Received: 23 April 2017 | Revised: 6 September 2017 | Accepted: 10 September 2017
DOI: 10.1111/chd.12541

ORIGINAL ARTICLE

WILEY Congenital Heart Disease

Time course of the changes in right and left ventricle function and associated factors after transcatheter closure of atrial septal defects

Byung W. Yoo MD[1] | Jung O. Kim MD[2] | Lucy Y. Eun MD, PhD[2] | Jae Y. Choi MD, PhD[2] | Dong S. Kim MD, PhD[3]

[1]Department of Clinical Pharmacology, Clinical Trial Center, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
[2]Division of Pediatric Cardiology, Department of Pediatrics, Yonsei University College of Medicine, Seoul, Korea
[3]Department of Pediatrics, Severance Children's Hospital, Yonsei University College of Medicine, Seoul, Korea

Correspondence
Lucy Youngmin Eun, Division of Pediatric Cardiology, Department of Pediatrics, Yonsei University College of Medicine, Seoul, Korea.
Email: lucyeun@yuhs.ac

Funding information
Yonsei University College of Medicine for 2007, Grant/Award number: 6-2007-0161

Abstract

Objective: The purpose of this study was to evaluate the changes in right ventricle (RV) and left ventricle (LV) function after transcatheter atrial septal defect (ASD) closure and to assess the influence of the age and the amount of shunt.

Design: Retrospective study

Patients: Fifty-three adult patients who underwent transcatheter closure were enrolled, then divided into subgroups according to the age ($<$ 40 years vs $\geq$ 40 years), and the amount of shunt flow (QpQs $<$ 2.5 vs QpQs $\geq$ 2.5).

Outcome Measures: Two-dimensional tissue Doppler imaging was performed in a four-chamber view at the basal ventricular septum (VS) and tricuspid valve annulus (TVA) before and at 1 month and 6 months after closure. Myocardial velocities, the myocardial performance index (MPI), and isovolumic acceleration (IVA) were assessed.

Results: At the TVA, the MPI decreased slightly and then greatly increased at 6 months after closure ($P = .002$). The IVA improved in all patients ($P < .001$), and the E'/A' ratio decreased, especially in the old age group ($P = .031$) and larger shunt group ($P = .035$). At the VS, S' and the IVA decreased and had not recovered until 6 months in the old age ($P = .02$) and larger shunt ($P = .02$). The Qp/Qs showed a significant reverse correlation with a decrease in the E'/A' at the TVA ($r = -0.37$, $P = .008$), and age of patient was correlated with a decrease in the IVA at the VS ($r = -0.32$, $P = .019$). The age at closure ($\beta = -0.36$, $P = .002$), the Qp/Qs ratio ($\beta = -0.45$, $P = .01$), and RV MPI changes ($\beta = -7.64$, $P < .001$) were found to be associated factors with IVA decrease at the VS.

Conclusions: After ASD closure, RV global function might be impaired. In elderly patients and patients with a large shunt, impairment of LV contractility developed until 6 months after closure. Close long-term observation is required after closure, especially in old-age patients with a large shunt.

KEYWORDS
atrial septal defect, isovolumic acceleration, myocardial performance index, tissue Doppler imaging, ventricular function

1 | INTRODUCTION

In patients with atrial septal defect (ASD), right ventricle (RV) volume overload causes alterations in chamber geometry and ventricular function at the RV and left ventricle (LV).[1–5] Transcatheter closure has replaced surgery as the primary treatment modality of ASD, and its clinical benefits and positive remodeling effects on cardiac chamber geometry are well demonstrated even in elderly patients.[1–5] With regard to ventricular function, it has been suggested that transcatheter closure leads to an improvement in ventricular performance.[3,6–8]

TABLE 1 Clinical and hemodynamic data of the subjects

		Age group			Qp/Qs group		
	Total (n = 53)	Group 1 (n = 20)	Group 2 (n = 33)	*P*	Group A (n = 25)	Group B (n = 28)	*P*
Age (yr)	42.2 ± 13.7	28.1 ± 7.8	50.8 ± 8.1		42.2 ± 15.6	42.3 ± 11.9	.98
ASO size	25.4 ± 7.0	27.8 ± 7.6	23.9 ± 6.3	.048	23.0 ± 7.1	27.5 ± 6.3	.020
BSA (m^2)	1.66 ± 0.16	1.72 ± 0.16	1.62 ± 0.15	.030	1.66 ± 0.15	1.66 ± 0.17	.93
Qp/Qs	2.76 ± 0.88	2.81 ± 0.86	2.73 ± 0.91	.76	2.04 ± 0.31	3.41 ± 0.71	
RAP (mm Hg)	7.6 ± 2.8	7.7 ± 3.2	7.6 ± 2.5	.96	6.4 ± 2.5	8.7 ± 2.6	.002
PAP (mm Hg)	33.4 ± 9.9	30.0 ± 7.6	35.4 ± 10.6	.053	32.7 ± 11.4	33.9 ± 8.4	.67

Abbreviations: ASO, atrial septal occluder; BSA, body surface area; n, number; PAP, preocclusional pulmonary systolic pressure; Qp/Qs, pulmonary-to-systemic flow ratio; RAP, preocclusional right atrial mean pressure; yr, years.

However, some studies have reported deterioration of systolic or diastolic ventricular function after the procedure; especially for the LV, an acute rise in the volume and filling pressure of both the LA and LV may cause left-sided heart failure, even without evident LV dysfunction prior to the intervention; however, this is rare.[9–11] As for the RV, it is not clear whether preocclusional systolic and diastolic dysfunction completely recovers after the procedure. In a previous study of patients who underwent surgical ASD closure, there were no survival benefits in patients older than 40 years at surgery.[12] Considering this result, influencing factors such as the age of patient and the amount of shunt flow could affect the remodeling of ventricles after transcatheter closure. Some studies have reported the effects of ASD device closure on regional RV and LV performance; however, the results were rather inconclusive and did not allow for a complete consensus.[13–19]

Among several methods for the quantitative analysis of regional ventricular performance, tissue Doppler imaging (TDI) is a feasible and useful tool with high reproducibility.[20,21] In particular, some nonvolumetric indices derived from TDI are less load-dependent. Among these indices, the myocardial performance index (MPI) can quantify global ventricular function, while isovolumic acceleration (IVA) represents myocardial contractility directly, more independent of ventricular loading conditions.[22,23]

The purpose of this study was to evaluate the changes in RV and LV performance after transcatheter ASD closure using TDI. In particular, we analyzed the changes according to age of patient at closure, the amount of shunt through the defect, and the time after closure.

