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Natural history of medium-sized atrial septal defect in pediatric cases

Takekatsu Saito (MD), Kunio Ohta (MD, PhD)*, Yuko Nakayama (MD), Yoko Hashida (MD), Akiko Maeda (MD), Keiko Maruhashi (MD, PhD), Akihiro Yachie (MD, PhD)

Department of Pediatrics, Angiogenesis and Vascular Development, Graduate School of Medical Science, Kanazawa University, Kanazawa, Japan

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ABSTRACT

Background: The indication for surgical repair of atrial septal defect (ASD) is pulmonary to systemic blood flow ratio (Q_p/Q_s) > 2.0, and therapeutic strategy depends on the facility in cases of Q_p/Q_s 1.5–2.0. Defect size increases with age, but hemodynamic changes of medium-sized ASD (Q_p/Q_s 1.5–2.0) are unknown.
Methods and results: From April 1, 1985 to March 31, 2008, we experienced 125 cases of cardiac catheterization for ASD. Twelve cases were re-evaluated without surgical repair. The first and second catheterizations were performed at median ages of 7 years (range, 2–13 years) and 16 years (range, 5–19 years), respectively. The mean follow-up period was 7 years. Q_p/Q_s increased from 1.6 to 2.0 during follow-up ($p < 0.05$). Of four cases with $Q_p/Q_s < 1.5$ at initial presentation, three had $Q_p/Q_s \geq 1.5$ at second inspection. Right ventricle diastolic volume (RVEDV/LVEDV) also increased.
Conclusions: Q_p/Q_s and RVEDV/LVEDV of medium-sized ASD increase together in childhood. Re-evaluation before adulthood should be considered in patients with no indications of ASD closure in childhood.

Introduction

Atrial septal defect (ASD) occurs at an incidence rate of 1 per 1500 live births. There are usually no symptoms in childhood, and ASD is discovered by chance due to a heart murmur [1]. However, ASD patients have age-related chronic volume overload of the right atrium and right ventricle due to left to right shunt through the defect, pulmonary hypertension, and atrial arrhythmia, and heart failure may occur later in life [2,3]. As there are no differences in prognosis or lifespan between patients and healthy subjects if the defect is closed in childhood [4], and the presence of right ventricular volume overload depends on significant left to right shunt through the defect, surgical repair is generally performed in childhood. The indication for surgical repair of ASD is generally $Q_p/Q_s > 1.5$ [5] or 2.0, indication for catheter treatment is $Q_p/Q_s > 1.5$ [6]. The strategy of treatment for ASD cases with Q_p/Q_s 1.5–2.0 depends on the policy of each facility. The strategy in our institution is that surgical repair is performed in cases with $Q_p/Q_s > 2.0$; in cases with Q_p/Q_s 1.5–2.0, the patient awaits the start of catheter treatment in Japan without surgical repair. Many previous reports regarding the natural history of small ASD defects described spontaneous closure [7–12]. However, defects larger than a certain threshold increase in size with age [13,14]. There have been few reports regarding the natural history of borderline cases. The aim of this study was to clarify the natural history of ASD with Q_p/Q_s 1.5–2.0 in childhood from a hemodynamic perspective.

Methods

Patients

During the period from April 1, 1985 to March 31, 2008, we experienced 125 cases of cardiac catheterization for ASD. Twelve of these cases were re-evaluated without surgical repair before school age or reaching adulthood. The diagnosis of ASD secundum was made by transthoracic echocardiography or transesophageal echocardiography. Subjects with partial anomalous pulmonary venous connection, pulmonary valve stenosis, and other cases of congenital heart disease were excluded from the study. Those with pulmonary hypertension in cardiac catheterization, Down's syndrome, and other chromosomal abnormalities were also excluded. These 12 cases were examined retrospectively for changes in hemodynamics using catheterization data and echocardiographic data.

