real-time three-dimensional (3D) TEE.[4,5] From the standpoint of echocardiographic options for transcatheter closure of an interatrial septum in the catheterization laboratory, the small size of the micro-TEE probe may be better tolerated without general anesthesia for a prolonged procedure such as ASD closure, as compared to a standard TEE probe. In addition, micro-TEE has some advantages compared to intracardiac echocardiography in terms of capability of multiplane, reusability, avoiding vascular complications and cost effectiveness. However, image quality of the current micro-TEE probe is inferior to that of a conventional adult TEE probe, and inability of 3D imaging by a micro-TEE probe can also be a limitation.

Micro-TEE could provide adequate information with a less invasive procedure even in patients with a large ASD. Micro-TEE has the potential to become a novel imaging option for interventions of the interatrial septum.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Movie clip S1: Short-axis view with micro-TEE shows a large atrial septal defect (ASD) and a deficient superior-anterior rim.

Movie clip S2: The micro-TEE shows that both disks are on the appropriate sides of the interatrial septum.

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Transcatheter Closure of Atrial Septal Defect in a Geriatric Population

Koji Nakagawa,[1] MD, Teiji Akagi,[2*] MD, PhD, FSCAI, Manabu Taniguchi,[2] MD, PhD, Yasufumi Kijima,[1] MD, Keiji Goto,[3] MD, PhD, Kengo F. Kusano,[1] MD, PhD, Hiroshi Itoh,[1] MD, PhD, and Shunji Sano,[4] MD, PhD

Objectives: To evaluate the efficacy and safety of transcatheter closure of atrial septal defects (ASD) in patients over 70 years of age. **Background:** Transcatheter closure of ASD is an established procedure in children and young adults, but the benefits of this procedure in geriatric patients are still unclear. **Methods:** Between 2005 and 2010, 430 patients with ASD underwent transcatheter closure in our hospital. Among those patients, 30 consecutive patients older than 70 years of age were prospectively evaluated. **Results:** Mean age at procedure was 75.8 ± 3.8 years (range: 70–85 years). Mean Qp/Qs was 2.4 ± 0.7 and mean ASD diameter was 20.3 ± 6.4 mm. Nine patients (30%) had a history of hospitalization due to heart failure. ASD closure was successfully performed in 28 patients (93%) without significant complications. During the follow-up period (mean period of 19.1 ± 11.3 months), New York Heart Association (NYHA) functional class was significantly improved in 20 patients (74%). Significant improvements of plasma BNP level, resting heart rate, and systolic pulmonary artery pressure were also observed. Improvement of tricuspid regurgitation was observed in 11 of 17 patients with moderate or severe regurgitation during the follow-up period. Conversely, worsening of mitral regurgitation was observed in 10 of the 27 patients. **Conclusion:** Transcatheter closure of ASD in geriatric patients can be performed safely. This procedure contributes to significant improvement of symptoms and positive cardiac remodeling. Long-term follow-up is mandatory, especially for patients with mitral regurgitation.

Key words: atrial septal defect; transcatheter closure; elderly

INTRODUCTION

The clinical features of atrial septal defect (ASD) in the elderly are significantly different from those in children and young adults. Elderly patients with ASD frequently present with hemodynamic abnormalities such as pulmonary hypertension, atrial arrhythmias, and valvular regurgitation, which cause congestive heart failure. Moreover, various comorbidities, such as hypertension, chronic obstructive pulmonary disease, coronary artery disease and left ventricular diastolic dysfunction often complicate the clinical features in this population. Left ventricular diastolic dysfunction, which is also seen as part of normal aging and frequently occurs in elderly individuals with hypertension or increased arterial stiffness [1,2], may cause acute

[1]Department of Cardiovascular Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
[2]Cardiac Intensive Care Unit, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
[3]Department of Anesthesiology and Resuscitology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
[4]Department of Cardiovascular Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Conflict of interest: Nothing to report.

*Correspondence to: Teiji Akagi, MD, PhD, FSCAI, Cardiac Intensive Care Unit, Okayama University Hospital, 2-5-1, Shikata-cho, Okayama 7008558, Japan. E-mail: t-akagi@cc.okayama-u.ac.jp

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congestive heart failure after ASD closure [3]. Therefore, ASD closure alone is sometimes insufficient for improvement of symptoms and heart failure in elderly ASD patients. Transcatheter ASD closure is a well-established alternative to surgical closure in children and young adults [4], and it has been shown to improve symptoms and hemodynamic abnormalities [5–11]. Recently, several studies have demonstrated that symptomatic reduction and cardiac remodeling can occur even in patients older than 60 years of age [12–15]. However, the benefits of transcatheter ASD closure in geriatric patients are still uncertain. In the present study, we focused on patients older than 70 years of age and assessed the clinical background of ASD and the feasibility of transcatheter ASD closure in this geriatric population.

METHODS

Study Population

From 2005 to 2010, transcatheter closure of ASD was attempted in 420 patients in our hospital. Of those patients, 30 patients who were older than 70 years were retrospectively assessed.