2 | METHODS

2.1 | Subjects

The study enrolled 53 adult patients who underwent successful transcatheter ASD closure in the Division of Pediatric Cardiology at Severance Cardiovascular Hospital, Yonsei University College of Medicine. Patients who had shunts other than ASD and significant PS were excluded, and there was no patient with significant arrhythmia (including atrial arrhythmia). For evaluating the effect of age of patient at the time of the procedure and the amount of shunt on ventricular performance, patients were divided according to their age (Group 1: < 40 years and Group 2: ≥ 40 years) and pulmonary-to-systemic flow ratio (Qp/Qs ratio; Group A: < 2.5 and Group B: ≥ 2.5). We compared the results of each group according to the time after closure (Table 1).

Transcatheter ASD closure was performed using an Amplatzer septal occluder (AGA Medical, Golden Valley, MN) and its delivery system. The procedure was performed by a single interventionist with the assistance of intracardiac echocardiography, and the hemodynamics of each patient was assessed before deploying the occluder. There was no case in which the procedure failed. The pulmonary arterial hypertension revealed in 13 patients before ASD closure and persisted in 5 of them after ASD closure.

This retrospective study was approved by the Institutional Review Board of Severance Hospital (Seoul, Korea).

2.2 | Echocardiography

Transthoracic echocardiographic evaluation was performed and 2D echo data were assessed including fractional area change of RV (RV FAC) and ejection fraction of LV (LV EF) within 3 months before and at 1 month and 6 months after the implantation of the occluder, using commercially available systems. TDI was performed in a four-chamber view at the basal part of the ventricular septum (VS) and tricuspid valve annulus (TVA). We used the pulsed-wave TDI with filters to exclude high-frequency signals and a 2-mm sample volume. Myocardial velocities were obtained at a sweep speed of 100 mm/s and frame rate of above 150 frames per second. We carefully aligned the ultrasound beam parallel to the direction of wall motion because of the angle dependency of TDI. However, we could not obtain the appropriate Doppler angle at the mitral valve annulus, as in most patients, the longitudinal ventricular axis was severely tilted to the left because of RV volume overload. Therefore, we could not obtain appropriate TDI data from the mitral valve annulus with reproducibility. For each image, myocardial velocities (E', A', S', peak isovolumic myocardial velocity) and time intervals (isovolumetric contraction time, isovolumetric relaxation time, ejection time, acceleration time) were averaged from three consecutive beats, and the MPI and IVA were derived from the data on off-line system (Echopac, GE-Vingmed, Horten, Norway). As described previously, the TDI-derived MPI was defined as the ratio of the sum of isovolumetric contraction time and isovolumetric relaxation time to the

TABLE 2 Myocardial velocities and tissue Doppler–derived indices in all the patients (n = 53)

	Ventricular septum				Tricuspid valve annulus			
	Preclosure	1 mo after	6 mo after	P*	Preclosure	1 mo after	6 mo after	P*
E'	9.92 ± 2.76	9.13 ± 2.24	8.48 ± 2.37	< .001	15.33 ± 3.78	12.04 ± 3.17	11.79 ± 3.52	< .001
A'	9.59 ± 2.49	8.89 ± 1.80	8.83 ± 2.20	.051	16.05 ± 4.43	12.98 ± 3.69	13.21 ± 3.61	< .001
E'/A'	1.12 ± 0.53	1.09 ± 0.41	1.05 ± 0.41	.079	1.05 ± 0.48	1.00 ± 0.41	0.92 ± 0.37	.045
S'	9.79 ± 1.44	8.64 ± 1.11	8.35 ± 1.28	< .001	15.78 ± 3.09	13.59 ± 3.37	12.79 ± 3.21	< .001
MPI	0.33 ± 0.05	0.32 ± 0.06	0.33 ± 0.04	.96	0.31 ± 0.07	0.29 ± 0.06	0.35 ± 0.06	.002
IVA (m/s^2)	2.20 ± 0.75	1.99 ± 0.86	2.08 ± 1.18	.50	2.29 ± 0.93	2.21 ± 1.23	3.73 ± 1.11	< .001
2D echo parameter								
RV FAC (%)	40.1 ± 6.9	34.9 ± 8.2	35.9 ± 8.2	.002				
LV EF (%)	65.6 ± 7.2	70.7 ± 5.8	69.6 ± 5.3	< .001				

Abbreviations: A', late diastolic myocardial velocity; E', early diastolic myocardial velocity; IVA, isovolumic acceleration; LV EF, ejection fraction of the left ventricle; mo, month; MPI, myocardial performance index; RV FAC, fractional area change of the right ventricle; S', systolic myocardial velocity.
*P values represent the statistical significance in the paired t test between the value at preclosure and the value 6 months later.

ejection time,[21,22] and IVA was measured as the mean slope of the isovolumic contraction velocity.[23] Echocardiographic data review and off-line analysis were performed by a single investigator.

2.3 | Statistics

Results are expressed as mean ± one standard deviation for normally distributed data. Comparisons of clinical data between groups were performed using the Student's t test. Changes in each parameter before and after the procedure were analyzed using the paired Student's t test. We evaluated the correlation between the differences in TDI parameters before and after closure, and we compared the frequency of the increase/decrease in each TDI parameter between each subgroup. To validate the influence of associated factors on the changes in TDI parameters, Pearson's correlation test, the chi-square test, or Fisher's exact test were performed, and to identify the independent associated factors with changes in TDI parameters, linear regression was used.

