ARCHIVES OF THE
TURKISH SOCIETY
OF CARDIOLOGY

Official journal of the
TURKISH
SOCIETY OF
CARDIOLOGY

Assessment of Bi-Atrial Mechanical Function in Patients with Isolated Atrial Septal Aneurysm

İzole Atriyal Septal Anevrizmalı Hastalarda Bi-Atriyal Mekanik Fonksiyonların Değerlendirilmesi

ABSTRACT

Objective: Atrial mechanical dysfunction may be an alternative mechanism underlying the increased risk of systemic embolism in patients with atrial septal aneurysm (ASA). This study aimed to evaluate left atrial (LA) and right atrial (RA) function using two-dimensional speckle tracking echocardiography (2D STE) in patients with isolated ASA.

Method: Fifty-four patients with ASA (mean age 50.3 ± 12.48, 37% male) and 48 healthy individuals of similar age and gender (mean age 48.3 ± 10.84, 39.6% male) were included in the study. To assess atrial mechanical function, measurements of left and right atrial reservoir strain (RS), peak contraction strain (PCS), and conduit strain (CS) were conducted using 2D STE, in addition to conventional evaluation with transthoracic echocardiography.

Results: LA RS and PCS values were significantly lower in the ASA group than in the controls (37.52 ± 2.89 vs. 40.16 ± 2.68%, $P < 0.001$ and 17.29 ± 2.5 vs. 19.18 ± 2.23%, $P < 0.001$, respectively). Similarly, RA RS and RA PCS were significantly lower in patients with ASA (36.97 ± 2.19 vs. 39.77 ± 2.36%, $P < 0.001$ and 16.78 ± 2.10 vs. 18.54 ± 2.43%, $P < 0.001$, respectively). A multivariate regression analysis revealed a strong independent association between ASA and the measures LA RS, LA PCS, RA RS, and RA PCS.

Conclusion: Our findings indicate that bi-atrial function are diminished in patients with isolated ASA. This may be a possible cause for the increased risk of arterial embolism in this patient group, aside from atrial arrhythmias and patent foramen ovale. Validating these results with larger studies may influence the treatment and follow-up strategies for patients with isolated ASA.

Keywords: Atrial septal aneurysm, atrial strain imaging, speckle tracking echocardiography

ÖZET

Amaç: Atriyal mekanik disfonksiyon, atriyal septal anevrizmalı (ASA) hastalarda artmış sistemik emboli riskini açıklayabilecek sebeplerden birisi olabilir. Bu çalışmanın amacı izole ASA'lı hastalarda iki boyutlu "speckle tracking" ekokardiyografi (2B STE) kullanarak sol atriyum (LA) ve sağ atriyum (RA) fonksiyonlarını değerlendirmektir.

Yöntem: Çalışmaya 54 ASA hastası (ortalama yaş 50,3 ± 12,48, erkek %37) ve benzer yaş ve cinsiyete sahip 48 sağlıklı birey (ortalama yaş 48,3 ± 10,84, erkek %39,6) dahil edildi. Atriyumların mekanik fonksiyonlarının değerlendirilmesi için transtorasik ekokardiyografi ile geleneksel değerlendirmeye ek olarak 2B STE kullanılarak sol ve sağ atriyal rezervuar strain (RS), pik kontraksiyon straini (PKS) ve konduit straini (KdS) ölçümleri yapıldı.

Bulgular: Sol atriyal RS ve PKS, ASA grubunda kontrollere göre anlamlı derecede düşüktü (sırasıyla, %37,52 ± 2,89 vs. 40,16 ± 2,68, $P < 0,001$; %17,29 ± 2,5 vs. 19,18 ± 2,23, $P < 0,001$). Benzer şekilde RA RS ve RA PKS, ASA hastalarında anlamlı derecede düşük bulundu (sırasıyla, %36,97 ± 2,19 vs. 39,77 ± 2,36, $P < 0,001$; %16,78 ± 2,10 vs. 18,54 ± 2,43, $P < 0,001$). Çok değişkenli lineer regresyon analizinde ASA ile LA RS, LA PCS, RA RS ve RA PCS arasında güçlü bir bağımsız ilişki gösterilmiştir.

Sonuç: Çalışmamızda izole ASA hastalarında bi-atriyal fonksiyonların azaldığı gösterildi. Bu durum, bu hasta grubunda atriyal aritmiler ve patent foramen ovale dışında artan arteriyel embolinin olası bir nedeni olabilir. Bu sonuçların daha büyük çalışmalarla desteklenmesi izole ASA hastalarına yönelik tedavi ve takip yaklaşımlarını değiştirebilir.