Indications for ASD closure were a significant left-to-right shunt, pulmonary and systemic blood flow ratio >1.5, volume overload of the right ventricle, and/or clinical symptoms of dyspnea, decompensation, or paradoxical embolism. Exclusion criteria included maximum defect diameter >38 mm evaluated by transesophageal echocardiography (TEE), other concomitant congenital heart disease, and pulmonary hypertension with pulmonary vascular resistance >8 Wood units.

Transcatheter ASD Closure

Transcatheter ASD closure was conducted under general anesthesia with the guidance of fluoroscopy and TEE. Amplatzer® Septal Occluder (St. Jude Medical; St. Paul, MN) was used for all closures, and the procedure was performed as previously described [16]. Because the largest device size available in Japan was 38 mm, the defect diameter >38 mm was included in exclusion criteria. For patients who had a history of heart failure and were considered to be hemodynamically highrisk, we placed a Swan-Ganz catheter into pulmonary artery from the other femoral vein and monitored pulmonary artery wedge pressure (PCWP) during subsequent procedure. And if mean PCWP increased >5 mm Hg from the baseline value during balloon occlusion of the defect (test balloon occlusion), the procedure was abandoned. All patients received 100 mg/day aspirin at least 48 hr before the procedure. After the procedure, the same dose of aspirin was continued for 6 months and clopidogrel was also given at 50 mg/day for 1 month in addition to aspirin. Other medications such as diuretics, warfarin, and antihypertension and antiarrhythmia drugs were continued at the same doses after the procedure. The procedure was explained and written informed consent was obtained from all patients.

Clinical Assessment and Follow-Up

All patients were assessed for medical history and comorbidity before ASD closure. Diagnostic cardiac catheter examinations including coronary angiography were performed before ASD closure. Pulmonary to systemic flow ratio (Qp/Qs) and pulmonary artery pressure were evaluated with cardiac catheterization. Mean pulmonary artery pressure =25 mm Hg at heart catheterization was considered as pulmonary artery hypertension. New York Heart Association (NYHA) functional class was assessed before and after ASD closure. Measurement of plasma B-type natriuretic peptide (BNP) and transthoracic echocardiographic evaluation were performed before ASD closure, 1 day and 6 to 12 months after the procedure, and annually thereafter. Both right ventricular end-diastolic dimension (RVEDD) and left ventricular end-diastolic dimension (LVEDD) were measured from two-dimensional parasternal long-axis views. Systolic pulmonary artery pressure was estimated by tricuspid regurgitation (TR) velocity and dimensions of the inferior vena cava [17]. The degrees of TR and mitral regurgitation (MR) were quantified by color Doppler imaging [18]. Early diastolic mitral valve flow velocity (E) and early diastolic septal mitral annular velocity (e') were obtained by pulse wave Doppler and Tissue Doppler imaging, respectively. The value of e' is an index of left ventricular diastolic function [19], and the ratio of E derived by e' (E/e') correlates closely with left ventricular filling pressure [20]. Residual shunt was evaluated by color Doppler signal width: <2 mm was considered as small, 2–4 mm as moderate and >4 mm as severe [21]. In patients with atrial fibrillation, echocardiographic data were derived from corresponding mean values of 10 continuous cardiac cycles.

Statistical Analysis

Statistical analysis was performed using SPSS (SPSS, Chicago, IL). Data are expressed as mean values ± SD. As appropriate, Student's t-test or Wilcoxon signed-rank test was performed to test for statistical differences between variables. Pearson's correlation coefficient was used to analyze relations between variables and NYHA functional class at the latest follow-up. The significant data obtained from univariate analysis were applied to multivariate linear regression analysis to

TABLE I. Patients Characteristics

Total patients	30
Gender, F/M	20/10
Age, (range), years	75.8 ± 3.8 (70–85)
BSA, m^2	1.5 ± 0.2
Hypertension	12 (40%)
Stroke	4 (13%)
CAD	2 (7%)
COPD	5 (17%)
Atrial fibrillation	16 (53%)
Paroxysmal	3 (10%)
Permanent	13 (43%)
RBBB	22 (74%)
Systolic PAP*, mm Hg	35.6 ± 11.8
PAH	16 (53%)
E′, cm/s	7.1 ± 1.9
E/E′	11.0 ± 3.9
Diuretic use	17 (57%)
Hospitalization for HF	9 (30%)
NYHA functional class, I/II/III	5/17/8
Qp/Qs*	2.4 ± 0.7
ASD diameter, mm	20.3 ± 6.4
Rim type	
Sufficient rim, *n* (%)	8 (27%)
Aortic rim deficient, *n* (%)	19 (63%)
Aortic and anterosuperior rim deficient, *n* (%)	1 (3%)
IVC rim deficient, *n* (%)	2 (7%)

BSA, body surface area; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; RBBB, right bundle branch block; PAP, pulmonary artery pressure; PAH, pulmonary artery hypertension; E, early diastolic mitral valve flow velocity; *E′*, early diastolic mitral annular velocity; HF, heart failure; NYHA, New York Heart Association; Qp, pulmonary flow; Qs, systemic flow; IVC, inferior vena cava.

assess factors independently associated with NYHA functional class at the latest follow-up. A value of $P < 0.05$ was considered to be statistically significant.