SPSS for Windows (version 18.0, SPSS Inc., Chicago, IL) was used for data analysis. A P value less than .05 was considered to indicate statistical significance.

3 | RESULTS

3.1 | 2D echo measurement

The RV FAC decreased after ASD closure in analysis of all subjects, and in subgroup analysis for old age group and lager shunt group. The LV EF increased after ASD closure in all subgroup analysis except for smaller shunt group (Tables 2–4).

3.2 | Changes in myocardial velocities

After ASD closure, early diastolic (E') and systolic (S') velocities significantly decreased at both the VS and TVA in all subjects and in all subgroup analyses (Tables 2–4). The late diastolic (A') velocity at the VS did not show any changes except for a decrease in the old age group. However, A' at the TVA significantly decreased in all subgroups, except for the young age group. The E'/A' ratio, a marker of diastolic function, demonstrated no change at the VS. However, the E'/A' ratio at the TVA decreased to less than 1 ($P = .045$) and decreased more significantly in the old age group than in the young age group and in the larger shunt group than in the smaller shunt group ($P = .031$ and $P = .035$, respectively).

Compared with the normal values according to age and gender,[24] the number of patients with normal E' at VS increased from 7 (13.2%) before the procedure to 10 (18.9%) after the procedure.

For the A' at VS, this number of patients (10 patients, 18.9%) did not change before and after the procedure, but for the S' and the E'/A' ratio at VS, the patients with normal value increased after the procedure [S', 7 (13.2%) to 12 (22.6%); E'/A' ratio, 4 (7.5%) to 6 (11.3%)]. Regarding the myocardial velocities at TVA, the patients with normal value increased after the procedure for all parameter [E', 7(13.2%) to 8 (15.1%); A', 2 (3.8%) to 7 (13.2%); S', 2 (3.8%) to 7 (13.2%); E'/A' ratio, 7 (13.2%) to 9 (17.0%)].

3.3 | Changes in TDI-derived indices

The MPI at the VS did not differ significantly before and after closure. However, the MPI at the TVA decreased slightly at 1 month after closure and then increased greatly at 6 months after closure ($P = .002$, Table 2). In subgroup analysis, these changes were more pronounced in the larger shunt group than in the smaller shunt group (Table 4, Figure 1).

The IVA at the TVA increased greatly relative to time in all subjects and in all subgroup analyses ($P < .001$). The IVA at the VS did not differ in the analysis of all subjects ($P = .50$). However, in the old age group and the larger shunt group, the IVA at the VS decreased significantly at 1 month after closure and persisted at 6 months after closure ($P = .029$ and $P = .026$, respectively, Figure 1).

TABLE 3 Myocardial velocities and tissue Doppler-derived indices in each age group

	Ventricular septum				Tricuspid valve annulus			
	Preclosure	1 mo after	6 mo after	P*	Preclosure	1 mo after	6 mo after	P*
Group 1 (< 40 years old, n = 20)								
E′	11.92 ± 2.11	10.21 ± 1.90	10.04 ± 2.37	.005	16.65 ± 3.05	13.75 ± 2.75	13.73 ± 3.76	.008
A′	8.02 ± 2.13	7.96 ± 1.83	8.30 ± 2.79	.85	14.94 ± 4.08	11.78 ± 3.67	12.59 ± 3.94	.11
E′/A′	1.54 ± 0.52	1.36 ± 0.44	1.36 ± 0.39	.088	1.27 ± 0.42	1.23 ± 0.52	1.17 ± 0.43	.51
S′	10.50 ± 1.43	8.84 ± 1.03	8.89 ± 1.42	.002	16.84 ± 2.80	13.96 ± 3.61	14.31 ± 3.77	.003
MPI	0.32 ± 0.04	0.33 ± 0.05	0.33 ± 0.04	.60	0.31 ± 0.07	0.31 ± 0.05	0.35 ± 0.06	.051
IVA (m/s^2)	2.48 ± 1.05	2.26 ± 0.85	2.75 ± 1.65	.64	2.45 ± 0.83	2.21 ± 1.00	3.73 ± 1.29	.001
2D echo parameter								
RV FAC(%)	38.8 ± 6.7	31.8 ± 5.5	34.9 ± 6.0	.050				
L V EF(%)	64.1 ± 6.5	69.9 ± 6.0	68.6 ± 5.6	.029				
Group 2 (≥40 years old, n = 33)								
E′	8.65 ± 2.37	8.45 ± 2.19	7.46 ± 1.75	.003	14.52 ± 4.01	10.99 ± 2.99	10.53 ± 2.73	< .001
A′	10.59 ± 2.18	9.47 ± 1.54	9.18 ± 1.68	.003	16.74 ± 4.56	13.73 ± 3.56	14.03 ± 3.37	< .001
E′/A′	0.86 ± 0.33	0.91 ± 0.28	0.84 ± 0.27	.47	0.94 ± 0.42	0.87 ± 0.31	0.76 ± 0.20	.031
S′	9.35 ± 1.28	8.49 ± 1.16	7.99 ± 1.06	< .001	15.13 ± 3.13	13.12 ± 3.06	11.88 ± 2.49	< .001
MPI	0.34 ± 0.06	0.31 ± 0.06	0.33 ± 0.04	.73	0.32 ± 0.07	0.29 ± 0.06	0.35 ± 0.05	.021
I VA (m/s^2)	2.11 ± 0.65	1.83 ± 0.84	1.73 ± 0.61	.029	2.19 ± 0.99	2.22 ± 1.36	3.69 ± 1.02	< .001
2D echo parameter								
RV FAC (%)	40.9 ± 7.0	36.7 ± 9.1	36.4 ± 9.3	.015				
LV EF (%)	66.2 ± 7.5	71.0 ± 5.8	70.1 ± 5.1	.003				

Abbreviations: *A′*, late diastolic myocardial velocity; *E′*, early diastolic myocardial velocity; IVA, isovolumic acceleration; LV EF, ejection fraction of the left ventricle; mo, month; MPI, myocardial performance index; RV FAC, fractional area change of the right ventricle; *S′*, systolic myocardial velocity.
**P* values represent the statistical significance in the paired *t* test between the value at preclosure and the value 6 months later.