Hemodynamic evaluation

To evaluate the hemodynamic data, the pulmonary to systemic blood flow ratio (Q_p/Q_s) was calculated using the Fick method based on data of cardiac catheterization. We used the superior vena cava as mixed venous blood data and the average values of

* Corresponding author at: 13-1 Takara-machi, Kanazawa 920-8641, Japan. Tel.: +81 76 265 2313; fax: +81 76 262 1866.
E-mail address: kohta@staff.kanazawa-u.ac.jp (K. Ohta).

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Table 1
Patient characteristics.

Case	12 cases		Male 7 cases, female 5 cases
Age	1st catheterization	Median	7 y (2–13 y)
	2nd catheterization	Median	16 y (5–19 y)
Follow-up period		Mean	7.1 y (3.0–12.9 y)
BSA	1st catheterization	Mean	0.97 m^2 (0.48–1.53)
	2nd catheterization	Mean	1.45 m^2 (0.70–1.92)
MPAp mean	1st catheterization	Mean	14 mmHg (10–20)
	2nd catheterization	Mean	15 mmHg (12–22) ns*
ΔMPAp-RVp	1st catheterization	Mean	5 mmHg (1–10)
	2nd catheterization	Mean	6 mmHg (1–18) ns*

MPAp, main pulmonary artery pressure; ΔMPAp-RVp, pressure gradient between main pulmonary artery and right ventricle.
* ns, not significant ($p > 0.05$).

right and left pulmonary artery as pulmonary artery blood data. In addition, we calculated the right ventricular end-diastolic volume (RVEDV) and right ventricular ejection fraction (RVEF) using the Simpson method [15] based on right ventricular angiography and calculated the left ventricular end-diastolic volume (LVEDV) using the area-length method [16] based on left ventricular angiography. To determine the extent of right ventricular volume overload, using Nakazawa's normal value [17], the ratio of end-diastolic right ventricular volume under the normal value (%RVEDV) and end-diastolic volume ratio (RVEDV/LVEDV) was calculated. With regard to echocardiographic data, we measured ASD defect size in end-diastole in four chamber view. Then, we calculated the ratio of ASD diameter for left ventricular end-diastolic dimension (ASD/LVEDD).

Statistical analysis

These data were calculated at the first and second inspections. Data are presented as the means ± SD (minimum–maximum). Comparisons between paired data were performed using Mann–Whitney *U*-test, and $p < 0.05$ was considered to indicate statistical significance.

Results

Patient profile

The profiles of the patients are shown in Table 1. The first catheterization was performed at a median age of 7 years (range, 2–13 years), and second catheterization was performed at a median age of 16 years (range, 5–19 years). The mean follow-up period was 7 years. Nine patients (75%) were diagnosed by heart murmur, and three patients were diagnosed by electrocardiogram abnormalities (IRBBB) detected on routine examination at school. None of the patients were taking any medication and all were asymptomatic. There were no patients with pulmonary hypertension, and the pressure gradient between the main pulmonary artery and right ventricle did not change through first and second inspections.

Q_p/Q_s

Hemodynamic changes are shown in Fig. 1 and the changes in right ventricular volume (%RVEDV and RVEDV/LVEDV) are shown in Table 2. Q_p/Q_s, RVEDV/LVEDV were also increased in cases that had Q_p/Q_s below 2.0 at the initial inspection ($p < 0.05$). Of four cases with Q_p/Q_s below 1.5 at the initial inspection, three cases had Q_p/Q_s of 1.5 or more at the second inspection.

