA lateral wall, RA roof, RA septal wall, and ending at the opposite tricuspid annulus.

RA STE curves were obtained using ECG R-R gating as the zero-strain reference. Phasic strain values were measured by RA reservoir (RASr), conduit (RAScd), and contraction strain (RASct). **(Figure 1)**

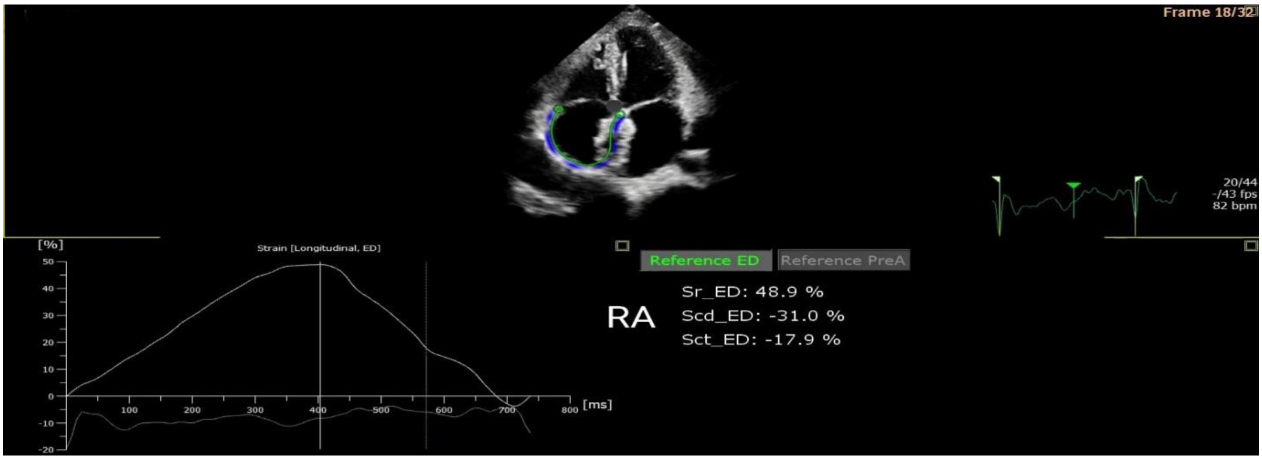

Figure (1): An example of RA strain measurement in a case of post-ASD transcatheter closure

Statistical Analysis:

Data were collected, coded, and analyzed using Microsoft Excel software and then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis with inferential and descriptive procedures. According to the type of data qualitative represented by number and percentage, and the quantitative continues group is represented by mean ± SD, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi-square test (X2). Differences between quantitative independent groups by t-test paired by paired t, correlation by Pearson's correlation. Results are presented as the 95% confidence interval (95% CI) and regression coefficient (β-coefficient). A p-value <0.05 was considered significant.

Results:

The mean age of the studied groups was (43.70±2.84 years) for the case group and (44.60±3.23 years) for the control group. The case group consisted of 24 females and 16 male patients, while the control group had 12 females and 8 males. The mean height of the case group was slightly lower at (170.9±7.53 cm), compared to (172.5±5.11 cm) for the control group. The mean BMI of the case group was slightly higher at (28.25±3.75 kg/m^2), compared to (27.11±2.59 kg/m^2) for the control group. (**Table 1**)

Table (1): Demographic and anthropometric data of the studied groups:

			Case	Control	t/ X^2	P
Age			**43.70±2.84**	**44.60±3.23**	**1.103**	**0.275**
Height			**170.9±7.53**	**172.5±5.11**	**0.855**	**0.396**
Weight			**83.2±16.02**	**80.85±9.86**	**0.600**	**0.551**
BSA			**1.95±0.21**	**1.94±0.13**	**0.029**	**0.977**
BMI			**28.25±3.75**	**27.11±2.59**	**1.222**	**0.226**
Sex	**Female**	**N**	**24**	**12**		
		%	**60.0%**	**60.0%**		
	Male	**N**	**16**	**8**	**0.0**	**1.0**
		%	**40.0%**	**40.0%**		
Total		**N**	**40**	**20**		
		%	**100.0%**	**100.0%**		