3.4 | Interdependency of ventricular function

The preocclusional *E′/A′* ratios at the VS and TVA showed a close correlation ($r = 0.57$, $P < .001$). Additionally, the preocclusional IVA at both sites showed the same relationship ($r = 0.37$, $P = .01$). As for the changes before and after closure, the changes in the MPI at the TVA showed a significant reverse correlation with the changes in the IVA at the VS ($r = -0.40$, $P = .004$, Figure 2).

TABLE 4 Myocardial velocities and tissue Doppler-derived indices in each pulmonary-to-systemic flow ratio group

	Ventricular septum				Tricuspid valve annulus			
	Preclosure	1 mo after	6 mo after	P*	Preclosure	1 mo after	6 mo after	P*
Group A (Qp/Qs < 2.5, n = 25)								
E′	9.98 ± 2.93	9.66 ± 2.00	8.23 ± 2.61	.001	15.00 ± 4.23	12.66 ± 3.82	12.04 ± 4.15	.016
A′	8.93 ± 2.63	9.09 ± 1.89	9.12 ± 2.32	.22	17.38 ± 4.81	14.51 ± 3.73	14.87 ± 4.27	.022
E′/A′	1.12 ± 0.55	1.13 ± 0.39	1.00 ± 0.41	.059	0.93 ± 0.38	0.99 ± 0.41	0.86 ± 0.38	.48
S′	9.89 ± 1.32	9.16 ± 1.11	8.38 ± 1.42	< .001	16.41 ± 3.66	14.53 ± 3.37	13.81 ± 3.75	.003
MPI	0.32 ± 0.04	0.33 ± 0.06	0.33 ± 0.04	.44	0.33 ± 0.09	0.31 ± 0.05	0.35 ± 0.06	.15
IVA (m/s^2)	2.40 ± 0.95	2.14 ± 0.96	2.50 ± 1.48	.82	2.60 ± 1.06	2.48 ± 1.46	3.86 ± 1.19	< .001
2D echo parameter								
RV FAC(%)	39.7 ± 7.3	36.2 ± 8.4	36.4 ± 8.7	.073				
LV EF(%)	66.9 ± 7.9	70.7 ± 5.1	69.5 ± 5.4	.073				
Group B (Qp/Qs ≥ 2.5, n = 28)								
E′	9.85 ± 2.66	8.62 ± 2.38	8.71 ± 2.16	.017	15.60 ± 3.44	11.56 ± 2.51	11.55 ± 2.93	< .001
A′	9.37 ± 2.37	8.70 ± 1.73	8.56 ± 2.11	.12	14.97 ± 3.85	11.86 ± 3.23	12.31 ± 2.54	.008
E′/A′	1.17 ± 0.58	1.05 ± 0.44	1.09 ± 0.41	.26	1.15 ± 0.52	1.08 ± 0.42	0.98 ± 0.36	.035
S′	9.70 ± 1.57	8.24 ± 0.98	8.32 ± 1.16	< .001	15.28 ± 2.51	12.57 ± 2.96	12.13 ± 2.50	< .001
MPI	0.34 ± 0.07	0.31 ± 0.04	0.32 ± 0.04	.35	0.30 ± 0.05	0.28 ± 0.06	0.35 ± 0.06	.005
IVA (m/s^2)	2.12 ± 0.46	1.81 ± 0.70	1.78 ± 0.50	.030	2.06 ± 0.78	1.95 ± 0.97	3.47 ± 0.88	< .001
2D echo parameter								
RV FAC (%)	40.4 ± 6.7	33.3 ± 7.8	35.0 ± 7.7	.009				
LV EF (%)	64.5 ± 6.5	70.7 ± 6.4	69.4 ± 5.3	.002				

Abbreviations: *A′*, late diastolic myocardial velocity; *E′*, early diastolic myocardial velocity; IVA, isovolumic acceleration; LV EF, ejection fraction of the left ventricle; mo, month; MPI, myocardial performance index; RV FAC, fractional area change of the right ventricle; *S′*, systolic myocardial velocity.
**P* values represent the statistical significance in the paired *t* test between the value at preclosure and the value 6 months later.