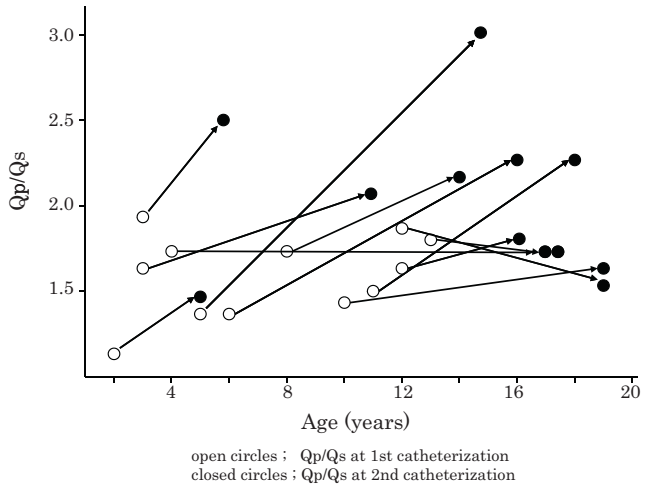

Fig. 1. Q_p/Q_s increased from 1.6 to 2.0 during the follow-up period ($p < 0.05$). Of four cases with Q_p/Q_s below 1.5 at the initial inspection, three cases had Q_p/Q_s of 1.5 or more at the second inspection. Open circles: Q_p/Q_s at 1st catheterization. Closed circles: Q_p/Q_s at 2nd catheterization.

RV volume overload

The changes in right ventricular volume (%RVEDV and RVEDV/LVEDV) are shown in Table 2. Q_p/Q_s, RVEDV/LVEDV were also increased in cases that had Q_p/Q_s below 2.0 at the initial inspection. When cases were divided into before school age (<7 years) and school age (>7 years), Q_p/Q_s, RVEDV/LVEDV tended to increase more in the before school age group.

Echocardiographic findings

Echocardiography was performed in the same period. We calculated ASD/LVEDD. The left ventricular end-diastolic dimension of ASD is smaller than the age-matched normal value due to right ventricular volume overload [18,19]. We evaluated the relative changes in ASD diameter with age. We hypothesized that ASD/LVEDD will be larger when ASD size has increased beyond the age-related changes. In fact, ASD diameter of a 2-year-old patient changed from 9 mm to 27 mm, and ASD/LVEDD changed from 0.39 to 0.75 over 9.5 years. However, the ASD diameter and ASD/LVEDD did not increase with age: 8.9 ± 1.9 mm to 11.5 ± 3.8 mm, $p = 0.20$; 0.27 ± 0.09 to 0.29 ± 0.09, $p = 0.68$).

Discussion

The indication for closure of ASD is determined by the ratio of pulmonary to systemic blood flow ratio (Q_p/Q_s) > 2.0 and generally there is no indication in cases in which Q_p/Q_s is lower than 1.5. When Q_p/Q_s is between 1.5 and 2.0, indication is considered based on pulmonary artery pressure and age [4]. Transcatheter

Table 2
Hemodynamic evaluation.

	1st catheterization	2nd catheterization	
Total ($n = 12$)			
Q_p/Q_s	1.6 ± 0.2 (1.1–1.9)	2.0 ± 0.5 (1.4–3.1)	$p < 0.05$
%RVEDV	129 ± 23 (96–182)	138 ± 21 (119–192)	ns*
RVEDV/LVEDV	1.35 ± 0.30 (1.04–1.88)	1.57 ± 0.18 (1.33–1.94)	$p < 0.05$
RVEF	0.62 ± 0.07 (0.51–0.79)	0.63 ± 0.08 (0.49–0.79)	ns*

RVEDV, % of normal value by Nakazawa's normal equation; RVEDV/LVEDV, ratio of right ventricular end-diastolic volume and left ventricular end-diastolic volume.
* ns, not significant ($p > 0.05$).

techniques for closure of ASD became available in the 1990s. The Amplatzer septal occluder (ASO) [20,21] is used worldwide for closure of ASD although systematic information about fluoroscopy time and radiation dosage applied during catheter intervention is still not enough [22]. Use of the ASO is considered in cases of ostium secundum defects with a rim of sufficient size, in which the defect is smaller than the size of the largest device. However, other indications for ASD closure (catheter closure and surgical closure) are the same. $Q_p/Q_s > 1.5$, and enlargement of the right atrium and ventricle are considered indications for use of ASO [6,23].

