Journal of Cardiology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Original article

Intergenerational differences in the effects of transcatheter closure of atrial septal defects on cardiac function

Hideki Tashiro (MD, PhD)[a,*], Kenji Suda (MD, PhD, FJCC)[b], Motofumi Iemura (MD, PhD)[c], Youzou Teramachi (MD)[c]

[a] *Division of Cardiology, St. Mary's Hospital, Kurume, Japan*
[b] *Department of Pediatrics, Kurume University, Kurume, Japan*
[c] *Division of Pediatric Cardiology, St. Mary's Hospital, Kurume, Japan*

ARTICLE INFO

Article history:
Received 13 August 2016
Received in revised form 14 March 2017
Accepted 19 March 2017
Available online xxx

Keywords:
Congenital heart disease
Transcatheter closure of atrial sepal defect
Diastolic dysfunction
Echocardiography

ABSTRACT

Background: Little is known regarding intergenerational differences in the effects of atrial sepal defect (ASD) closure on the left heart. We therefore analyzed age-related serial changes in the left heart following ASD closure.
Methods: We studied 50 patients with an isolated ASD who underwent successful transcatheter closure using Amplatzer septal occluders (St. Jude Medical, Little Canada, MN, USA) between June 2007 and June 2013. Patients were divided into three age groups: young patients aged ≤17 years; middle-aged patients aged 18–50 years; and older patients aged >50 years. Multi-modal echocardiographic studies with different views were performed before and at 1 day, 1–3 months, and 6–12 months after ASD closure. Echocardiographic variables were compared among the groups at different time points after closure.
Results: Left ventricular end-diastolic and end-systolic volume indices (EDVI and ESVI) in the older group were significantly smaller than those in the other groups before closure. EDVI and ESVI increased with time after closure in all groups with stable ejection fractions. However, EDVI and ESVI remained significantly smaller in the older group compared with the other groups. There was a significant interaction among the age groups only in terms of left atrial volume index (LAVI). LAVI increased significantly with time in the older group, but did not change in the other groups.
Conclusion: Although the left ventricle enlarged with time after ASD closure in all age groups, left ventricular size in older patients never reached that in younger patients. In addition to this inadequate enlargement of the left ventricle, diastolic dysfunction might also result in late left atrial enlargement in older patients following ASD closure.

Secundum-type atrial septal defect (ASD) is a common form of congenital heart disease [1]. Transcatheter closure has been established as an alternative treatment to surgical closure for isolated secundum-type ASD [2,3], and several studies have described transcatheter closure as a safe and minimally invasive therapy for ASD [4,5]. Although transcatheter repair is associated with low risk and can be definite in older patients [6], differences among generations in terms of left-heart responses to disappearance of the left-to-right shunt following ASD closure remain unclear. We therefore analyzed serial echocardiographic changes in the left heart in different generations to compare the age-related chronic effects of ASD closure on left ventricular (LV) diastolic and systolic volumes and functions.

Methods

We retrospectively studied 50 patients with an isolated ASD who underwent successful transcatheter closure at St. Mary's Hospital between June 2007 and June 2013, and for whom sufficient data were available. This study complied with the Declaration of Helsinki. ASD closure was performed using Amplatzer septal occluders (St. Jude Medical, Little Canada, MN, USA) in all patients. All patients were in sinus rhythm at the time of echocardiography and without ischemic heart disease at ASD closure. The definitions of hypertension were based on the Japanese Society of Hypertension Guidelines for the Management of Hypertension 2014. Development of heart failure was diagnosed

* Corresponding author at: Division of Cardiology, St. Mary's Hospital, 422 Tubuku-honmachi, Kurume 830-8543, Japan.
E-mail address: tashiro@st-mary-med.or.jp (H. Tashiro).

http://dx.doi.org/10.1016/j.jjcc.2017.03.014
0914-5087/© 2017 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

by apparent heart failure symptoms, cardiomegaly, or effusion on chest X-ray, and laboratory data. In this retrospective analysis, the patients were divided into three groups according to their age: a young group ≤17 years ($n = 17$, 6 males); a middle-aged group aged 18–50 years ($n = 19$ patients, 4 males); and an older group aged >50 years ($n = 14$ patients, 3 males).

All patients underwent multi-modal echocardiography before and 1 day, 1–3 months, and 6–12 months after ASD closure. Echocardiographic images, including 2-dimensional and Doppler studies, were obtained using a Vivid 7 (General Electric Company, Fairfield, CT, USA) with standard parasternal and apical views.

LV end-diastolic and end-systolic volumes were measured in conventional 2-dimensional echocardiography using the biplane-modified Simpson's method, and the ejection fraction (EF) was calculated. Cardiac output was calculated as follows: (LV end-diastolic volume − end-systolic volume) × heart rate. Left atrial (LA) volume was determined by the biplane area–length method. Right atrial (RA) area was estimated by planimetry at the end of ventricular systole in the apical 4-chamber view [7]. All these values were measured using the EchoPac PC (General Electric Company) and indexed to body surface area.

Transmitral inflow velocity was recorded from conventional pulsed wave Doppler in the apical view. Deceleration time, peak velocity of early diastolic inflow (E), and peak flow velocity of late diastolic inflow (A) were measured [8] and the E/A ratio was calculated.