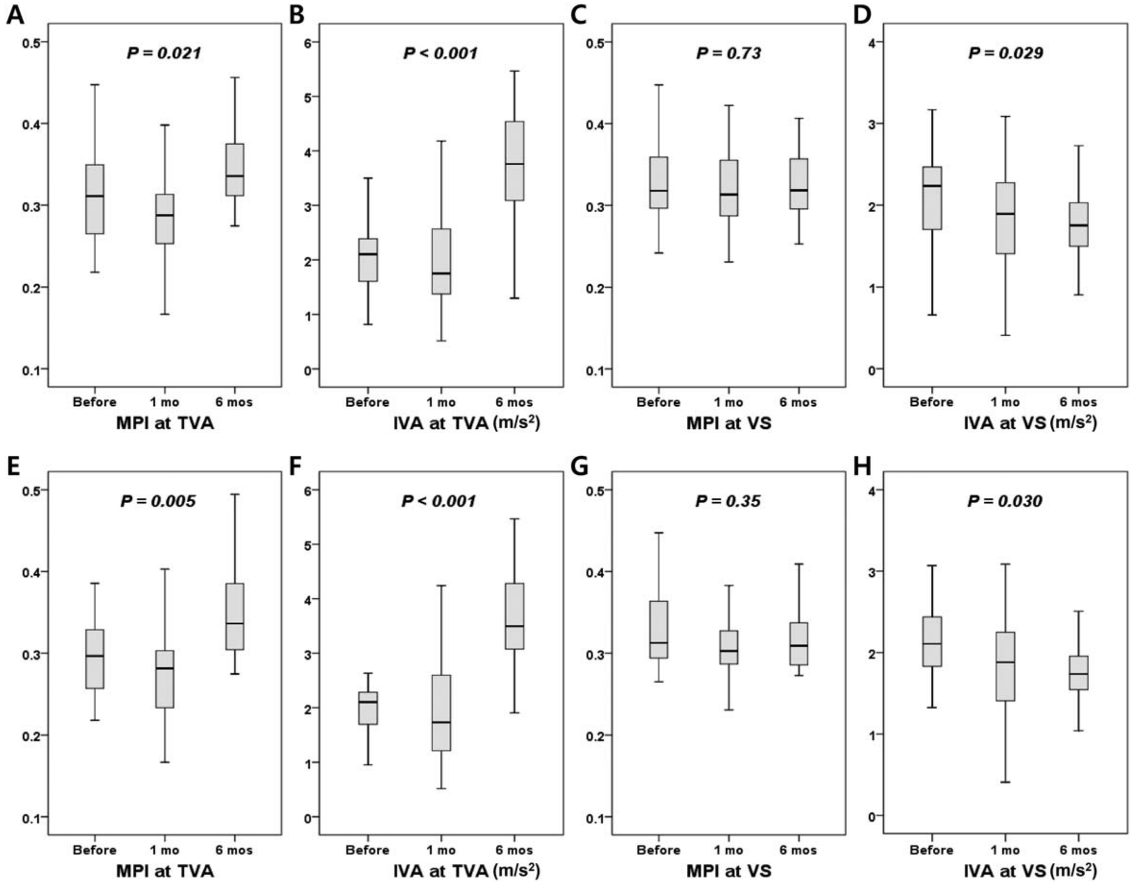

FIGURE 1 The time course of changes in TDI parameters. The paired *t* test was performed between the parameters before and 6 months after ASD closure. (A) Changes in MPI at tricuspid valve annulus with time in the old age group (≥ 40 years old). (B) Changes in IVA at tricuspid valve annulus with time in the old age group. (C) Changes in MPI at interventricular septum with time in the old age group. (D) Changes in IVA at interventricular septum with time in the old age group. (E-H) Same as (A-D), but in the larger shunt group (Qp/Qs ≥ 2.5)

3.5 | Relationship of associated factors

In the evaluation of the factors that influence the decrease in the E'/A' ratio at the TVA after closure, the Qp/Qs ratio showed a significant reverse correlation ($r = -0.37$, $P = .008$, Figure 3), and the frequencies of the decrease in the E'/A' ratio at the TVA were 44.0% in the smaller shunt group and 77.8% in the larger shunt group ($P = .012$; relative risk (RR), 1.77; 95% CI, 1.09-2.87). The age of patient at closure was not significantly correlated with the decrease in the E'/A' ratio at the TVA.

As for the increase in the MPI at the TVA, age of patient and the Qp/Qs ratio did not show a direct correlation. The frequency of the decrease in the E'/A' ratio at the TVA was higher in patients with MPI increase (38.5% in patients with a decrease in MPI vs 76.5% in patients with an increase in MPI; Fisher's exact test, $P = .018$). In multivariate analysis, only IVA decrease at the VS was found to be a predictor of RV MPI increase ($\beta = -0.035$, $P < .001$).

As for the decrease in the IVA at the VS, age of patient at closure showed a significant correlation ($r = -0.32$, $P = .019$, Figure 3). The amount of shunt did not show any significant correlation with the decrease in the IVA, but the frequency of IVA decrease was higher in the larger shunt group than in the smaller shunt group (75.0% vs 48.0%; $P = .043$). In multivariate analysis, age of patient at closure ($\beta = -0.36$, $P = .002$), the Qp/Qs ratio ($\beta = -0.45$, $P = .01$), and RV MPI changes ($\beta = -7.64$, $P < .001$) were found to be independent predictors of IVA decrease at the VS.

4 | DISCUSSION

A longstanding atrial shunt may result in atrial arrhythmias and dysfunction of both ventricles.[25] Therefore, optimal timing of treatment is essential to avoid the progression of ventricular dysfunction. Because transcatheter closure is able to avoid confounding factors that affect ventricular function, such as cardiopulmonary bypass and pericardiotomy, it is valuable to evaluate hemodynamic changes caused by pure atrial shunts in patients with transcatheter ASD closure.[6,14] Many previous studies have shown that cardiac geometric changes or hemodynamic improvements occur after the procedure.[1–4] According to the results, cardiac remodeling, decrement of the RV size, and increase in LV volume were early postinterventional changes, occurring even within 1 hour after the procedure.[4,5,17] Although it was suggested that these acute changes in ventricular hemodynamics may affect