RESULTS

Baseline Characteristics

Patient characteristics, clinical, hemodynamic and echocardiographic data, and ASD morphology are shown in Table I. The patients in this study included 10 males and 20 females with a mean age of 75.8 ± 3.8 years and age range of 70–85 years. Eighteen of the 30 patients had been diagnosed with ASD within 2 years before transcatheter closure was attempted but the others well before that. Most of the patients had at least one major comorbidity, including systemic hypertension, stroke, coronary artery disease, and atrial fibrillation. Mean systolic pulmonary artery pressure at the time of diagnostic catheterization was 35.6 ± 11.8 mm Hg. Mean early diastolic mitral annular velocity (*e'*) and the ratio of early diastolic mitral valve flow velocity (*E*) to *e'* (*E/e'*) were 7.1 ± 1.9 cm/s and 11.0 ± 3.9, respectively, suggesting that our cohort generally had impaired myocardial relaxation [19]. More than half of the patients were being treated with a diuretic for congestive heart failure, and 30% of the patients had a history of hospitalization due to heart failure. Seventeen patients were classified as NYHA functional class II and eight patients were classified as class III. Only five patients had no symptoms despite significant shunt flow and were classified as NYHA functional class I. One patient had two defects. Mean defect diameter was 20.3 ± 6.4 mm, and a circumferentially sufficient rim (>5 mm rim around the defect) was observed in only eight patients. Mean pulmonary-systemic flow ratio (Qp/Qs) calculated by using the Fick principle was 2.4 ± 0.7.

TABLE II. Procedural and Mid-Term Results

Procedural results (*n* = 30)	
Success deployment, *n* (%)	28 (93%)
Device size, mm	23.3 ± 6.0
Acute complication, *n* (%)	0 (0%)
Mid-term results (*n* = 28)	
Mean follow-up period, *m*	19.1 ± 11.3
Residual shunt, *n* (%)	2 (8%)
Small, *n* (%)	2 (8%)
Major events	
Death, *n* (%)	2 (8%)
Unknown cause, *n* (%)	1 (4%)*
Prostate cancer, *n* (%)	1 (4%)
Pacemaker implantation, *n* (%)	1 (4%)
TIA, *n* (%)	1 (4%)*
Persistent AF, *n* (%)	1 (4%)

*The same case.
TIA, transient ischemic attack; AF, atrial fibrillation.

Procedural and Mid-Term Results

Table II shows the procedural and mid-term results. The first procedure was successful in 27 of 30 cases in which transcatheter ASD closure was attempted. On the other hand, the procedure was abandoned in three cases.

Before to ASD closure, test balloon occlusion were performed in 7 of 30 cases. As a result, the procedure was abandoned in one case due to a significant elevation of PCWP during test occlusion of the ASD. This patient was an 84-year-old thin woman who had permanent atrial fibrillation, hypertension, chronic kidney disease, chronic anemia, and severe TR. She had been repeatedly hospitalized with congestive heart failure in past years. Her ASD diameter was 24 mm and Qp/Qs was 2.6. During test balloon occlusion, her PCWP immediately increased from 8 mm Hg to 22 mm Hg and remained at 16 mm Hg after 20 min. At that point, we decided to abandon the procedure. In the other two cases, the device was difficult to deploy because of large size defect. One of those cases proceeded to surgical closure, and the other case was successfully closed in the second attempt of catheter intervention

TABLE III. Changes in Clinical Echocardiographic Parameters

	Pre-procedure ($n = 27$)	Follow-up ($n = 27$)	P value
NYHA functional class, n (%)			
I	3 (11%)	21 (78%)	<0.001
II	17 (63%)	5 (18%)	
III	7 (26%)	1 (4%)	
Plasma BNP level, pg/mL	175.9 ± 249.7	99.2 ± 83.2	0.013
HR at rest, bpm	74.4 ± 14.5	66.7 ± 8.7	0.005
Estimated systolic PAP, mm Hg	38.5 ± 12.7	27.2 ± 7.3	<0.001
RVEDD, mm	40.8 ± 6.0	31.6 ± 4.5	<0.001
LVEDD mm	39.7 ± 4.8	45.3 ± 4.6	<0.001
RVEDD/LVEDD ratio	1.05 ± 0.24	0.70 ± 0.12	<0.001
LAD, mm	46.1 ± 9.9	44.3 ± 9.3	0.128
LVEF, %	70.5 ± 6.1	70.5 ± 5.7	0.611
TR, n (%)			
≤Mild	10 (37%)	20 (74%)	0.002
Moderate	13 (48%)	7 (26%)	
Severe	4 (15%)	0 (0%)	
MR, n (%)			
None or trivial	18 (67%)	8 (30%)	0.004
Mild	6 (22%)	16 (59%)	
>Moderate	3 (11%)	3 (11%)	

BNP, brain natriuretic peptide; PAP, pulmonary artery pressure; RVEDD, right ventricular end-diastolic dimension; LVEDD, left ventricular end-diastolic dimension; LAD, left ventricular dimension; LVEF, left ventricular ejection fraction; TR, tricuspid regurgitation; MR, mitral regurgitation.

on a later day. Finally, 28 (93%) of the 30 patients were treated successfully by catheter closure. A single device was placed in 27 patients. In the remaining patient with multiple defects, two devices were deployed at the time of the same procedure. Mean device diameter was 23.3 ± 6.0 mm. Mean follow-up period was 19.1 ± 11.3 months.

