

Atrial function after treatment of atrial septal defects in children under 5 years

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Research

Keywords: atrial septal defect, echocardiography, atrial function

Posted Date: March 9th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-16328/v1>

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Abstract

Background

Recently, the patient's age of atrial septal defect (ASD) treatment has been gradually decreasing. However, the most appropriate age and treatment method remain controversial. We hypothesized that treatment of ASDs in patients under 5 years would be able to adequately normalize bi-atrial function over one year after treatment. The purpose of this study is to confirm the normalization of hypothesized atrial function.

Methods

Data of fifteen patients who underwent surgical ASD closure under 5 years of age (Operation group), 15 patients who underwent percutaneous ASD closure (Device group), and 15 age- and gender-matched normal control patients (Control group) were extracted from our echocardiographic data. Conventional 2D images and 2D speckle tracking method were used to evaluate bi-atrial function.

Results

Left atrial function, ϵ_S , ϵ_E , and ϵ_A showed no significant differences in the three groups. Indicators representing the right atrial function varied with the three groups. However, there were no significant differences in the global longitudinal strain of the right atrium between the Operation and Device groups.

Conclusions

After ASD treatment, right atrial function recovery is less than that of the left atrium. The function of the right atrium is not normalized after more than one year of treatment for ASD in patients under 5 years. After ASD treatment, further follow-up of the bi-atrial function is necessary.

Introduction

An atrial septal defect (ASD) is a relatively common disease of congenital heart defects. If the ratio of pulmonary blood flow and systemic blood flow through the ASD is more than 2:1 or if the patient has symptoms of ASD, treatment is performed by surgery or percutaneous trans-catheter closure. The purpose of treating ASD is to block the volume overload of the right atrium (RA) and right ventricle (RV) in order to reduce heart failure symptoms and prevent complications caused by secondary lung injury or arrhythmia caused by ASD. Infants and preschoolers rarely develop symptoms due to ASD, and more often they follow the natural course. However, hemodynamically significant ASDs require treatment during infancy and preschool ages. Recently, as percutaneous ASD closure has become more common, many cases of percutaneous device closure have been attempted except in early preschool ages because at that age, the patient's physique and vessel diameter is small, which increases the risk of various complications due to percutaneous intervention. Moreover, there is a risk of complications following surgical ASD closure. Despite these adverse factors, few studies have been conducted on how atrial

function is restored in patients with ASD who underwent surgical or percutaneous device closure during the preschool age. The purpose of this study was to compare the atrial function of patients who underwent surgical ASD closure under the age of 5 years, those who underwent percutaneous device closure of ASD, and normal controls.

Methods

Population

Among patients who have undergone cardiac echocardiography using a GE Vivid-E95 or GE Vivid-E9 ultrasound scanner (GE Vingmed Ultrasound AS, Horten, Norway) within the last 3 years, fifteen patients who had undergone an ASD operation under 5 years of age at least 1 year ago (Operation group), fifteen patients who had undergone percutaneous device closure of ASD under 5 years of age at least 1 year ago (Device group), and fifteen healthy age- and gender-matched patients were selected (Control group). Clinical information of patients and controls included in the study was retrospectively obtained through a review of medical records. The institutional review board of Sejong general hospital approved this study and waived the need for informed consent due to the retrospective nature (Approval number: 1964)

Echocardiographic data

There are three functions of the atria: the reservoir, conduit, and contraction functions. Left atrial (LA) volume and RA volume were measured by the area-length method using apical four-chamber view-obtained standard grayscale images. The maximum volume (V_{max}), minimum volume (V_{min}), and volume just before the P wave emerges from the surface electrocardiogram (ECG) (V_{preP}) of the RA and LA were measured by three pediatric experts (J.K., S.P., J.Y.). The calculated values are shown in Table 1.

Table 1
Indicators of the three atrial functions

Reservoir function	Emptying volume = $V_{max} - V_{min}$
	Emptying fraction = $100 - (V_{max} - V_{min}) / V_{max}$
Conduit function	Passive emptying volume = $V_{max} - V_{preP}$
	Passive emptying fraction = $100 * (V_{max} - V_{preP}) / V_{max}$
Pump function	Active emptying volume = $V_{preP} - V_{min}$
	Active emptying fraction = $100 * (V_{preP} - V_{min}) / V_{preP}$

RA and LA 2D speckle tracking analysis was obtained using a grayscale apical four-chamber view. Offline analysis of these images was performed using the EchoPAC software (GE Ultrasound AS, Horten,

Norway), according to the current guidelines. Strain of the RA and LA was measured during peak systole (ϵ S), early diastole (ϵ E), and late diastole (ϵ A; Fig. 1).