***** P value was <0.05 for significant results, BMI: Body mass index & BSA: Body surface area.

The mean systolic blood pressure (SBP) in the case group was (115.75±14.25 mmHg), which was slightly lower than the control group (117.0±8.64 mmHg), but the difference was not statistically significant (p=0.720). However, the mean heart rate (HR) in the case group was significantly higher at (93.75±8.15 beats/min) compared to (81.25±7.58 beats/min) in the control group (p<0.001). Most patients (34) had no risk factors, while 2 patients were hypertensive. **(Figure 2)**

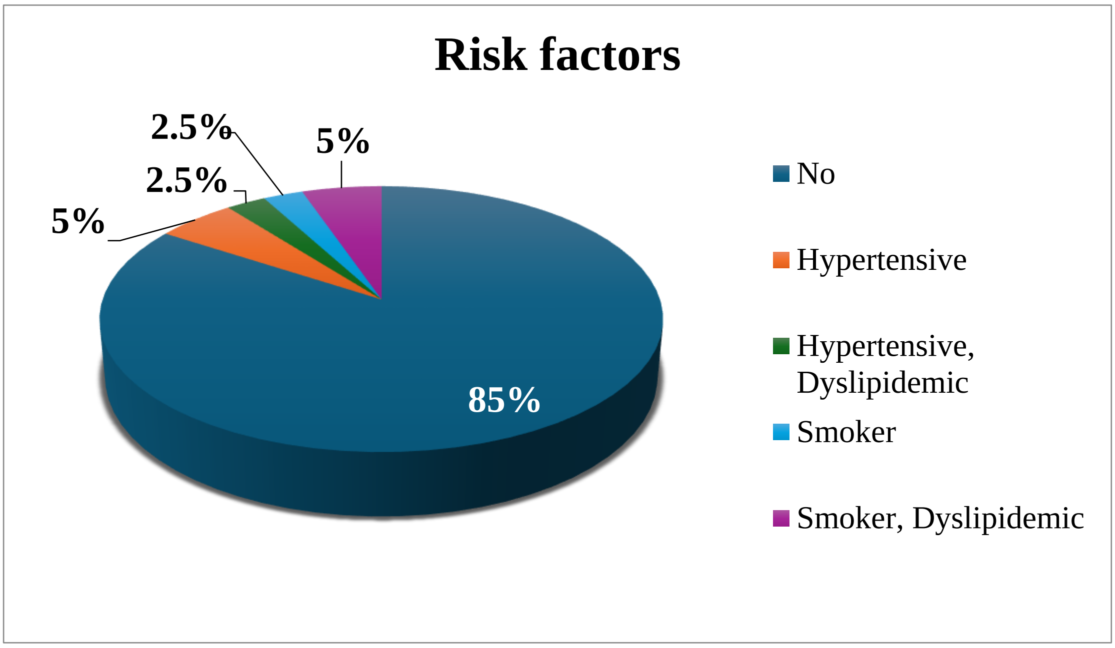

Figure (2) Risk factors distribution among patients of the ASD group.

The conventional echocardiographic parameters for the right side of the heart showed that the case group had significantly higher values for tricuspid regurgitation (TR) velocity, right atrial (RA) volume, RA volume index (RAVI), RV dimensions, tricuspid valve A wave (TV A), and TAPSE, but significantly lower values for, tricuspid valve E wave (TV E), TV E/A ratio, and TV E/e'. **(Table 2)**

There was no statistically significant difference between the groups in terms of LA volume, LA volume index (LAVI), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), or ejection fraction (EF).