Anahtar Kelimeler: Atriyal septal anevrizma, atriyal gerilim görüntüleme, benek izleme ekokardiyografi

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

Betül Cengiz Elçioğlu
Saide Aytekin

Department of Cardiology, Koç University Hospital, İstanbul, Türkiye

Corresponding author:
Betül Cengiz Elçioğlu
✉ betulcengiz@yahoo.com

Received: September 25, 2023
Accepted: October 21, 2023

Cite this article as: Cengiz Elçioğlu B, Aytekin S. Assessment of bi-atrial mechanical function in patients with isolated atrial septal aneurysm. *Turk Kardiyol Dern Ars.* 2024;52(2):103-109.

DOI:10.5543/tkda.2023.87922

Interatrial septal aneurysm (ASA) is an abnormality often detected during routine echocardiography. It may be found in asymptomatic patients, either in isolation or concomitantly with other cardiac disorders such as mitral valve prolapse and patent foramen ovale (PFO).[1,2] ASA is defined as a protrusion of the interatrial septum towards the left or right atrium by more than 10 mm.[3,4] Although the incidence of ASA varies considerably across different series, it is estimated to be approximately 1% based on transthoracic echocardiography (TTE) findings.[5]

Various studies have demonstrated a relationship between ASA and ischemic cerebrovascular events (CVE).[6,7] While the development of paradoxical embolisms in the presence of PFO and atrial arrhythmias is often implicated, the exact mechanism linking ASA with CVE remains elusive.[8] The rare occurrence of deep vein thrombosis (DVT) in these patients, combined with the emergence of cardio-embolic events even in those with a regular sinus rhythm, hints at other underlying mechanisms.[9,10] Recent studies have shifted their focus towards the potential role of atrial cardiomyopathy in the etiology of cardiac embolism and cryptogenic stroke.[11,12] Measuring atrial strain values using speckle tracking echocardiography (STE) offers an accurate and reliable evaluation of atrial functions, potentially signaling early deterioration that aligns with histologically confirmed atrial fibrosis.[13,14] Yet, the mechanical functions of the atria, particularly using STE, have not been thoroughly investigated in patients with ASA. Current studies mainly focus on left atrial (LA) functions.[12,15]

The main objective of this research was to evaluate both left and right atrial mechanical function by measuring reservoir, contraction, and conduit strains using two-dimensional (2D) STE in patients with ASA. Moreover, the study sought to compare strain parameters across different ASA types.

ABBREVIATIONS

2D STE	Two-dimensional speckle tracking echocardiography
AF	Atrial fibrillation
ASA	Atrial septal aneurysm
BSA	Body surface area
CS	Conduit strain
CVD	Cardiovascular disease
CVE	Cerebrovascular events
DVT	Deep vein thrombosis
ECG	Electrocardiogram
ICC	Intra-class correlation coefficient
LA	Left atrial
LAVI	Left atrial volume index
LV	Left ventricle
LV GLS	Left ventricular global longitudinal strain
PCS	Peak contraction strain
PFO	Patent foramen ovale
RA	Right atrial
ROI	Region of interest
RS	Reservoir strain
SEC	Spontaneous echo contrast
STE	Speckle tracking echocardiography
TTE	Transthoracic echocardiography

Materials and Methods

Study Design and Patient Selection

In this retrospective study, we included 54 subjects diagnosed with ASA and 48 age- and sex-matched individuals as the control group. We searched transthoracic echocardiograms, which were conducted for various indications in our center's echocardiography laboratory between 2019 and 2022, from the central database of our institute. Among these, individuals diagnosed with ASA formed the patient group, while those without ASA and devoid of any obvious cardiovascular disease (CVD) constituted the control group. We excluded patients with ischemic heart disease, heart failure, moderate to severe heart valve disease, congenital heart diseases (excluding ASA), history of CVE, arrhythmias and conduction abnormalities evident on electrocardiography, poor echogenicity, and those who reported palpitations as a primary complaint.

Our study adhered to the principles of the Declaration of Helsinki, and Ethics Committee of Koç University granted approval for the study protocol (Approval Number: 2022.338.IRB1.127, Date: 04.10.2022).

Echocardiographic Assessment

We performed transthoracic echocardiographic examinations using the Epiq 7C ultrasound system (Philips, Andover, MA, USA) equipped with a 2.3-3.5 MHz transducer probe, and this was done alongside simultaneous electrocardiogram (ECG) recordings. We measured left ventricle (LV) wall thicknesses and heart chamber diameters using B-mode and M-mode images, captured from standard parasternal and apical windows, in line with the recommendation guidelines from the American Society of Echocardiography.[16] We employed the modified two-dimensional biplane Simpson's rule to determine the left ventricular ejection fraction (LVEF) and the left atrial volume (LAV).[17] The left atrial volume index (LAVI) was derived by dividing the LAV value by the body surface area (BSA). For assessing LV diastolic function, we utilized pulse wave Doppler measurements from trans-mitral velocities and tissue Doppler imaging measurements from the mitral annulus.