Indicators of left ventricular (LV) function presented in the previously reported echocardiography results were used.

Statistical Analysis

SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA) was used for statistical analyses. Continuous variables are described as a mean and standard deviation. Categorical variables are described as a frequency and percentage. To test whether the variables differ between groups, variance analysis was performed for continuous variables and a chi-squared test for categorical variables. Covariance analysis was performed to analyze the difference in echocardiography results that corrected the body surface area (BSA) variables. For post-hoc analysis, the TUKEY test was performed.

Results

Baseline Characteristics

Each group (Operation, Device and Control) was age- and gender-matched (10 girls and 5 boys). There were no significant differences in weight, height, and BSA between groups. At the time of echocardiography, the Operation group was on average 46.95 months after surgery and the Device group was 26.53 months after percutaneous ASD device closure. Most of the patients included in the Control group underwent echocardiography as part of an assessment for functional heart murmur. None of the patients included in the study had definite arrhythmias or other systemic disease. The basic characteristics of the study populations are summarized in Table 2. There was no significant difference in age and the sex ratio between groups, and there was also no significant difference in weight, height, and BSA. Although there was a difference between the elapsed time after surgery in the Operation group and after percutaneous device closure in the Device group, this study analyzed echocardiography performed after more than one year in all patients.

Table 2
Basic characteristics of the study population

	Control group (n = 15)	Operation group (n = 15)	Device group (n = 15)	P- value
Echocardiography Age (years)	5.62 ± 1.38	5.97 ± 1.49	6.00 ± 1.42	0.719 ¹⁾
Female/male	10/5	10/5	10/5	
Body weight (kg)	19.22 ± 3.34	20.57 ± 4.73	19.61 ± 3.31	0.621 ¹⁾
Height (cm)	112.06 ± 9.04	112.69 ± 8.94	113.29 ± 9.5	0.935 ¹⁾
Body surface area (m ²)	0.77 ± 0.10	0.80 ± 0.11	0.78 ± 0.09	0.719 ¹⁾
Postoperative or post-procedure periods (months)		46.95 ± 28.11	26.53 ± 14.19	0.02 ²⁾
1) Analysis of variance (ANOVA) test				
2) Independent sample T-test				

Conventional echocardiographic indicators

There were no structural abnormalities nor pericardial or pleural effusion. There was no evidence of significant chamber enlargement or ventricular dysfunction. However, the Operation group had smaller systolic left ventricular dimension (LVIDs) than the Control group. There was no significant difference in mitral inflow Doppler pattern and mitral annular velocity measurements using tissue Doppler imaging (TDI) between groups. However, the tricuspid annular velocity measurement using TDI revealed significant differences between the Operation and Device groups (Table 3).

Table 3
Conventional echocardiographic parameters

	LSMEANS			P-value ¹⁾	P-value ²⁾		
	Control Group	Operation Group	Device Group		C vs O	C vs D	O vs D
LVIDd	35.79	34.44	35.83	0.234	0.311	0.999	0.288
LVIDs	23.04	21.12	22.07	0.035*	0.027*	0.365	0.382
EF	65.92	69.74	69.41	0.106	0.135	0.181	0.984
FS	35.63	38.58	38.39	0.108	0.142	0.0176	0.991
E	1.01	1.08	1.03	0.339	0.324	0.897	0.571
A	0.58	0.59	0.55	0.710	0.999	0.767	0.742
E/A	1.8	1.97	2.06	0.460	0.715	0.434	0.892
Medial e'	13.74	13.92	12.42	0.218	0.981	0.332	0.248
Medial a'	7.48	5.52	5.75	0.009*	0.013*	0.030*	0.934
Medial s'	7.95	6.85	7.27	0.094	0.080	0.362	0.672
Mitral e'	17.88	16.04	16.86	0.083	0.067	0.416	0.560
Mitral a'	7.17	6.09	6.31	0.190	0.196	0.350	0.928
Mitral s'	9.06	9.07	8.28	0.501	>.999	0.569	0.561
Tricuspid e'	13.20	11.76	14.46	0.027*	0.307	0.394	0.020*
Tricuspid a'	9.17	5.90	9.03	<.001*	<.001*	0.979	<.001*
Tricuspid s'	11.47	8.94	11.79	<.001*	<.001*	0.872	<.001*
1) Analysis of Covariance (ANCOVA) are adjusted for BSA							
2) The Tukey-Kramer test was performed for post-hoc comparisons							