The mean RA volume in the case group was significantly higher at (119.63±28.6 ml) compared to (50.97±7.77 ml) in the control group (p<0.001), the mean RAVI in the case group was significantly higher at (60.41±18.69 ml/m^2) compared to (26.19±2.98 ml/m^2) in the control group (p<0.001). The mean tricuspid E wave velocity was significantly lower in the case group at (69.82±11.64 cm/s) compared to (95.60±16.0 cm/s) in the control group (p<0.001). Conversely, the mean tricuspid A wave velocity was significantly higher in the case group at (57.50±11.03 cm/s) compared to (41.40 ± 8.77 cm/s) in the control group (p<0.001). Consequently, the mean tricuspid E/A ratio was significantly lower in the case group at (1.28±0.41) compared to (2.37±0.49) in the control group (p<0.001).

The mean tricuspid e' wave velocity, a parameter of RV diastolic function, was lower in the case group (12.75±2.15 cm/sec), compared to the control group (13.95±3.03 cm/sec), though the difference was not statistically significant (p=0.082). In contrast, the mean tricuspid E/e' ratio, another parameter of diastolic function, was significantly lower in the case group (5.69±1.56) compared to the control group (7.10±1.78) (p=0.003).

The mean RV S' wave velocity, a measurement of RV systolic function, was slightly lower in the case group (16.40±3.74 cm/sec) than in the control group (16.95±2.72 cm/sec), but the difference was not statistically significant (p=0.562). However, the mean tricuspid regurgitation (TR) velocity, a measurement of right ventricular systolic pressure, was significantly higher in the case group (2.85±0.13 m/sec) compared to the control group (2.02±0.16 m/sec) (p<0.001). **(Table 2)**

Table (2): Conventional echocardiographic data distribution between studied groups

	Case (n=40)	Control (n=20)	t	P
	Mean ± SD	Mean ± SD		
RA Volume (ml)	**119.63±28.6**	**50.97±7.77**	**6.002**	**<0.001****
RA Volume index (ml/m^2)	**60.41±18.69**	**26.19±2.98**	**6.702**	**<0.001****
Tricuspid Valve (TV) E (cm/sec)	**69.82±11.64**	**95.60±16.0**	**7.114**	**<0.001****
TV A (cm/sec)	**57.50±11.03**	**41.40±8.77**	**5.680**	**<0.001****
TV E/A	**1.28±0.41**	**2.37±0.49**	**8.999**	**<0.001****
TV e' (cm/sec)	**12.75±2.15**	**13.95±3.03**	**1.768**	**0.082**
TV E/e'	**5.69±1.56**	**7.10±1.78**	**3.146**	**0.003***
TAPSE (mm)	**26.52±1.92**	**24.20±3.33**	**2.101**	**0.040***
RVS' (cm/sec)	**16.40±3.74**	**16.95±2.72**	**0.584**	**0.562**
TR velocity (m/sec)	**2.85±0.13**	**2.02±0.16**	**20.373**	**<0.001****

*P value was set at <0.05 for significant results, **P value <0.001 was set for highly significant results, P value >0.05 for non-significant results, TAPSE: Tricuspid annular plane systolic excursion, TR: Tricuspid regurge & TV: Tricuspid valve.

The mean RA strain in the reservoir phase (RAS-r) was significantly lower in the case group (37.35±6.02) than in the control group (42.66±4.89) (p=0.001). The mean RAS-ct, the right atrial strain in the contractile phase, was significantly lower in the case group (-13.89±3.87) compared to the control group (-18.46±2.03) (p<0.001). However, the mean RAS-cd, the right atrial strain in the conduit phase, was slightly lower than the control group but without a significant difference between the two groups (p=0.633). **(Table 3)**

Table (3): Right atrial strain parameters of the studied groups

	Case (n=40)	Control (n=20)	t	P
	Mean ± SD	Mean ± SD		
RAS-r	**37.35±6.02**	**42.66±4.89**	**3.411**	**0.001****
RAS-cd	**-23.46±6.30**	**-24.22±4.67**	**0.480**	**0.633**
RAS-ct	**-13.89±3.87**	**-18.46±2.03**	**3.930**	**<0.001****

*P value was set at <0.05 for significant results, **P value <0.001 was set for highly significant results. RAScd: Right atrial conduit strain, RASct: Right atrial contractile strain & RASr: Right atrial reservoir strain.