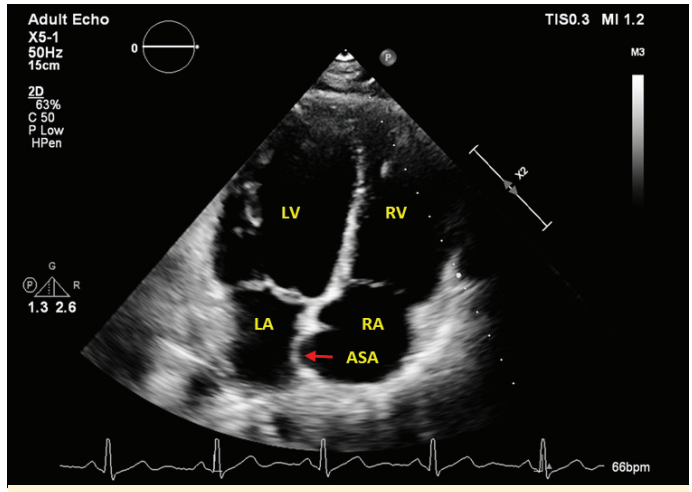

Figure 1. Apical four-chamber view image. The red arrow indicates a type 2 atrial septal aneurysm (ASA) in a study subject. LA, left atrium; RA, right atrium; LV, left ventricle; RV, right ventricle.

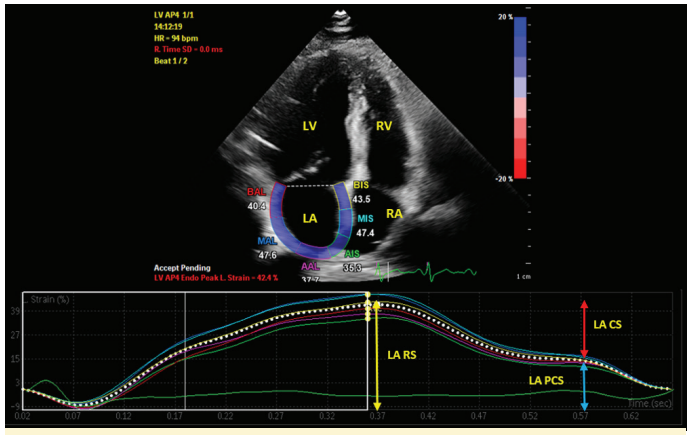

Figure 2. Left atrial strain imaging using 2D speckle-tracking echocardiography from the apical four-chamber view in a study patient. The yellow arrow indicates reservoir strain (RS), the blue arrow indicates peak contraction strain (PCS), and the red arrow indicates conduit strain (CS).

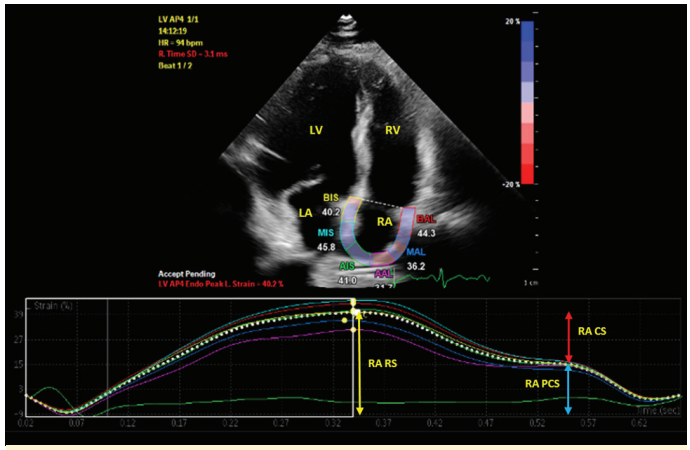

Figure 3. Right atrial strain imaging using 2D speckle-tracking echocardiography from the apical four-chamber view in a study patient. The yellow arrow indicates reservoir strain (RS), the blue arrow indicates peak contraction strain (PCS), and the red arrow indicates conduit strain (CS).