Two patients died during the follow-up period. One died of prostatic cancer 20 months after ASD closure. The other patient died 2 months after the procedure. This patient was a 70-year-old woman who had permanent atrial fibrillation, severe chronic obstructive pulmonary disease, mild left ventricular dysfunction, history of pacemaker implantation for sick sinus syndrome, and mitral valve replacement and was in NYHA functional class III. Her ASD was 22 mm with a sufficient atrial rim, and a 26 mm device was used for closure. She died from unknown cause at home; however, a history of transient cerebral ischemic attack was reported one week before her death. Autopsy was not performed. Two patients were complicated with new arrhythmia. One patient who had permanent atrial fibrillation underwent pacemaker implantation for slow ventricular response 6 months after ASD closure. The other patient with paroxysmal atrial fibrillation before ASD closure developed persistent atrial fibrillation during the follow-up period. The remaining 24 patients had no late complication during the follow-up period. No patient had hemodynamically significant residual shunt.

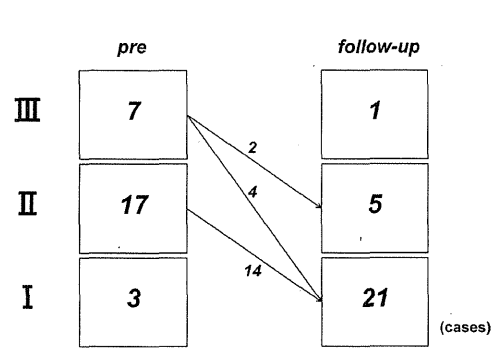

Fig. 1. NYHA functional class before the procedure and at follow-up.

Table III shows time course changes in clinical and echocardiographic parameters. Follow-up data (at more than 6 months after the procedure) were available in all of the 28 patients with exception of one patient who died 2 months after the procedure. NYHA functional class was significantly improved in 20 (74%) of the 27 patients at the latest follow-up (Fig. 1). One patient who remained in NYHA class III was complicated with severe chronic obstructive pulmonary disease. There was also a significant improvement in plasma BNP level (175.9 ± 64.7 vs. 99.2 ± 83.2 pg/ml, $P = 0.013$). Resting heart rate also decreased significantly (74.4 ± 14.5 vs. 66.7 ± 8.7 beats/min, $P = 0.005$), although no cardiac chronotropic drug was administered to any of the patients.

Cardiac Remodeling

RVEDD and estimated systolic pulmonary artery pressure decreased significantly (40.8 ± 6.0 vs. 31.6 ± 4.5 mm, $P < 0.001$, 38.5 ± 12.7 vs. 27.2 ± 7.3 mm Hg, $P < 0.001$, respectively). At the same time, LVEDD increased significantly (39.7 ± 4.8 vs. 45.3 ± 4.6 mm, $P < 0.001$). Therefore, the RVEDD/LVEDD ratio significantly decreased (1.05 ± 0.24 vs. 0.70 ± 0.12 mm, reduction of 67%, $P < 0.001$), indicating ventricular reverse remodeling. Left atrial dimension, above the normal level at baseline, did not change significantly during the follow-up period. Left ventricular ejection fraction also did not change.

AV Valve Regurgitation

Improvement of TR was observed in 11 of 17 patients (65%) with moderate or severe degree of regurgitation during the follow-up period (Fig. 2). On the other hand, MR was increased in 10 (37%) of the 27 patients and

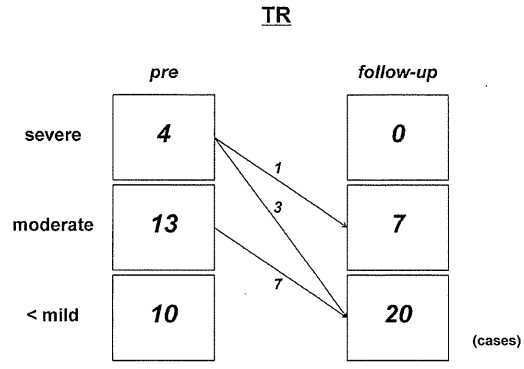

Fig. 2. Degrees of TR before the procedure and at follow-up.

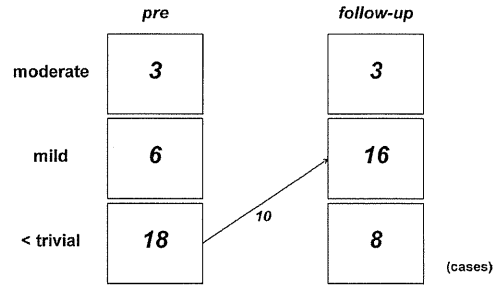

Fig. 3. Degrees of MR before the procedure and at follow-up.

was unchanged in the others (63%) during the follow-up period (Fig. 3). In our cohort, there was no patient with mitral valve prolapse as a cause for MR.

Associations Between NYHA Functional Class and Echocardiographic Parameters in the Follow-Up Period

Table IV shows associations of clinical and echocardiographic parameters with NYHA functional class. In the follow-up period, RVEDD/LVEDD ratio was identified as a factor associated with NYHA functional class. On the other hand, *E/e'*, *e'*, degree of TR or MR and increase in MR were not associated with NYHA functional class.