After ASD closure, RAS-ct increased significantly, indicating improved right atrial contractile function (p= 0.032). In contrast, no statistically significant difference existed between RAS-r and RAS-cd before and after ASD closure. **(Table 4)**

Table (4): Comparison between cases regarding right atrial strain values before and after ASD closure

	Pre-Closure	**Post-Closure**	**Paired t**	**P**
	Mean ± SD	Mean ± SD		
RAS-r	**37.35±6.02**	**38.71±8.20**	**0.932**	**0.357**
RAS-cd	**-23.46±6.30**	**-22.54±8.57**	**0.616**	**0.541**
RAS-ct	**-13.89±3.87**	**-16.16±4.57**	**2.220**	**0.032***

***** P value was set at <0.05 for significant results, RAScd: Right atrial conduit strain, RASct: Right atrial contractile strain & RASr: Right atrial reservoir strain.

Regarding the method of ASD closure, there was no significant difference in pre-closure RAS-r and RAS-ct between the catheter and surgical groups. However, post-closure RAS-r and RAS-ct increased more in the catheter group than in the surgical group (p<0.001 and p=0.048, respectively). For RAS-cd, there was no significant difference in the pre-closure values, but the post-closure values were significantly higher in the catheter group compared to the surgical group (p<0.001). **(Table 5)**

Table (5): Comparison between catheter and surgical closure regarding right atrial strain parameters, before and after ASD closure

	Catheter closure (n=26)	**Surgical closure** (n=14)	**T**	**P**
RAS-r pre-closure	**36.52±5.89**	**38.74±6.18**	**1.134**	**0.264**
RAS-r post-closure	**42.64±6.10**	**32.18±7.08**	**4.938**	**<0.001****
P	**0.00****	**0.027**		
RAS-cd pre-closure	**-23.00±5.01**	**-24.22±8.15**	**0.586**	**0.562**
RAS-cd post-closure	**-26.22±8.59**	**-16.42±3.73**	**4.166**	**<0.001****
P	**0.012***	**0.01***		
RAS-ct pre-closure	**-13.52±4.19**	**-14.51±4.56**	**0.603**	**0.550**
RAS-ct post-closure	**-16.42±4.93**	**-15.74±4.04**	**0.450**	**0.655**
P	**0.048***	**0.47**		

**P value <0.001 was set for highly significant results, RAScd: Right atrial conduit strain, RASct: Right atrial contractile strain & RASr: Right atrial reservoir strain.

Discussion:

In our present study, we enrolled 40 ostium secundum ASD adult patients and 20 age-matched healthy individuals as a control group. The mean age of the studied groups was distributed as (43.70 ± 2.84 years) and (44.60 ± 3.23 years) respectively, 24 patients were females, and 16 patients were males in the case group matched with 12 females and 8 males in the control group.

ASD can manifest in early childhood or remain asymptomatic until adulthood. If left untreated, chronic RV volume overload due to left-to-right shunting leads eventually to pulmonary hypertension and Eisenmenger syndrome [9]. Patients who do not undergo ASD closure have worse long-term outcomes, including atrial arrhythmias, reduced functional capacity, and eventually greater degrees of pulmonary hypertension [10].

Up to 80% of patients with secundum ASD are amenable to device closure and due to the established safety and efficacy of the procedure, with a very low rate of serious complications (<1%), it has been the first choice for defect closure [11]. Patients who undergo ASD closure before the age of 25 years have the best outcome, while closure after the age of 40 doesn't seem to alter the incidence of atrial tachyarrhythmias [12]. However, symptomatic improvement and regression in pulmonary artery pressure and RV dimensions were observed in all age groups [12].

In the present study, there was no statistically significant difference between groups concerning age, sex, BMI, BSA, weight, height, and sex (p-value > 0.05). Our demographic results agree with Vitarelli et al., 2018, who studied right atrial function by two-dimensional and three-dimensional speckle-tracking echocardiography in patients with ASD before and after percutaneous transcatheter closure and hypothesized that they could predict paroxysmal atrial fibrillation (PAF) development. Seventy-three patients with hemodynamically significant secundum ASD were prospectively studied and followed up for 6 months after occluder insertion and compared with a normal age-matched group [13].