Atrial septal aneurysm is defined as the movement of the atrial septum by more than 10 mm to one side from its normal septal plane (Figure 1). ASA is categorized into five types based on the direction of septal protrusion. Type 1 R is characterized by the bulging towards the right atrium (RA) only, while Type 2 L is defined by its protrusion towards the LA only. In Type 3 R-L, the septum predominantly moves towards the RA, and in Type 4 L-R, it predominantly shifts towards the LA. Type 5 is distinguished by the septum's equal movement towards both atria during the cardiorespiratory cycle.[18]

For the two-dimensional speckle tracking echocardiography (2DSTE) assessment, apical four- and two-chamber images, recorded over three cycles in grayscale with frame rates between 60-100 frames/s, were used. Left ventricular, left atrial, and right atrial strain analyses were executed by the same investigator using dedicated software (Qlab Advanced Quantification Software version 10.1, Philips Medical Systems, Bothell, WA, USA). After the region of interest (ROI) was automatically generated by the software and any necessary manual adjustments were made, strain parameters were calculated by taking the average of all segments. The left ventricular global longitudinal strain (LV GLS) and atrial peak longitudinal strain, which reflects reservoir function, as well as peak contraction strain (PCS) denoting atrial pump function, were calculated from strain curves with the QRS onset as a reference. The atrial conduit strain (CS) was also evaluated by computing the difference between reservoir strain (RS) and PCS values (Figure 2 and Figure 3).

Statistical Analysis

Data from the study were analyzed using the Statistical Package for the Social Sciences (SPSS) (version 26.0; SPSS Inc., Chicago, Illinois, USA). The Kolmogorov-Smirnov test was used to determine the normality of the distribution. Results are presented as numbers and percentages for categorical variables and as mean ± standard deviation for continuous variables. Variables with a normal distribution were compared using the Student's t-test, while the Mann-Whitney U test was employed to compare continuous variables that were not normally distributed. The chi-square test was utilized to compare categorical variables. A p-value of <0.05 was considered statistically significant. The association between two continuous variables was measured using Pearson's correlation, and Spearman's rank correlation was used to compare categorical variables. The correlation coefficient (r) was calculated for both tests.

Both univariate and multivariate linear regression analyses were conducted to pinpoint the independent determinants of left and right atrial strain values.

For the evaluation of intra-observer variability, analyses of LV, LA, and RA strain measurements were performed on ten randomly chosen participants by the same experienced echocardiographer on two different days. To evaluate intra-observer variability, the intra-class correlation coefficient (ICC) was calculated. ICC values between 0.5 and 0.75 indicate moderate reliability, those between 0.7 and 0.9 suggest good reliability, and values over 0.9 denote excellent reliability.

Results

The study comprised 54 patients with ASA (mean age 50.3 ± 12.48 yeras, 37% male) and a control group of 48 individuals, similar in age and gender (mean age 48.3 ± 10.84 years, 39.6% male). Demographic characteristics, baseline clinical observations, and cardiovascular (CV) risk factors were similar between the groups (Table 1).

While there were no significant differences between the two groups in conventional echocardiographic measurements, the E and E' wave velocity values of LV diastolic function parameters were found to be significantly lower in the patient group. Measurements for LAV and LAVI were similar in both groups. In assessing atrial mechanical functions, the strain measurements for LA RS, LA PCS, RA RS, and RA PCS were observed to be significantly lower in the ASA group (Table 2).

Patients were divided into two groups based on ASA type: Group 1 consisted of 21 patients with right-predominant septal bulging (14 patients with type 1 R ASA and 7 with type 3 R-L ASA), and

Table 1. Demographic and Clinical Features of the Study Group

Parameter	ASA patients (n = 54)	Control group (n = 48)	*P*
Age (years)	50.3 ± 12.48	48.3 ± 10.84	0.402
Male, % (n)	37 (20)	39.6 (19)	0.792
SBP (mmHg)	115.83 ± 13.34	117.5 ± 14.98	0.554
DBP (mmHg)	73.14 ± 7.09	74.06 ± 8.79	0.563
Heart rate (beat/m)	74.66 ± 8.94	71.97 ± 9.32	0.141
BSA (m^2)	1.80 ± 0.22	1.82 ± 0.20	0.585
BMI (kg/m^2)	24.89 ± 3.99	26.12 ± 3.49	0.102
Hypertension, % (n)	16.7 (9)	29.4 (14)	0.132
Hyperlipidemia, % (n)	3.7 (2)	10.4 (5)	0.181
Diabetes mellitus, % (n)	3.7 (2)	8.3 (4)	0.321
Smoking, % (n)	7.4 (4)	8.3 (4)	0.862
ACEI/ARB, % (n)	7.4 (4)	14.6 (7)	0.244
Beta blockers, % (n)	5.6 (3)	8.3 (4)	0.580
CCB, % (n)	3.7 (2)	8.3 (4)	0.321
Statin, % (n)	1.9 (1)	8.3 (4)	0.130

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; BSA, body surface area; CCB, calcium channel blocker; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table 2. Comparison of Echocardiographic Measurements of the Groups