On the other hand, reports from some facilities [13,14,24] indicated that ASD size may become larger while waiting for ASO treatment, and it may deviate from the indications for treatment. Totrtoriello [24] reported that small ASD (defect size 3–4 mm) enlarged to 24 mm after 6 years. We also treated an infant with a defect size that enlarged from 9 mm to 27 mm over a period of 9 years. The male patient underwent surgical repair because his posterior rim was too short for ASO closure by transesophageal echocardiography at 9 years of age.

The natural history of ASDs like those reported here was seen in previous echocardiographic evaluations, many of which showed spontaneous closure [7–12]. The rate of spontaneous closure varied, ranging from 4% [13] to 70% [10]. These differences can be explained by varying selection of study populations. In addition, the rate of defect enlargement varied, ranging from 29% [14] to 65% [13]. However, none of our cases showed spontaneous closure of ASD or shrinkage of the defect; moreover, in 11 of 12 cases, Q_p/Q_s increased to above 1.5 at second catheterization. This was considered due to right ventricular volume overload in all cases, and the defect size at the initial echocardiographic examination was approximately > 6 mm. This defect size was classified as moderate to large [13]. It is generally believed that increases in diameter of ASD are related to increased compliance of the right ventricle, increased blood flow-through defects, and the increased right atrium size with age [13]. Liberthon [25] reported that right ventricular volume overload was increased and right ventricular ejection function was decreased in adult ASD. Bonow [18] reported that decreased compliance of the left ventricle with aging affects the increase in left-to-right shunt flow-through defects. Helgason [8] reported that the short axis of the defect was extended gradually in echocardiographic assessment. Graham [15] reported right ventricle volume overload by angiographic examination. He reported that cases of congenital heart disease with right ventricular volume overload, such as ASD, showed significant increases in RVEDV/LVEDV. Our cases in pediatric patients showed a tendency for an increase in RVEDV/LVEDV with no change in RVEF, while the other reported the cases in adults where increased RVEDV/LVEDV tends to reduce RVEF [25].

Many previous reports [9,11,12,14,24] based on echocardiography indicated that the size of the ASD defect on initial examination is related to the increase of the ASD defect size. Especially, larger defects expand easily because the increased blood flow through larger defects is responsible for right atrium and ASD expansion [13]. However, the changes in shunt flow with age cannot be re-evaluated by catheterization after surgical closure. Therefore, there have been few reports of hemodynamic data. Tsuchioka [26] divided patients into five groups according to age before intracardiac repair, and Q_p/Q_s values were compared in each group; he reported that there were no chronological changes in Q_p/Q_s. There have been only a few reports from the 1960s and 1970s [27,28] regarding hemodynamic changes in the same case. Andersen [28] reported that Q_p/Q_s increased with age in 4 of 39 cases with Q_p/Q_s 1.3–1.9, but did not describe the reasons for these findings. In our cases, ASD diameter and ASD/LVEDD did not change. The increasing ASD shunt in childhood may be related to factors other than increasing ASD diameter (i.e. expansion of RVEDV by increased RV compliance).

Study limitations

The major limitation of this study is that it was a retrospective study with a small number of cases.

Conclusions

Q_p/Q_s and RVEDV/LVEDV of medium size ASD (Q_p/Q_s 1.5–2.0) increase together in childhood. Especially, of four cases with Q_p/Q_s below 1.5 at initial inspection, three cases had a Q_p/Q_s of $\geq$1.5 at second inspection. The number of cases of ASD awaiting ASO closure in childhood will likely increase in future [28]. Therefore, re-evaluation before adulthood should be considered in patients with no indication of ASD closure in childhood, because patients with right ventricular volume overload in childhood will be indicated for ASD closure with increased Q_p/Q_s.

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