The right atrium has multiple important roles during the cardiac cycle: it functions as a reservoir for systemic venous return when the tricuspid valve is closed, provides a passive conduit for blood flow during early diastole when the tricuspid valve opens, and actively expels blood during late diastole with atrial contraction [14]. The right atrium has an unusual geometry and thin walls. Assessment of atrial dimensions and volume using 2D echocardiographic parameters has limitations. Measurement of atrial dimensions with M-mode and 2D echocardiography assumes the atria have an elliptical geometry, [15] but this is not completely true, and the variable and non-uniform geometry of the atria leads to significant differences in the measurement of atrial volumes using the biplane area-length method and biplane modified Simpson's rule. [15] Anatomical and functional assessment of the RA is therefore difficult [16].

In our study, there was a statistically significant difference between the case and control group regarding RA volume, RA volume index, RV basal, mid-dimensions, TR velocity, and PASP (p-value < 0.05). which agrees with the results of (El-Sherbeny WS et al., 2022) and (Arat N et al., 2008) [17-18].

One of the new applications of strain echocardiography is the assessment of RA myocardial function. We assessed the RA function including reservoir, conduit, and contractile function and we found that RA function decreased in the ASD group when compared to the control group and we also found no statistically significant difference between the RA reservoir function and RA conduit function before and after ASD closure (p-value 0.357 & 0.541 respectively), but the RA contractile function increased significantly after ASD closure at 3 months post closure follow-up (p-value <0.05).

In 2022, El-Sherbeny et al., studied atrial function by quantifying longitudinal strain in patients with chronic RV volume overload due to ASD before and after percutaneous closure using 2D-STE in a study included 13 pediatric patients (46.4%) and 15 adult patients (53.5%), whose age ranged between 4 and 35 years and found significant increase in peak RA longitudinal systolic strain and strain rate after percutaneous ASD closure, due to relief of the volume overload with improvement of RA wall velocity after closure of the shunt. This agrees with our results regarding RA function.

In 2008**,** Arat N et al., studied left and right atrial myocardial deformation properties in patients with ASD, in a study involved 24 patients with a secundum type ASD and 22 healthy subjects with a mean age for the control group was 43.4 ± 13.5 years, had similar results to our study; color Doppler myocardial imaging has been used to calculate left and right atrial myocardial systolic strain and strain rate values in their research; they found significant increase in RA peak systolic strain and strain rate after ASD closure.

In our study, the catheter group post-closure strain values increased significantly when compared to the post-closure strain values of surgically treated patients, RA (reservoir & conduit) (p-value < 0.05). Also, RA contractile function increased post-closure in the catheter group more than in surgically treated patients but statistically non-significant increase (p-value 0.655). Ozturk O et al., 2017, demonstrated that peak RA longitudinal strain which determines the reservoir phase increased significantly after percutaneous closure of secundum ASD in adults whose age was 34.6±8.2 years [19].

Limitations:

The study had several limitations such as the small number of patients included in the study. The widespread of diagnostic tools e.g. echocardiography made ASD diagnosis at a younger age common, and the number of older patients (>40 years) without diagnosis is rare. Finally, the short duration of follow-up is one of our important limitations, so a long-term follow-up is recommended to assess the long-term effects of ASD closure.

Conclusion:

Reduced right atrial (RA) mechanical function assessed by speckle tracking echocardiography due to long-standing ASD in adults. Improved RA contractile function after ASD closure. Also, the RA geometrical reverse remodeling was evident at 3 months following ASD closure. Finally, In the catheter-treated patients, RA function improvement was greater than in the surgically treated patients.