Parameter	ASA patients (n = 54)	Control group (n = 48)	*P*
IVS (cm)	1.03 ± 0.66	0.91 ± 0.11	0.250
PW (cm)	0.95 ± 0.36	0.9 ± 0.11	0.317
LVEDD (cm)	4.52 ± 0.33	4.56 ± 0.37	0.663
LVESD (cm)	2.91 ± 0.27	2.92 ± 0.25	0.790
LV EF (%)	60.88 ± 1.38	60.81 ± 1.49	0.789
LAD (cm)	3.55 ± 0.21	3.60 ± 0.18	0.229
RAD (cm)	3.39 ± 0.23	3.45 ± 0.19	0.168
RVD (cm)	3.24 ± 0.23	3.27 ± 0.22	0.541
sPAP (mmHg)	23.61 ± 2.94	23.33 ± 2.56	0.614
TRV (m/s)	2.42 ± 0.15	2.41 ± 0.13	0.640
E wave velocity (cm/s)	**73.53 ± 17.65**	**79.56 ± 14.62**	**0.036**
A wave velocity (cm/s)	73.13 ± 20.14	71.06 ± 15.13	0.526
E/A ratio	1.14 ± 0.31	1.12 ± 0.23	0.752
DT (msn)	182.41 ± 36.78	182.29 ± 24.04	0.985
IVRT (msn)	93.72 ± 15.07	92.14 ± 10.18	0.435
E' wave velocity (cm/s)	**12.92 ± 3.06**	**14.31 ± 3.21**	**0.033**
E/E' ratio	6.11 ± 2.22	5.70 ± 1.06	0.257
LV GLS (%)	-20.94 ± 1.54	-21.12 ± 1.48	0.551
LAV (ml)	38.63 ± 11.16	39.75 ± 9.27	0.586
LAVI (ml/ m^2)	21.24 ± 4.87	21.72 ± 4.46	0.603
LA RS (%)	**37.52 ± 2.89**	**40.16 ± 2.68**	**<0.001**
LA PCS (%)	**17.29 ± 2.51**	**19.18 ± 2.23**	**<0.001**
LA CS (%)	20.29 ± 2.99	20.98 ± 3.95	0.106
RA PLS (%)	**36.97 ± 2.19**	**39.77 ± 2.36**	**<0.001**
RA PCS (%)	**16.78 ± 2.10**	**18.54 ± 2.43**	**<0.001**
RA CS (%)	20.18 ± 2.59	21.23 ± 3.50	0.080

CS, conduit strain; DT, deceleration time; IVRT, isovolumetric relaxation time; IVS, interventricular septal thickness; LAD, left atrial end systolic diameter; LAV, left atrial volume; LAVI, left atrial volume index; LVEDD, left ventricular end diastolic diameter; LV EF, left ventricular ejection fraction; LVESD, left ventricular end systolic diameter; LV GLS, left ventricular global longitudinal strain; PCS, peak contraction strain; PW, posterior wall thickness; RAD, right atrial end systolic diameter; RS, Reservoir strain; RVD, right ventricular end diastolic diameter; sPAP, systolic pulmonary artery pressure; TRV, tricuspid regurgitation velocity.

Table 3. Multivariate Linear Regression Analysis for Atrial Strain Values

Variables	B	Standard error	Beta	t	*P*
	Dependent	**Variable**	**LA RS**		
Age	-0.042	0.030	-0.183	-1.404	0.164
Gender	0.249	0.527	0.044	0.473	0.637
BSA	0.570	1.450	0.045	0.393	0.695
HT	-0.923	0.759	-0.141	-1.216	0.227
DM	-0.524	1.330	-0.047	-0.394	0.695
ASA	-1.823	0.527	-0.336	-3.462	**0.001**
E' wave velocity	0.071	0.102	0.084	0.697	0.487
	Dependent	**Variable**	**LA PCS**		
Age	0.027	0.030	0.125	0.909	0.366
Gender	-0.879	0.524	-0.166	-1.677	0.097
BSA	-1.722	1.443	-0.145	-1.193	0.236
HT	-0.668	0.755	-0.108	-0.885	0.379
DM	0.002	1.323	0.001	0.002	0.999
ASA	-1.634	0.524	-0.319	-3.119	**0.002**
E' wave velocity	-0.040	0.101	-0.049	-0.391	0.697
	Dependent	**Variable**	**RA RS**		
Age	-0.035	0.028	-0.149	-1.245	0.216
Gender	-0.267	0.496	-0.046	-0.539	0.591
BSA	0.120	1.364	0.009	0.088	0.930
HT	-0.616	0.714	-0.091	-0.863	0.390
DM	-0.182	1.251	-0.016	-0.145	0.885
ASA	-2.919	0.495	-0.523	-5.896	**<0.001**
E' wave velocity	0.076	0.096	0.087	0.796	0.428
	Dependent	**Variable**	**RA PCS**		
Age	0.066	0.031	0.300	2.154	0.054
Gender	-0.424	0.543	-0.078	-0.780	0.437
BSA	0.529	1.495	0.043	0.354	0.724
HT	-1.224	0.783	-0.193	-1.563	0.122
DM	0.357	1.371	0.033	0.261	0.795
ASA	-1.472	0.543	-0.281	-2.713	**0.008**
E' wave velocity	-0.010	0.105	-0.013	-0.100	0.921

ASA, atrial septal aneurysm; BSA, body surface area; DM, diabetes mellitus; HT, hypertension.