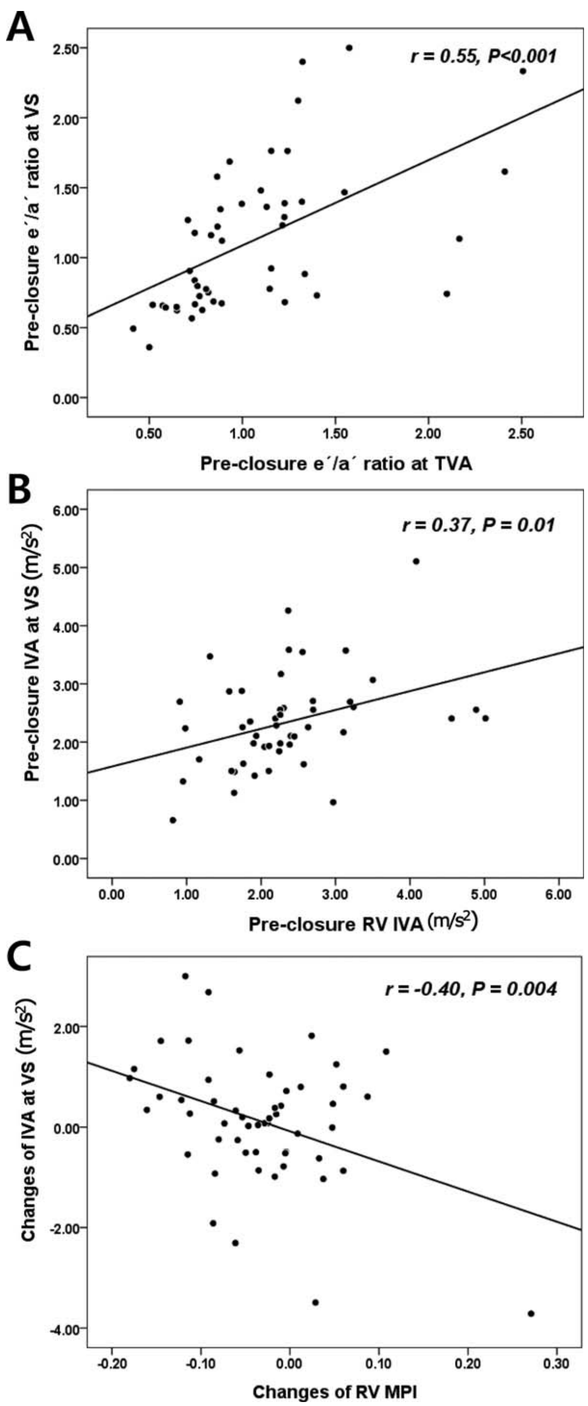

FIGURE 2 The interdependency of TDI parameters between both ventricles. (A) The preocclusional *E′*/*A′* ratios at the interventricular septum and tricuspid valve annulus showed a close correlation. (B) The preocclusional IVA at the interventricular septum and tricuspid annulus were significantly correlated. (C) The differences in the MPI at the tricuspid annulus before and 6 months after closure showed a significant reverse correlation with the differences in the IVA at the interventricular septum

ventricular function, consequences of ventricular function after the procedure were not completely understood.

In the evaluation of ventricular function, conventional Doppler echocardiography depends greatly on preloads and is, therefore, limited in the assessment of pure ventricular function in the volume loading condition. Although TDI is not free from the effects of volume load, some nonvolumetric markers derived from TDI are recognized as sensitive and less load-dependent indicators of ventricular function. Among them, we used the MPI and IVA as easily measurable parameters. Isovolumic acceleration is thought to correlate with intrinsic myocardial contractility[26] and has been validated as a sensitive load-independent index of LV and RV systolic function.[27] In our study, RV contractility (IVA at TVA) improved in all subgroups after ASD closure, in addition to RV volume-overload relief. Previous studies using magnetic resonance imaging (MRI) and three-dimensional echocardiography reported improvements in the RV EF after transcatheter ASD closure, which is consistent with our data.[7,16] The systolic myocardial velocity (*S′*) of the RV decreased significantly, reflecting a confounding effect of the volume load.[2,23] These results demonstrate that the IVA is a reliable index in the assessment of RV contractility, despite a loading condition.

Our study showed that RV global function (MPI) was impaired after closure in the old age group and larger shunt group. Additionally, the marker of diastolic function (the *E′*/*A′* ratio) simultaneously decreased in patients who showed worsening of the RV MPI. Some studies reported that the RV and/or LV MPI improved after transcatheter ASD closure,[3,7,8]; whereas, few studies reported an increase in the RV MPI after closure, which is consistent with our results.[18] We thought that this disagreement among previous studies was attributable to the heterogeneity of time intervals from closure and associated factors, such as age of patient and the amount of shunt flow. Therefore, we tried to assess the changes in ventricular performance according to the time course and associated factors, and only old-age patients and those with a large shunt showed deterioration in the RV MPI. A previous MRI study on RV function after transcatheter ASD closure[16] demonstrated that a rapid decrease in RV volume and relatively slow regression of RV mass could result in an increase in the mass/volume ratio, which might affect diastolic compliance. This physiologic finding might have reduced RV compliance, which resulted in an increase in the MPI, and it might depend on the amount of shunt and might be magnified in old-age patients with underlying diastolic dysfunction. In comparison, RV EF measured using MRI increased constantly after closure,[16] and this finding is consistent with the increase in the RV IVA in our study.

It has been suggested that LV dysfunction after ASD closure is mainly caused by the restrictive physiology of the LV.[9–11] However, in our study, impairment in LV systolic function developed in the old age group and the larger shunt group, which has been reported in a previous study using the strain rate.[19] Although LV EF improved in both the old age group (before closure, 66.2 ± 7.5%; 6 months after, 70.1 ± 5.1%; $P = .003$) and the larger shunt group (before closure, 64.5 ± 6.5%; 6 months after, 69.4 ± 5.3%; $P = .002$), *S′* and IVA decreased and were maintained until 6 months after ASD closure. It is not evident whether a LV, which has been deprived of volume for a lifetime, can promptly adapt to acute volume overload. In our study, age at closure, the Qp/Qs ratio, and RV global dysfunction were associated with