References:

1. Kusumoto FM, Schoenfeld MH, Barrett C, et al., ACC/AHA/HRS Guideline on the Evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2019 Aug 20;74(7):e51-e156.
2. Altindag T, Roos-Hesselink J, Cuypers J, et al., Transcatheter device closure of atrial septal defects in patients aged 40 years and older. Cardiologie (Hoogland). 2010;18(11):537-542.
3. Takaya Y, Akagi T, Kijima Y, et al., Nakagawa K, Sano S, Ito H. Long-term outcome after transcatheter closure of the atrial septal defect in older patients: impact of age at the procedure. JACC Cardiovasc Interv. 2015 Apr 20;8(4):600-6.
4. Khan AA, Tan JL, Li W, et al., The impact of transcatheter atrial septal defect closure in the older population: a prospective study. JACC Cardiovasc Interv. 2010, 3:276-281.

5. Cameli M, et al. Speckle tracking echocardiography as a new technique to evaluate right ventricular function in patients with primary pulmonary hypertension. J Am Soc Echocardiogr. 2008;21(6):686-691.
6. Saraiva RM, et al. Right and left atrial strain evaluated by speckle tracking echocardiography in patients with and without pulmonary hypertension. J Am Soc Echocardiogr. 2014;27(10):1043-1049.
7. Baumgartner H, De Backer J, Babu-Narayan SV, et al., ESC Scientific Document Group. 2020 ESC Guidelines for the management of adult congenital heart disease. European Heart J 2021; 42:563–645.
8. Tadic M. The right atrium, a forgotten cardiac chamber: an updated review of multimodality imaging. J Clin Ultrasound 2015; 43:335-45.
9. Konstam MA, Kiernan MS, Bernstein D, et al., Evaluation and Management of Right-Sided Heart Failure: A scientific statement from the American Heart Association. Circulation, 2018, 137(20).
10. Vitarelli A, Mangieri E, Gaudio C, et al., Right atrial function by speckle tracking echocardiography in atrial septal defect: Prediction of atrial fibrillation. Clin Cardiol. 2018 Oct;41(10):1341-1347.
11. Hafez MS, Abdelrahman MI, El Sayed MH et al., Transcatheter Atrial Septal Defect Closure Before Versus After Adulthood. J Saudi Heart Assoc. 2022 Sep 5;34(3):148-152.
12. Seo JS, Park YA, Wi JH, et al., Long-Term Left Atrial Function after Device Closure and Surgical Closure in Adult Patients with Atrial Septal Defect. J Cardiovasc Imaging. 2021 Apr;29(2):123-132.
13. Muzaffer Aslan, Mehmet Erturk, Selahattin Turen, et al., Effects of percutaneous closure of atrial septal defect on left atrial mechanical and conduction functions, European Heart Journal - Cardiovascular Imaging, Volume 15, Issue 10, October 2014, Pages 1117–1124.
14. Sakata K, Uesugi Y, Isaka A, et al. Evaluation of right atrial function using right atrial speckle tracking analysis in patients with pulmonary artery hypertension. J Echocardiogr. 2016; 14:30-8.
15. Teo KSL, Dundon BK, Molaee P, et al. Percutaneous closure of atrial septal defects leads to the normalization of atrial and ventricular volumes. J Cardiovasc Magn Reson. 2008; 10:55.
16. Timóteo AT, Branco LM, Rosa SA, et al. The usefulness of right ventricular and right atrial two-dimensional speckle tracking strain to predict late arrhythmic events in adult patients with repaired Tetralogy of Fallot. Rev Port Cardiol. 2017; 36:21---9.
17. El-Sherbeny WS, Elhefnawy SB. Assessment of atria function after percutaneous closure of atrial septal defect using 2D speckle tracking echocardiography. J Echocardiogr, 2022, 20, 33–41.
18. Arat N, Sökmen Y, Altay H, et al., Left and right atrial myocardial deformation properties in patients with an atrial septal defect. Echocardiography. 2008 Apr;25(4):401-7.
19. Ozturk O, Ozturk U, Ozturk S. et al., Assessment of right atrial function with speckle tracking echocardiography after percutaneous closure of an atrial septal defect. Rev Port Cardiol. 2017 Dec;36(12):895-900.