RA and LA function

LA function, using 2D imaging, showed significant differences between the LA emptying volume and fraction. LA function, using 2D speckling tracking imaging, showed no significant difference in the ϵ_S , ϵ_E , and ϵ_A values between groups. Although it did not reach statistical significance, the LA volume/BSA, ϵ_S , ϵ_E , and ϵ_A were higher in the Control group than the Operation and Device groups.

In contrast, RA functional evaluation showed differences among the three groups. Values of the RA emptying volume, emptying fraction, passive emptying volume, passive emptying fraction, and active emptying fraction were significantly different. The global longitudinal strain values (ϵ_S , ϵ_E , and ϵ_A) also showed significant differences among the groups. There was no significant difference in the global longitudinal strain of the RA between the Operation and Device groups. However, the Operation group had significantly lower ϵ_S and ϵ_E values than the Control group and the Device group had lower ϵ_S , ϵ_E , and ϵ_A values than the Control group (Table 4).

Table 4
Comparison of the left and right atrial functions between groups

	LSMEANS			P-value ¹⁾	P-value ²⁾		
	Control Group	Operation Group	Device Group		C vs O	C vs D	O vs D
LA emptying volume/BSA	13.90	11.87	10.99	0.029*	0.156	0.025*	0.693
LA emptying fraction	68.04	61.99	68.15	0.005*	0.012*	0.998	0.010*
LA passive emptying volume/BSA	9.77	8.42	8.56	0.424	0.0459	0.530	0.991
LA passive emptying fraction	48.54	44.38	52.06	0.246	0.633	0.715	0.216
LA active emptying volume/BSA	2.37	1.96	1.44	0.224	0.725	0.197	0.591
LA active emptying fraction	32.41	29.39	30.20	0.629	0.643	0.729	0.988
LA GLS ϵ S	43.59	37.30	37.62	0.502	0.551	0.580	0.998
LA GLS ϵ E	32.11	25.83	27.21	0.379	0.382	0.550	0.953
LA GLS ϵ A	11.47	11.48	10.41	0.809	>.999	0.840	0.840
RA emptying volume/BSA	7.77	6.57	8.35	0.023*	0.151	0.630	0.019*
RA emptying fraction	63.83	46.32	60.16	<.001*	<.001*	0.484	<.001*
RA passive emptying volume/BSA	6.86	6.55	9.63	0.018*	0.958	0.050	0.026*
RA passive emptying fraction	35.02	29.96	43.47	0.011	0.173	0.131	0.008*
RA active emptying volume/BSA	5.53	3.99	3.87	0.078	0.140	0.104	0.989
RA active emptying fraction	43.09	25.52	30.62	0.001*	0.001*	0.017*	0.474
RA GLS ϵ S	45.30	31.2	31.24	<.001*	0.001*	0.001*	1

1) Analysis of Covariance (ANCOVA) are adjusted for BSA

2) The Tukey-Kramer test was performed for post-hoc comparisons

	LSMEANS			P-value ¹⁾	P-value ²⁾		
	Control Group	Operation Group	Device Group		C vs O	C vs D	O vs D
RA GLS εE	29.52	18.83	20.23	0.002*	0.002*	0.008*	0.884
RA GLS εA	15.79	12.37	11.01	0.005*	0.051	0.004*	0.598
1) Analysis of Covariance (ANCOVA) are adjusted for BSA							
2) The Tukey-Kramer test was performed for post-hoc comparisons							

Discussion

Secundum ASD is a relatively common congenital heart disease, and as echocardiography is becoming more common, the age at diagnosis is gradually decreasing. Recently, percutaneous trans-catheter ASD device closure has been increasing in prevalence. More than 80% of ASD closures have recently been performed by non-open-heart surgery.¹ However, ASD device closure in infants and children with low weight remains a technical problem and often requires surgical ASD closure. In this study, we matched subjects by their age and gender, but the elapsed time after ASD closure was different between the Operation (46.95 ± 28.11 months) and Device (26.53 ± 14.19 months) groups. In our center, surgical ASD closure is more common than device closure if the child is under 3 years old or weighs less than 10 kg.