Group 2 had 33 patients with left-predominant septal bulging (29 with type 2 L ASA and 4 with type 4 L-R ASA). No patients were diagnosed with type 5 ASA. No differences were observed in echocardiographic measurements, including strain assessments, between the two groups.

In the correlation analysis, neither LA nor RA strain parameters showed statistically significant correlations with other echocardiographic measurements. However, age had a significant negative correlation with both LA and RA reservoir strain, conduit strain values, and LV GLS (r = -0.263, P = 0.008; r = -0.330, P = 0.001; r = -0.306, P = 0.002; r = -0.392, P < 0.001; and r = 0.446, P < 0.001, respectively). Moreover, no significant correlations were observed between atrial strain values and other demographic and clinical characteristics.

Univariate linear regression analysis indicated that ASA was a predictor of decreased LA RS and LA PCS, as well as RA RS and RA PCS values (r = 0.459, P < 0.00; r = 0.391, P < 0.001; r = 0.564, P < 0.001; and r = 0.480, P < 0.001, respectively). In a multivariate regression analysis model, which included age, sex, ASA, hypertension, diabetes mellitus, and E' wave velocity, ASA demonstrated a strong independent association with LA RS, LA PCS, RA RS, and RA PCS (Table 3).

For intra-class correlation, there was a high degree of reliability in measurements for LV GLS, LA RS, LA PCS, RA RS, and RA PCS. The average ICC for LV GLS was 0.96, with a 95% confidence interval ranging from 0.81 to 0.98. For LA RS, the ICC was 0.94 with a 95% confidence interval ranging from 0.79 to 0.98, and for LA PCS, it was 0.92 with a 95% confidence interval from 0.68 to 0.98. The ICC values for RA RS and RA PCS were 0.91 and 0.92, with a 95% confidence interval of 0.65 to 0.98 and 0.66 to 0.98, respectively.

Discussion

In our study evaluating atrial mechanical function in ASA patients, we found that both left and right atrial reservoir and contraction strain values were significantly lower than those of the control group. Furthermore, within our study group, ASA was found to be the strongest determinant of both left and right atrial reservoir and contraction strain values. These observations imply that decreased atrial function may contribute to the increased risk of systemic embolism in ASA patients.

Numerous studies have indicated that arterial embolisms of cardiac origin occur more frequently in ASA patients than in the general population. In a study by Mattioli et al.[19], patients who experienced CVE were assessed for the presence of ASA using transesophageal echocardiography (TEE) and were compared to a healthy control group. ASA was identified in roughly one-third of the patients who had experienced a CVE and had no other discernible source of embolism. One suggested mechanism for this relationship involves the onset of paradoxical embolisms in patients with PFO and DVT. However, studies indicate that DVT is not commonly observed in patients with CVE and PFO.[20]

In ASA patients, another disorder related to systemic embolism is atrial arrhythmia. Although its pathophysiology is not clearly understood, studies have shown that atrial arrhythmias are more common in patients with ASA than in controls.[21,22] Additionally, the incidence of paroxysmal atrial fibrillation (AF) in patients with ASA is reported to be approximately 3-17% across different cohorts.[23,24] Impairment of atrial function and cardiac autonomic dysfunction may be associated with the development of atrial arrhythmias. Atrial dysfunction can be seen as both a cause and a consequence of AF in patients with ASA. However, studies suggest that atrial dysfunction may develop in these patients regardless of the presence of AF.[25] Rigatelli et al.[12] investigated patients with ischemic stroke accompanied by PFO who were scheduled for percutaneous closure. Using the volumetric method by TTE, the LA functional parameters of these patients in sinus rhythm were evaluated and compared with those of chronic AF and healthy subjects. These measurements were found to be similar between patients with PFO accompanied by ASA and AF. However, they appeared impaired compared to isolated PFO patients and the healthy control group. Additionally, LA spontaneous echo contrast (SEC) was observed in all ASA patients, while none of the patients with only PFO developed SEC. These findings suggest that atrial thrombus formation may occur in ASA patients in sinus rhythm due to pathophysiological mechanisms akin to those in AF. Although hemodynamic changes are expected to affect both atria in patients with ASA, the right atrium has often been overlooked in previous studies. Demir et al.[26] demonstrated that the functions of both atrial appendages, evaluated with TEE, were impaired in ASA patients without PFO compared to the control group. Strain analysis using STE is a sensitive and reliable method for detecting early changes in the myocardium. In our study, both the left and right atrial global reservoir and contraction strain values were found to be significantly lower in patients with ASA than in healthy individuals, regardless of other atrial dimensions. Reduced atrial function may predispose these patients to embolic events. Consistent with our findings, cases demonstrating the development of atrial thrombus and CVE in low-risk, isolated ASA patients have been reported in the literature.[27,28]

In this study, atrial strain measurements across different ASA types were also evaluated, presumably for the first time in the literature. No significant difference was observed in echocardiographic measurements between different ASA types.