DISCUSSION

In this study, we demonstrated that transcatheter ASD closure can be performed safely and contributes to symptom reduction and cardiac remodeling even in patients older than 70 years of age.

Twelve of the 30 patients had been diagnosed with ASD well before trascatheter closure was attempted

TABLE IV. Associations of Clinical and Echocardiographic Parameters with NYHA Functional Class in the Follow-Up Period

Variable	*r*	Univariate *P* value	Multivariate *P* value
Age		0.349	
Qp/Qs		0.807	
HR at rest		0.260	
plasma BNP level		0.146	
Estimate systolic PAP		0.382	
RVEDD/LVEDD ratio	0.491	0.009	0.009
LVEF, %		0.971	
E'		0.962	
E/E'		0.688	
Degree of TR		0.282	
Degree of MR		0.682	
Increase in MR		0.764	

but they had refused or hesitated to receive ASD closure. We think that this was partially because they had no recognizable symptom, but mainly because surgical closure was the only treatment at the time when they had been first diagnosed with ASD.

Device closure was successfully performed in 28 (93%) of the 30 patients without acute complications. In the other two patients, the procedures were abandoned because of technical issues. While only eight (27%) of the 30 patients had sufficient rim type ASD, 19 (63%) had aortic rim deficient type. However, there was not much difference in our device selection between sufficient rim and aortic rim deficient type. Therefore, we think that the small percentage of patients with sufficient rim did not have a great impact on device size selection in the present study. Although the majority of our patients were complicated with various comorbidities, such as pulmonary artery hypertension, systemic hypertension and atrial fibrillation, high procedural success rate can be expected even in this aged group. Also, significant improvement of NYHA functional class was observed after closure even though about 30% of the patients in this study had a history of hospitalization for congestive heart failure. No patient required additional hospitalization for congestive heart failure during the follow-up period.

Several studies have suggested that development of acute congestive heart failure is due to abrupt elevation in left ventricular preload following transcatheter ASD closure, especially in elderly patients with impaired left ventricular systolic or diastolic function [3,22,23]. In our study, despite the fact that our patients had impaired left ventricular diastolic function estimated by decreased *e'* and increased *E/e'* [19,20] as well as various comorbidities such as systemic hypertension, pulmonary artery hypertension and atrial fibrillation, acute congestive heart failure after the ASD closure did not

develop in any of the patients except in one patient in whom the procedure was abandoned due to PCWP elevation during test balloon occlusion. Schubert et al. reported that periprocedural anticongestive medication was effective in preventing congestive heart failure after ASD closure in elderly patients [24]. In our study, 57% of the 30 patients previously used oral diuretics, and this high rate of diuretic usage might have contributed to prevention of acute congestive heart failure after closure.

During the follow-up period, NYHA functional class significantly improved in 20 (74%) of the 27 patients. Our data also demonstrated significant decreases of heart rate, pulmonary artery pressure and plasma BNP level, and these changes contributed to the improvement of NYHA functional class. Decrement of heart rate is presumably evidence of increment of left ventricular stroke volume following increased left ventricular preload after abolishment of left-to-right shunt. Significant decrease in RVEDD/LVEDD ratio was observed even in our geriatric patients, although RVEDD did not reach the normal level. Interestingly, percentage change in RVEDD/LVEDD ratio in our cohort was equivalent to results of other studies in younger populations [6,23]. Furthermore, it was revealed that RVEDD/LVEDD ratio was independently correlated with NYHA functional class in the follow-up period.

In this study, the degree of TR was decreased in 11 patients (41%) and exacerbation of TR was not observed during the follow-up period. Interestingly, in the case of moderate or severe TR before ASD closure, the degree of TR was improved in 11 (65%) of the 17 patients. TR can be improved functionally following decrement of right ventricular preload after ASD closure. Improvement of TR also can be expected following improvement of right ventricular geometric abnormality [25]. Our results suggest that TR can be improved even in geriatric patients and that the severity of TR does not become a factor to exclude them as candidates for transcatheter ASD closure. On the other hand, the degree of MR was slightly increased in 10 patients (37%) and unchanged in the others (63%) during the follow-up period. Wilson et al. reported that the degree of MR was unchanged in 83% and increased in 10% of their 194 patients, including 78 patients aged younger than 15 years, after transcatheter ASD closure [26]. In elderly ASD patients, the severity of MR might be masked by the presence of ASD effectively reducing left ventricular preload. Additionally, degenerated change of the mitral valve leaflet also influenced the increase in MR. Although the degree of MR and the increase in MR were not associated with NYHA functional class in the follow-up period in our study, further long-term follow-up is mandatory.

During the follow-up period, three complications occurred. One patient who was complicated with several cardiac comorbidities died 2 months after the procedure. An autopsy was not performed and it was therefore not known whether the cause of sudden death was ASD device-associated. Pacemaker implantation was required in one patient 6 months after the procedure, even though bradycardia was not observed before or just after ASD closure. In one patient, paroxysmal atrial fibrillation progressed into persistent atrial fibrillation 2 years after ASD closure. In previous studies, the incidence of atrial fibrillation in patients after transcatheter ASD closure was estimated to be 5% to 18% [27–29]; however, especially in elderly patients, atrial fibrillation is one of the expected findings for their natural course after ASD closure.