Unlike adult patients who have surgical or device closure of an ASD, in children, there are few cases of post-operative death and very few serious complications. Additionally, atrial fibrillation and pulmonary hypertension are rarely seen. Unlike adult patients, while the period of exposure to the left to right shunt is short, the hemodynamic significance of ASD required closure in children under 5 years also means that the amount of shunt is significantly larger to show clinical symptoms, which means that they are exposed to excessive volume overload. So far, there have been reports that the degree of RA and LA functional recovery varies according to the age at ASD treatment.²⁻⁴ After the treatment of these ASDs, the question remains whether the function of the RA and LA can be normalized after some time. Indeed, the number of studies regarding atrial and ventricular function after ASD closure in childhood are very few.⁵⁻¹²

In general, e' velocity is an indicator of the diastolic function of the ventricle and a' velocity is considered to be associated with the atrial function. As shown in Table 3, tricuspid e' and a' are significantly different between groups, and there are also significant differences between the Operation and Device groups, while mitral e' and a' show no significant differences. This is because ASD itself is a disease that mainly affects the right ventricle and RA. However, even after treatment for ASD, the LA and RA function of patients with ASD are reported to be inferior to those of normal subjects.^{7,13-14}

To compare the reservoir, conduit, and pump functions, which are the three functions of the atria, V_{\max} , V_{\min} , $V_{\text{pre-P}}$ of the RA and LA were calculated using the obtained standard grayscale images of an apical four-chamber view by area-length methods. Although there are many limitations in this process, there were significant differences between groups in the LA reservoir function. On the other hand, the conduit and pump functions did not show significant statistical difference. However, the reason for the difference between groups may be an error in the process of comparing the calculated values with the assumption that the shape of the left atrium is constant. One unchanging principle is that both the Operation and Device groups have lower LA volumes than the Control group.

The Operation and Device groups showed significant differences in RA reservoir and conduit functions, but this difference was very small between the Device and Control groups. These results suggest that device closure of ASD can maintain conduit and reservoir functions of the RA relatively well, even at ages less than five years, compared to surgical closure. The reason for this may be related to scarring of the RA which inevitably occurs during surgical closure of ASD.

In the case of the RA active emptying fraction, which is the pump function of the RA, there was no significant difference between the Operation and Device groups, but the value was lower in each of those groups than in the Control group. These results may be attributed to the deterioration of interatrial wall motion occurring after device closure and scarring which remain at the RA incision site and interatrial septal patch.

2D speckle tracking analysis has been widely used to evaluate ventricular function,¹⁵⁻¹⁶ but similar methods can be used to evaluate the atrial function. The ϵ_S , ϵ_E , and ϵ_A values obtained using EchoPAC software can be considered as indices representing the reservoir, conduit, and pump functions, respectively. The ϵ_S , ϵ_E , and ϵ_A of the LA did not differ significantly between groups. Perhaps it is because the structural and functional changes of the heart due to ASD have relatively little effect on the LA.

In spite of the data obtained through the echocardiography conducted at least one year after the operation or device closure of the ASD, in the case of the RA, the ϵ_S , ϵ_E , and ϵ_A were all reduced in the Device group compared to the Control group. The Operation group showed significantly decreased ϵ_S and ϵ_E compared to the Control group. These results can be interpreted as a failure to normalize the LA and RA function even after one year of repair.

As a study conducted in adults reported that the RA strain during the reservoir phase is a predictor of atrial fibrillation development¹⁷, the possibility of future arrhythmias in the Operation and Device groups with decreased ϵ_S may be considered. Therefore, ASD patients treated under 5 years of age require long-term follow-up with the possibility of arrhythmia and reduced atrial function.