In conclusion, the findings of this study suggest that ASA is associated with decreased atrial function, presenting another possible mechanism for embolic events independent of arrhythmias and the presence of PFO. Evaluating atrial function with STE may provide early detection of atrial myocardial changes in this congenital disorder. Further large-scale observational and follow-up studies that support these results may reshape treatment and follow-up strategies for these patients.

The main limitation of this study was its small sample size. Being a retrospective study, TEE evaluations were not performed on patients unless deemed necessary. Although patients with sinus rhythm on ECG and no palpitation history were included in the study, paroxysmal atrial fibrillation could not be definitely ruled out without ambulatory ECG Holter monitoring. Another limitation is that this study did not assess the effect of ASA size on atrial function. Furthermore, atrial strain analyses were performed using the QLAB software system, which was originally developed for left ventricular analysis. Although current guidelines recommend the use of software specifically designed for atrial analysis,[29] several studies have demonstrated that atrial strain analysis using QLAB software is reliable and offers good reproducibility.[30,31]

Ethics Committee Approval: Ethics Committee of Koç University granted approval for the study protocol (Approval Number: 2022.338.IRB1.127, Date: 04.10.2022).

Informed Consent: Informed consent was not obtained due to the retrospective nature of the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – B.C.E.; Design – B.C.E.; Supervision – S.A.; Resource – S.A.; Materials – B.C.E; Data Collection and/or Processing – B.C.E; Analysis and/or Interpretation – B.C.E., S.A.; Literature Review – B.C.E., S.A.; Writing – B.C.E.; Critical Review – S.A.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

References

1. Iliceto S, Papa A, Sorino M, Rizzon P. Combined atrial septal aneurysm and mitral valve prolapse: detection by two-dimensional echocardiography. *Am J Cardiol*. 1984;54(8):1151-1153. [CrossRef]