Limitations

This study has several limitations. The main limitation of our study is the small number of patients and lack of a control group. In addition, the follow-up period was relatively short. Long-term, randomized comparisons with large numbers of subjects are required to establish the survival benefit of transcatheter ASD closure in elderly patients. Another limitation is that our conclusion about improvement in exercise capacity was made on the basis of the patients' subjective impressions and not on the basis of oxygen uptake or other functional measurement. However, especially in elderly patients, performance in cardiopulmonary exercise testing is affected by lower-extremity muscle weakness. Thus, improvement of NYHA functional class can be considered as improvement of exercise tolerance in this patient population.

CONCLUSION

Even in elderly patients older than 70 years, transcatheter closure of ASD can be performed safely and contributes to significant improvement of NYHA functional class and positive cardiac remodeling. Further investigation is required especially for the outcome of MR.

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Usefulness of the Right Parasternal Approach to Evaluate the Morphology of Atrial Septal Defect for Transcatheter Closure Using Two-Dimensional and Three-Dimensional Transthoracic Echocardiography

Nobuhisa Watanabe, RDCS, Manabu Taniguchi, MD, Teiji Akagi, MD, Yasuharu Tanabe, RDCS, Norihisa Toh, MD, Kengo Kusano, MD, Hiroshi Ito, MD, Norio Koide, MD, and Shunji Sano, MD, *Okayama, Japan*

Background: The aim of this study was to demonstrate the feasibility and usefulness of addition of the right parasternal approach to the conventional left parasternal and apical approaches using two-dimensional (2D) and three-dimensional (3D) transthoracic echocardiography (TTE) for morphologic evaluation in cases of transcatheter closure of atrial septal defects (ASDs).

Methods: In 112 consecutive patients with ASDs, the morphology of the defects was evaluated for transcatheter closure in the right parasternal view in addition to the conventional left views using 2D and 3D TTE. Measurements of the maximal ASD diameter and detection of deficient rim obtained on 2D TTE were compared with those obtained by 2D transesophageal echocardiography. The shapes and locations of ASDs visualized by 3D TTE were compared with those visualized by 3D transesophageal echocardiography.

Results: In 88 patients (80.0%), optimal images from the right parasternal approach for morphologic evaluation of ASDs were obtained. Although there was a significant difference in maximal ASD diameter obtained only in the conventional left approach compared with transesophageal echocardiographic measurements ($P < .05$), when the right parasternal approach was applied, a significant difference was not found ($P = .18$), and the diagnostic concordance of the rim deficiency was improved from 85.2% to 90.9%. Three-dimensional TTE from the right parasternal approach improved visualization of the shape and location of ASDs from 65.5% to 74.5%.

Conclusions: Additional use of the right parasternal approach enables detailed morphologic evaluation for transcatheter closure of ASDs. In patients with suboptimal images on 3D TTE in the left conventional approach, additional 3D TTE in the right parasternal approach can improve the feasibility of obtaining optimal 3D images to evaluate the shapes and locations of ASDs. (J Am Soc Echocardiogr 2012;25:376-82.)

Keywords: Right parasternal approach, Transthoracic echocardiography, Transesophageal echocardiography, Atrial septal defect

Transcatheter closure of atrial septal defects (ASDs) has recently become established as a safe and effective treatment, and the procedure has become an alternative to a surgical approach.[1-5] Appropriate patient selection for transcatheter closure is the most important factor for success in this procedure,[4] and morphologic evaluation, including evaluation of maximal ASD diameter and surrounding rims by echocardiography, is essential. Although two-dimensional (2D) transthoracic echocardiography (TTE) in the left parasternal, apical, and subcostal views is routinely used for this purpose, previous studies have demonstrated that these views enable only limited morphologic evaluation of ASDs.[6-9] Real-time three-dimensional (3D) echocardiography, in which a comprehensible en face view of ASDs is obtained, has been available in a clinical setting.[10-12] Three-dimensional TTE is expected to improve understanding of the morphology of ASDs, but data are limited, and it is difficult to obtain good-quality images on 3D TTE using the left parasternal and apical approaches.[13-15] In this regard, 2D transesophageal echocardiography (TEE) and 3D TEE have been widely accepted and established as diagnostic modalities in evaluation of the morphology of ASDs for transcatheter closure because of their high-quality imaging[16-21]; however, TEE has a semi-invasive nature.

The right parasternal approach, in which the transducer is placed to the right of the sternum in the right lateral decubitus position, was

From the Division of Medical Support (N.W., Y.T.) and the Division of Cardiac Intensive Care Unit (M.T., T.A.), Okayama University Hospital, Okayama, Japan; the Department of Cardiovascular Medicine (N.T., K.K., H.I.), the Department of Laboratory Medicine (N.K.), and the Department of Cardiovascular Surgery (S.S.), Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan.

Reprint requests: Manabu Taniguchi, MD, 2-5-1 Kita-ku Shikata-Cho, Okayama 700-8558, Japan (E-mail: *tmnb@md.okayama-u.ac.jp*).