Study Limitations

This is a retrospective study with a low sample size. Since the area-length method was used to calculate the volume of the RA and LA, it may not accurately reflect the actual volume. When measuring global longitudinal strain using 2D speckle tracking, the values measured by the three pediatric cardiologists were averaged and did not solve the problem of inter- and intra-observer variation.

Conclusion

After ASD treatment, the recovery of RA function was less than that of the LA. In children under five years, RA function was not normalized after more than one year after treatment for ASD. After ASD treatment, further follow-up of the RA and LA function is necessary.

Abbreviations

ASD:atrial septal defect; BSA:body surface area; ECG:electrocardiogram; LA:left atrium; LV:left ventricle; LVIDs:systolic left ventricular dimension; RA:right atrium; RV:right ventricle; TDI:tissue Doppler imaging

Declarations

Acknowledgements

Thank you very much to professor Hyoung-gin An (Department of Biostatistics, college of medicine, Korea University) for your advice and data processing, and Yun-Hui Han for your help in drawing. We would like to thank Editage (www.editage.co.kr) for English language editing.

Authors's contributions

EC data analysis and writing of article. EK and CN guiding and interpretation of data. JK, SP and JY collected data.

Funding

None to declare.

Availability of data and materials

Please contact author for data requests.

Ethics approval and Consent to Participate

The authors confirm that all procedures contributing to this work comply with ethical standards of the national guidelines and the institutional review board of Sejong general hospital approved this study and waived the need for informed consent due to the retrospective nature (Appraisal number: 1964)

Consent for publication

Not applicable

Competing interests

None to declare.

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Figures

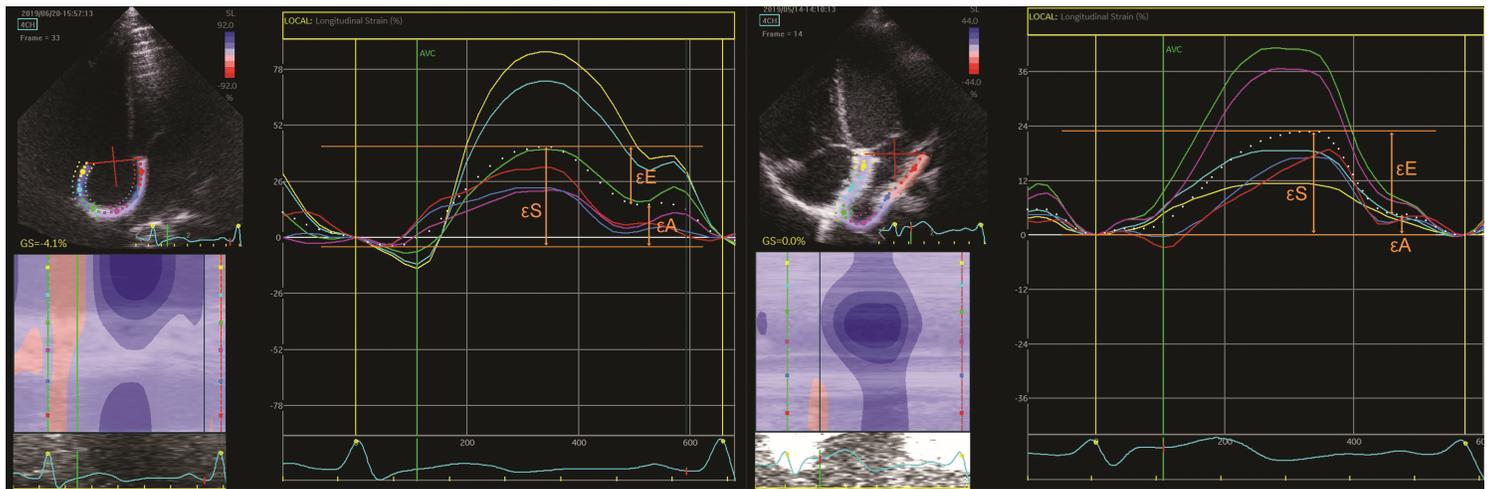


Figure 1

Method for measuring global longitudinal strain in the right atrium and left atrium. The white dotted line is the average of the six atrial segments. The peak systolic (ϵ_S) and early (ϵ_E) and late diastolic (ϵ_A) strains are markers of the reservoir, conduit, and pump functions of the atrium, respectively.