2. Krumsdorf U, Keppeler P, Horvath K, Zadan E, Schrader R, Sievert H. Catheter closure of atrial septal defects and patent foramen ovale in patients with an atrial septal aneurysm using different devices. *J Interv Cardiol*. 2001;14(1):49-55. [CrossRef]
3. Gondi B, Nanda NC. Two-dimensional echocardiographic features of atrial septal aneurysms. *Circulation*. 1981;63(2):452-457. [CrossRef]
4. Mügge A, Daniel WG, Angermann C, et al. Atrial septal aneurysm in adult patients. A multicenter study using transthoracic and transesophageal echocardiography. *Circulation*. 1995;91(11):2785-2792. [CrossRef]
5. Silver MD, Dorsey JS. Aneurysms of the septum primum in adults. *Arch Pathol Lab Med*. 1978;102(2):62-65.
6. Mas JL. Patent foramen ovale, atrial septal aneurysm and ischaemic stroke in young adults. *Eur Heart J*. 1994;15(4):446-449. [CrossRef]
7. Manning WJ. Role of transesophageal echocardiography in the management of thromboembolic stroke. *Am J Cardiol*. 1997;80(4C):19D-28D; discussion 35D-39D. [CrossRef]
8. Agmon Y, Khandheria BK, Meissner I, et al. Frequency of atrial septal aneurysms in patients with cerebral ischemic events. *Circulation*. 1999;99(15):1942-1944. [CrossRef]
9. Lethen H, Flachskampf FA, Schneider R, et al. Frequency of deep vein thrombosis in patients with patent foramen ovale and ischemic stroke or transient ischemic attack. *Am J Cardiol*. 1997;80(8):1066-1069. [CrossRef]
10. Kamel H, Healey JS. Cardioembolic stroke. *Circ Res*. 2017;120(3):514-526. [CrossRef]
11. Sanchis L, Montserrat S, Obach V, et al. Left atrial function is impaired in some patients with stroke of undetermined etiology: potential implications for evaluation and therapy. *Rev Esp Cardiol (Engl Ed)*. 2016;69(7):650-656. English, Spanish. [CrossRef]
12. Rigatelli G, Aggio S, Cardaioli P, et al. Left atrial dysfunction in patients with patent foramen ovale and atrial septal aneurysm: an alternative concurrent mechanism for arterial embolism? *JACC Cardiovasc Interv*. 2009;2(7):655-662. [CrossRef]
13. Cameli M, Miglioranza MH, Magne J, et al. Multicentric atrial strain comparison between two different modalities: MASCOT HIT study. *Diagnostics (Basel)*. 2020;10(11):946. [CrossRef]
14. Her AY, Choi EY, Shim CY, et al. Prediction of left atrial fibrosis with speckle tracking echocardiography in mitral valve disease: a comparative study with histopathology. *Korean Circ J*. 2012;42(5):311-318. [CrossRef]
15. Demir M, Aktaş İ, Çamci S. Left atrial mechanical function and stiffness in patients with atrial septal aneurysm: a speckle tracking study. *Cardiol J*. 2015;22(5):535-540. [CrossRef]
16. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr*. 2015;28(1):1-39.e14. [CrossRef]
17. Feigenbaum H, Armstrong WF, Ayan T. *Feigenbaum's Echocardiography.* 6th ed. Philadelphia: Lippincotts Williams & Wilkins;2005:355-356.
18. Olivares-Reyes A, Chan S, Lazar EJ, Bandlamudi K, Narla V, Ong K. Atrial septal aneurysm: a new classification in two hundred five adults. *J Am Soc Echocardiogr.* 1997;10(6):644-656. [CrossRef]
19. Mattioli AV, Aquilina M, Oldani A, Longhini C, Mattioli G. Atrial septal aneurysm as a cardioembolic source in adult patients with stroke and normal carotid arteries. A multicentre study. *Eur Heart J.* 2001;22(3):261-268. [CrossRef]
20. Lamy C, Giannesini C, Zuber M, et al. Clinical and imaging findings in cryptogenic stroke patients with and without patent foramen ovale: the PFO-ASA Study. *Atrial Septal Aneurysm. Stroke*. 2002;33(3):706-711. [CrossRef]
21. Russo V, Rago A, Di Meo F, et al. Atrial septal aneurysms and supraventricular arrhythmias: the role of atrial electromechanical delay. *Echocardiography*. 2015;32(10):1504-1514. [CrossRef]
22. Deveci OS, Aytemir K, Okutucu S, et al. Evaluation of the relationship between atrial septal aneurysm and cardiac arrhythmias via P-wave dispersion and signal-averaged P-wave duration. *Ann Noninvasive Electrocardiol*. 2010;15(2):157-164. [CrossRef]
23. Yetkin E, Ileri M, Korkmaz A, Ozturk S. Association between atrial septal aneurysm and arrhythmias. *Scand Cardiovasc J*. 2020;54(3):169-173. [CrossRef]
24. Janion M, Kurzawski J. Atrial fibrillation in patients with atrial septal aneurysm. *Cardiol J*. 2007;14(6):580-584.
25. Goch A, Banach M, Piotrowski G, Szadkowska I, Goch JH. Echocardiographic evaluation of the left atrium and left atrial appendage function in patients with atrial septum aneurysm: implications for thromboembolic complications. *Thorac Cardiovasc Surg*. 2007;55(6):365-370. [CrossRef]
26. Demir M, Ozmen G, Keçoğlu S, Günay T, Melek M. Right and left atrial appendage function in patients with atrial septal aneurysm without patent foramen ovale. *Acta Cardiol*. 2012;67(4):457-460. [CrossRef]
27. Demirci S, Dönmez MC, Aslan SM. Lone atrial septal aneurysm with spontaneous echo contrast: an increased stroke risk. *Turk J Med Sci.* 2008;38(5):473-476.
28. Zahdi O, El Bouhali S, El Hamraoui I, et al. Isolated atrial septal aneurysm: Exceptional cause of digital ischemia - a case report. *Ann Cardiol Angeiol (Paris).* 2020;69(2):100-102. French. [CrossRef]
29. Badano LP, Kolias TJ, Muraru D, et al.; Industry representatives; Reviewers: This document was reviewed by members of the 2016–2018 EACVI Scientific Documents Committee. Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *Eur Heart J Cardiovasc Imaging*. 2018;19(6):591-600. Erratum in: *Eur Heart J Cardiovasc Imaging*. 2018;19(7):830-833. [CrossRef]
30. Vianna-Pinton R, Moreno CA, Baxter CM, Lee KS, Tsang TS, Appleton CP. Two-dimensional speckle-tracking echocardiography of the left atrium: feasibility and regional contraction and relaxation differences in normal subjects. *J Am Soc Echocardiogr*. 2009;22(3):299-305. [CrossRef]
31. Cameli M, Caputo M, Mondillo S, et al. Feasibility and reference values of left atrial longitudinal strain imaging by two-dimensional speckle tracking. *Cardiovasc Ultrasound.* 2009;7:6. [CrossRef]