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Abbreviations

ASD = Atrial septal defect

TEE = Transesophageal echocardiography

3D = Three-dimensional

TTE = Transthoracic echocardiography

2D = Two-dimensional

reported to enable better visualization of ASDs and evaluation of the direction of shunt flow in patients with ASDs because it obtains a longitudinal vena cava superior-inferior plane of the interatrial septum.[22-26] In addition, 3D TTE in this approach might improve the feasibility of obtaining optimal en face images of ASDs. However, there have been limited data on the usefulness of the right parasternal approach using 2D and 3D TTE for morphologic evaluation in cases of transcatheter closure. Therefore, we sought to assess the usefulness of the right parasternal approach in addition to the conventional left parasternal and apical approaches in evaluating ASD morphology for the suitability of transcatheter closure using 2D and 3D TTE.

METHODS

Study Population

A total of 112 consecutive patients (40 men and 72 women) were prospectively evaluated for transcatheter closure of ASDs using the Amplatzer Septal Occluder (AGA Medical Corporation, Plymouth, MN) with 2D and 3D TTE. Two patients with ASDs other than the secundum type were excluded from this study (one had a superior sinus venosus ASD and the other had an unroofed coronary sinus ASD). Therefore, 110 patients were included in the study. All patients except for one were referred from other hospitals to our institution for transcatheter ASD closure. Age at the examination ranged from 6 to 84 years (mean, 46.1 ± 20.5 years). Two-dimensional TEE and 3D TEE were performed <3 days after TTE by a blinded observer. The study was approved by the local ethics committee.

Two-Dimensional TTE

Two-dimensional TTE was performed using a commercially available ultrasound system with a 3.5-MHz transducer (Vivid 7; GE Healthcare, Wauwatosa, WI). Right ventricular midcavity diameter was measured in the apical four-chamber view according to the guideline of American Society of Echocardiography.[27] In all patients, the morphology of ASDs was evaluated using TTE in the left lateral decubitus position from the left parasternal and apical approaches (conventional left approach). Then a transducer was positioned on the right parasternal border with the patient in the right lateral decubitus position (right parasternal approach). Maximal ASD diameter and the minimal diameter of surrounding rims were measured at end-systole by carefully sweeping the transducer from right to left and top to bottom of the interatrial septum in both approaches. Regarding the maximal ASD diameter, first, the ASD diameter was measured using the conventional left approach (ASD_L diameter), and then the ASD diameter was measured by the right parasternal approach (ASD_R diameter). The maximal ASD diameter was considered the maximal value from measurements by both approaches. The surrounding rims were classified according to location as superoanterior, inferoanterior, superoposterior, or inferoposterior. The superoanterior rim was measured as the distance between the aorta and the defect. The inferoanterior rim was measured as the distance from the atrioventricular valves. The inferoposterior rim was measured as the distance from the left atrial wall. The superoposterior rim was measured as the distance from the defect to the superior vena cava and to determine the inferoposterior rim as the distance from the defect to the inferior vena cava (Figure 1). Any rim length < 5 mm was considered deficient. First, the presence or absence of a deficient rim was evaluated using the conventional left approach, and then the right parasternal approach was used.

Three-Dimensional TTE

Three-dimensional TTE was performed after 2D TTE using a commercially available ultrasound system with a 3V transducer (Vivid 7). In all patients, the left parasternal approach was first chosen and optimized, and then loops from five consecutive cycles were acquired and digitally stored. In cases with suboptimal 3D images by the left parasternal approach, we attempted to obtain optimal 3D images using the right parasternal approach. In all patients, at least three acquisitions were performed, and the data set with the best image quality was chosen for analysis. The shapes and locations of ASDs were visually evaluated on the best 3D images.

Two-Dimensional and 3D TEE

Two-dimensional and 3D TEE were performed using a commercially available ultrasound system (iE33; Philips Medical Systems, Andover, MA). Maximal ASD diameter (ASD_{TEE} diameter) and minimal diameter of the surrounding rims were assessed at end-systole using both 2D TEE and 3D TEE, as previously reported.[18] To evaluate surrounding rims using 2D TEE, the superoanterior rim was measured as the distance between the aortic annulus and the defect in the horizontal plane at 0° to 30°. The inferoanterior rim was measured as the distance between the defect and atrioventricular valves in the four-chamber view at 135°. The longitudinal plane around 90° was used to determine the superoposterior rim as the distance from the defect to the superior vena cava and to determine the inferoposterior rim as the distance from the defect to the inferior vena cava (Figure 1). The rim length was considered deficient if the length was <5 mm.

Real-time 3D transesophageal echocardiographic data were obtained after a complete 2D transesophageal echocardiographic study. Real-time 3D zoom mode, which displays a smaller, magnified pyramidal data set, was used to evaluate the shapes and locations of ASDs as well as the rough relation to surrounding structures.

Two-dimensional and 3D transesophageal echocardiographic data were considered reference standards. In patients with optimal images obtained on both approaches, ASD_{TEE} diameter and detection of deficient rims obtained on 2D TEE were compared with those obtained on 2D TTE. The shapes and locations of ASDs using 3D TTE were compared with those obtained using 2D and 3D TEE.

Measurement Variability

ASD diameter and the minimal diameter of the surrounding rims obtained using TTE were measured by two independent observers and by one observer two times 1 month apart in 10 randomly selected patients to determine interobserver variability and intraobserver variability. Variability was assessed as the absolute difference between two measurements expressed as a percentage of their mean values.