In tissue Doppler imaging, the sampling volume was placed at the basal lateral wall in the apical 4-chamber view [8,9] and peak early diastolic mitral annular velocity (e′) was recorded.

LV mass before ASD closure was calculated in B-mode using the area–length method [10] according to American Society of Echocardiography recommendations, and indexed to body surface area. The ratio of LV mass divided by end-diastolic volume was determined for each patient.

Demographic variables at ASD closure, including height and weight, and comorbidities, such as diabetes, hypertension, and paroxysmal atrial fibrillation, were determined. Hemodynamic variables, including mean pulmonary artery pressure, systolic and diastolic aortic pressures, mean LA pressure, pulmonary-to-systemic flow ratio, and pulmonary vascular resistance were measured by cardiac catheterization. Transesophageal echocardiography was performed at ASD closure and the device sizes were determined. The defect widths on the major and minor axes were measured. The area of the defect was calculated by assuming its shape to be an ideal ellipse and using the formula: area of the defect = $\pi ab/4$, where a is width on the major axis and b is width on the minor axis [11]. ASD area and device size were indexed to body surface area.

All variables are expressed as the mean ± standard deviation. Data before ASD closure were compared with data 1 day, 1–3 months, and 6–12 months after closure by repeated analysis of variance (ANOVA). Post hoc comparisons were analyzed by Tukey's test. Causes of changes in LA volume and end-diastolic volume index (EDVI) before and at 6–12 months after ASD closure were analyzed by stepwise multiple regression analysis. Data were analyzed using the JMP software package for Windows (version 8, SAS institute, Cary, NC, USA). A value of $p < 0.05$ was considered to be significant.

Results

The patients' backgrounds are shown in Table 1. As expected, body height and body surface area were significantly lower in the young group compared with the other groups ($p < 0.001$). Body weight was significantly lower in the young group compared with the middle-aged group ($p = 0.001$) (Table 1). Mean pulmonary artery pressure was significantly lower in the middle-aged group ($p = 0.012$) and LA pressure was significantly higher in the young group compared with the older group ($p = 0.012$) (Table 1). The incidences of hypertension ($p = 0.019$) and paroxysmal atrial fibrillation ($p < 0.001$) were significantly higher in the older group compared with the other groups (Table 1).

Echocardiographic and Doppler indices before ASD closure are shown in Table 2. Before ASD closure, EDVI ($p < 0.001$) and end-systolic volume index (ESVI) ($p = 0.004$) were significantly smaller, but left atrial volume index (LAVI) ($p < 0.001$) was significantly larger in the older group compared with the other groups. Cardiac index was lower in the older group than in the other groups ($p < 0.001$). The E/A ratio ($p < 0.001$) and e' ($p < 0.001$) were significantly lower but E/e' was significantly higher in the older group compared with the other groups ($p = 0.008$), and the deceleration time was significantly longer in the older group compared with the young group ($p = 0.014$). There was no significant difference in LV mass index among the groups ($p = 0.129$), but the LV mass divided by end-diastolic volume

Table 1
Patient characteristics.

	Young group	Middle-aged group	Older group	p-value
Number of patients	17	19	14	
Age (years)	11.9 ± 3.1*,#	28.3 ± 8.0#	63 ± 9	<0.001
Mean PA (mmHg)	15 ± 3	13 ± 3#	16 ± 4	0.012
Systolic Ao (mmHg)	92 ± 15	91 ± 12	97 ± 26	0.590
Diastolic Ao (mmHg)	51 ± 7	53 ± 9	50 ± 12	0.666
Mean LA (mmHg)	9 ± 3#	7 ± 3	7 ± 2	0.012
Qp/Qs	2.2 ± 1.0	2.3 ± 1.0	2.7 ± 1.0	0.379
Shunt Ratio (%)	49.2 ± 18.4	50.5 ± 18.8	52.9 ± 23.9	0.860
PVRI (dyne sec cm^{-5} m^{-2})	59.8 ± 32.6	47.1 ± 18.8	70.4 ± 35.6	0.082
Device size index (mm/m^2)	14.1 ± 4.7*	11.1 ± 3.6	14.1 ± 3.5*	0.037
Height (cm)	143.5 ± 18.3* #	162.0 ± 7.5	156.0 ± 6.9	<0.001
Weight (kg)	40.6 ± 18.2*	57.8 ± 8.9	51.9 ± 9.8	0.001
BSA (kg/m^2)	1.2 ± 0.3* #	1.6 ± 0.2	1.5 ± 0.2	<0.001
Heart Failure	0%	0%	7%	0.270
Hypertension	0%#	5%#	29%	0.019
Diabetic Mellitus	0%	5%	14%	0.185
Paroxysmal Atrial Fibrillation	0%#	0%#	36%	<0.001

PA, pulmonary artery; Ao, aorta; LA, left atrium; Qp/Qs, pulmonary-to-systemic flow ratio; PVRI, pulmonary vascular resistance index; BSA, body surface area.
* $p < 0.05$ vs middle-aged group.
# $p < 0.05$ vs. older group.