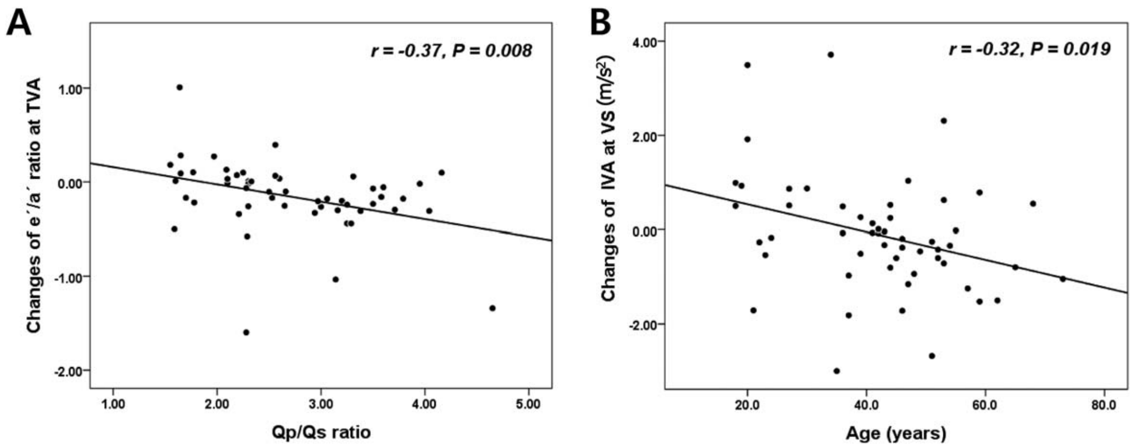

FIGURE 3 The influence of clinical factors on TDI parameters after atrial septal defect closure. (A) The Qp/Qs ratio was inversely correlated with the changes of the E'/A' ratio at the tricuspid annulus after ASD closure. (B) The age of patient was inversely correlated with the changes of the IVA at the ventricular septum after ASD closure

worsening of LV systolic function. According to the hypothesis by Ryan et al, it is possible that the duration of the volume deprived period and the magnitude of the acute volume load for the LV influenced LV systolic dysfunction after ASD closure. Although our study was not able to affirm the mechanism of LV systolic dysfunction after ASD closure, it validated the necessity of close observation for LV systolic dysfunction in elderly patients and patients with large shunts.

In our study, TDI parameters for both ventricles inconsistently changed with time. Previous studies on ventricular function after ASD closure involved different and inconsistent follow-up periods; therefore, the results were rather inconclusive.[28–30] Takaya et al reported that the improvement in exercise capacity was delayed to 6 months after ASD closure in patients older than 40 years.[30] Additionally, our results showed that the alteration and adaptation of ventricular function for the acute changes in volume status and geometry can be delayed and persist several months after closure, with differential times in both ventricles. Therefore, a long-term follow-up study of patients after ASD closure at both ventricles is needed.

4.1 | Limitations

As a limitation of our study, the LV was not fully evaluated by TDI and the TDI parameters at mitral annulus including E/E' could not be investigated. Because the axis of the ventricles severely tilted to the left due to the huge dilated RV, the angle between the ultrasound beam and the direction of wall motion at the mitral annulus was not acceptable in a considerable number of subjects. To overcome this limitation, studies using two-dimensional strain and strain rate are suggested. These newly developed tools directly measure two-dimensional movement with angle-independency. Also this study did not present the information on RV mass and pulmonary hypertension that associated RV function.

In previous studies, the intraobserver variability of measurements by pulsed-wave TDI was reported as 6–12%.[31,32] However, the reproducibility of TDI was concerned in some reports especially for the slope measurement,[33] and some researchers have suggested about the superiority of color coded TDI. In our study, we did not assess the intraobserver variability and it is the limitation in terms of reliability of measurements.

This study was conducted retrospectively, and the follow-up period of our study was relatively short and the number of subjects was relatively small. Considering that ventricular remodeling in patients after ASD closure is differential relative to the time course, a long-term follow-up evaluation with a larger number of subjects is needed.

5 | CONCLUSIONS

After transcatheter ASD closure, in addition to the elimination of RV volume overload, RV function by IVA improved. However, in old-age patients and those with large shunts, global function was impaired with deterioration of RV diastolic markers. LV systolic function decreased after the procedure. With regard to the time course of the alteration in ventricular function, it can be delayed and persist several months after closure, with differential times in both ventricles. Therefore, a close long-term observation of RV and LV dysfunction is required after transcatheter ASD closure, especially in old-age patients and those with large shunts.

ACKNOWLEDGMENT

None

AUTHOR CONTRIBUTIONS

Manuscript writing: Yoo, Kim, Eun
Data management: Yoo, Kim
Data analysis: Yoo, Eun
Manuscript review: Eun, Choi, Kim
Data collection: Choi, Kim

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ORCID

Lucy Y . Eun http://orcid.org/0000-0002-4577-3168

REFERENCES

[1] Jategaonkar S, Scholtz W, Schmidt H, Horstkotte D. Percutaneous closure of atrial septal defects: echocardiographic and functional results in patients older than 60 years. *Circ Cardiovasc Interv*. 2009;2:85–89.

[2] Khan AA, Tan JL, Li W, et al. The impact of transcatheter atrial septal defect closure in the older population. *J Am Coll Cardiol Interv*. 2010;3:276–281.

[3] Salehian O, Horlick E, Schwerzmann M, et al. Improvements in cardiac form and function after transcatheter closure of secundum atrial septal defects. *J Am Coll Cardiol*. 2005;45:499–504.

[4] Du ZD, Cao QL, Koenig P, Heitschmidt M, Hijazi ZM. Speed of normalization of right ventricular volume overload after transcatheter closure of atrial septal defect in children and adults. *Am J Cardiol*. 2001;88:1450–1453.

[5] Thilén U, Persson S. Closure of atrial septal defect in adult cardiac remodeling is an early event. *Int J Cardiol*. 2006;108:370–375.

[6] Cheung YF, Lun KS, Chau AK. Doppler tissue imaging analysis of ventricular function after surgical and transcatheter closure of atrial septal defect. *Am J Cardiol*. 2004;93:375–378.

[7] Ding J, Ma G, Huang Y, et al. Right ventricular remodeling after transcatheter closure of atrial septal defect. *Echocardiography*. 2009;26:1146–1152.

[8] Ding J, Ma G, Wang C, et al. Acute effect of transcatheter closure on right ventricular function in patients with atrial septal defect assessed by tissue Doppler imaging. *Acta Cardiol*. 2009;64:303–309.

[9] Ewert P, Berger F, Nagdyman N, et al. Masked left ventricular restriction in elderly patients with atrial septal defects: a contraindication for closure? *Cather Cardiovasc Interv*. 2001;52:177–180.

[10] Schubert S, Peters B, Abdul-Khaliq H, Nagdyman N, Lange PE, Ewert P. Left ventricular conditioning in the elderly patient to prevent congestive heart failure after transcatheter closure of atrial septal defect. *Catheter Cardiovasc Interv*. 2005;64:333–337.

[11] Masutani S, Taketazu M, Mihara C, et al. Usefulness of early diastolic mitral annular velocity to predict plasma levels of brain natriuretic peptide and transient heart failure development after device closure of atrial septal defect. *Am J Cardiol*. 2009;104:1732–1736.

[12] Murphy JG, Gersh BJ, McGoon MD, et al. Long-term outcome after surgical repair of isolated atrial septal defect. Follow-up at 27 to 32 years. *N Engl J Med*. 1990;323:1645–1650.

[13] Pascotto M, Caso P, Santoro G, et al. Analysis of right ventricular Doppler tissue imaging and load dependence in patients undergoing percutaneous closure of atrial septal defect. *Am J Cardiol*. 2004;94:1202–1205.

[14] Abd El Rahman MY, Hui W, Timme J, et al. Analysis of atrial and ventricular performance by tissue doppler imaging in patients with atrial septal defects before and after surgical and catheter closure. *Echocardiography*. 2005;22:579–585.

[15] Pascotto M, Santoro G, Caso P, et al. Global and regional left ventricular function in patients undergoing transcatheter closure of secundum atrial septal defect. *Am J Cardiol*. 2005;96:439–442.

[16] Schoen SP, Kittner T, Bohl S, et al. Transcatheter closure of atrial septal defects improves right ventricular volume, mass, function, pulmonary pressure, and functional class: a magnetic resonance imaging study. *Heart*. 2006;92:821–826.

[17] Burgstahler C, Wöhrle J, Kochs M, et al. Magnetic resonance imaging to assess acute changes in atrial and ventricular parameters after transcatheter closure of atrial septal defects. *Imaging*. 2007;25:1136–1140.

[18] Wu ET, Akagi T, Taniguchi M, et al. Differences in right and left ventricular remodeling after transcatheter closure of atrial septal defect among adults. *Cather Cardiovasc Interv*. 2007;69:866–871.

[19] Eyskens B, Ganame J, Claus P, Boshoff D, Gewillig M, Mertens L. Ultrasonic strain rate and strain imaging of the right ventricle in children before and after percutaneous closure of an atrial septal defect. *J Am Soc Echocardiogr*. 2006;19:994–1000.

[20] Cannesson M, Jacques D, Pinsky MR, Gorcsan J. 3rd. Effects of modulation of left ventricular contractile state and loading conditions on tissue Doppler myocardial performance index. *Am J Physiol Heart Circ Physiol*. 2006;290:1952–1959.

[21] Su HM, Lin TH, Voon WC, et al. Correlation of TEI index obtained from tissue Doppler echocardiography with invasive measurements of left ventricular performance. *Echocardiography*. 2007;24:252–257.

[22] Vogel M, Schmidt MR, Kristiansen SB, et al. Validation of myocardial acceleration during isovolumic contraction as a novel noninvasive index of right ventricular contractility: comparison with ventricular pressure-volume relations in an animal model. *Circulation*. 2002;105:1693–1699.

[23] Pauliks LB, Chan KC, Chang D, et al. Regional myocardial velocities and isovolumic contraction acceleration before and after device closure of atrial septal defects: A color tissue Doppler study. *Am Heart J*. 2005;150:294–301.

[24] Yao GH, Zhang M, Yin LX, et al. Doppler Echocardiographic Measurements in Normal ChineseAdults (EMINCA): a prospective, nationwide, and multicentre study. *Eur Heart J Cardiovasc Imaging*. 2016;17:512–522.

[25] Walker RE, Moran AM, Gauvreau K, Colan SD. Evidence of adverse ventricular interdependence in patients with atrial septal defects. *Am J Cardiol*. 2004;93:1374–1377.

[26] Vogel M, Derrick G, White PA, et al. Systemic ventricular function in patients with transposition of the great arteries after atrial repair: a tissue Doppler and conductance catheter study. *J Am Coll Cardiol*. 2004;43:100–106.

[27] Vogel M, Cheung MM, Li J, et al. Noninvasive assessment of left ventricular force-frequency relationships using tissue Doppler-derived isovolumic acceleration: validation in an animal model. *Circulation*. 2003;107:1647–1652.

[28] Eroglu E, Cakal SD, Cakal B, et al. Time course of right ventricular remodeling after percutaneous atrial septal defect closure: assessment of regional deformation properties with two-dimensional strain and strain rate imaging. *Echocardiography*. 2013;30:324–330.

[29] Kaya MG, Baykan A, Dogan A, et al. Intermediate-term effects of transcatheter secundum atrial septal defect closure on cardiac remodeling in children and adults. *Pediatr Cardiol*. 2010;31:474–482.

[30] Takaya Y, Taniguchi M, Akagi T, et al. Long-term effects of transcatheter closure of atrial septal defect on cardiac remodeling and exercise capacity in patients older than 40 years with a reduction in cardiopulmonary function. *J Interv Cardiol*. 2013;26:195–199.

[31] Olsen NT, Mogelvang R, Sogaard P, et al. Pulsed-wave tissue Doppler and color tissue Doppler echocardiography: calibration with M-

mode, agreement, and reproducibility in a clinical setting. *Echocardiography*. 2009;26:638–644.

[32] Cetiner MA, Sayin MR, Yildirim N, et al. Right ventricular isovolumic acceleration in acute pulmonary embolism. *Echocardiography*. 2014; 31:1253–1258.

[33] Punn R, Behzadian F, Tacy TA. Tissue Doppler-derived measurement of isovolumic myocardial contraction in the pediatric population. *Pediatr Cardiol*. 2012;33:720–727.

How to cite this article: Yoo BW, Kim JO, Eun LY, Choi JY, Kim DS. Time course of the changes in right and left ventricle function and associated factors after transcatheter closure of atrial septal defects. *Congenital Heart Disease*. 2018;13:131–139. https://doi.org/10.1111/chd.12541