Statistical Analysis

Categorical data are expressed as numbers and percentages and continuous data as mean ± SD. The significance of baseline differences

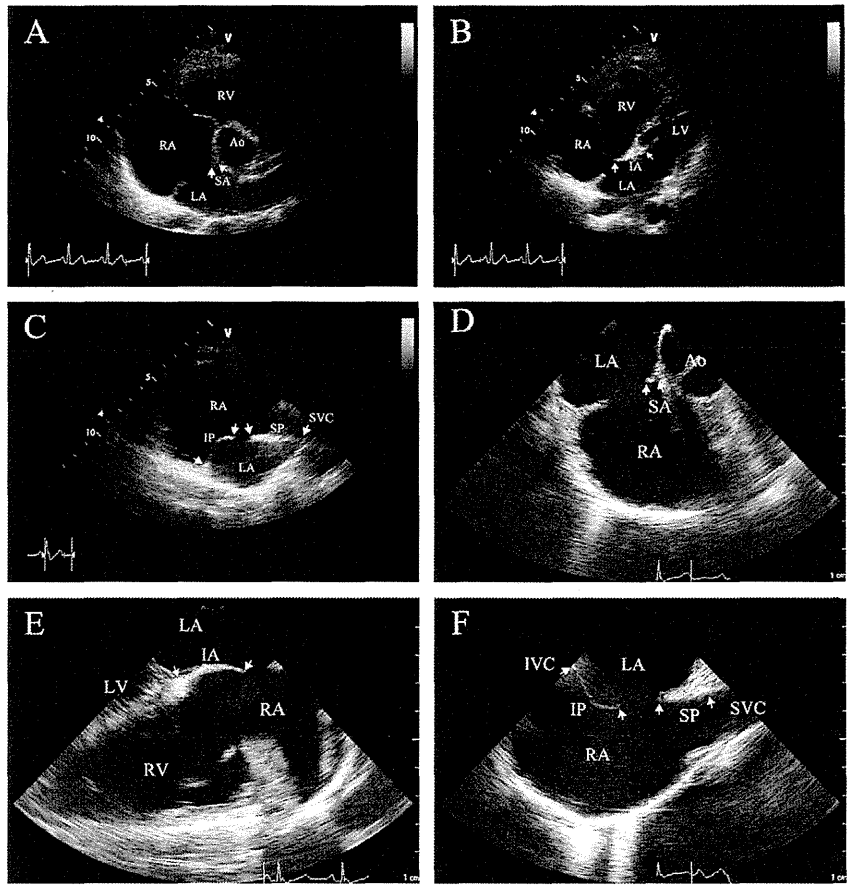

Figure 1 Measurement of maximal ASD diameter and the surrounding rims on 2D TTE and 2D TEE. The surrounding rim is measured from mark (*white arrow*) to mark (*white arrow*). **(A)** Left parasternal short-axis view, **(B)** left parasternal four-chamber view, **(C)** right parasternal longitudinal view, **(D)** short-axis transesophageal echocardiographic view (0°–30°), **(E)** four-chamber transesophageal echocardiographic view (135°), **(F)** biatrial transesophageal echocardiographic view (90°). The surrounding rims are measured at end-systole (*white arrow*). *Ao*, Aorta; *IA*, inferoanterior rim; *IP*, inferoposterior rim; *IVC*, inferior vena cava; *LA*, left atrium; *LV*, left ventricle; *RA*, right atrium; *RV*, right ventricle; *SA*, superoanterior rim; *SP*, superoposterior rim; *SVC*, superior vena cava.

was determined using paired and unpaired *t* tests as appropriate. Categorical variables are expressed as counts and percentages and were compared using χ^2 or Fisher's exact tests as appropriate. Comparisons between measurements were done using Pearson's linear regressions analysis. The agreement of the two methods was evaluated using the Bland-Altman test. *P* values $< .05$ were considered statistically significant. Statistical analyses were done using SPSS version 18.0 (SPSS, Inc., Chicago, IL).

RESULTS

Baseline Characteristics of Study Population

Table 1 shows the baseline characteristics and 2D transthoracic echocardiographic parameters of the study population. All patients showed hemodynamically significant atrial shunts or the presence of right atrial and ventricular volume overload.

Feasibility of 2D TTE in the Right Parasternal Approach

Two-dimensional TTE with the conventional left approach enabled the detection of shunt flow on color-flow Doppler imaging and visualization of the optimal images for the measurement of defects in all patients. Detection of shunt flow in the right parasternal approach on color-flow Doppler images was successful in 102 patients (92.7%). Optimal images with the right parasternal approach for measurements of defects and surrounding rims were visualized in 88 patients (80.0%). When all patients were divided into two groups according to age, <40 years ($n = 42$; mean age, 24.1 ± 10.4 years) and ≥40 years ($n = 68$; mean age, 59.6 ± 11.5 years), the percentage of patients in whom optimal images to measure ASD diameter and surrounding

Table 1 Baseline characteristics and transthoracic echocardiographic parameters of the study population ($n = 110$)

Variable	Value
Men/women	39/71
Age (y)	46.1 ± 20.5 (6–84)
Height (m)	1.58 ± 0.12 (1.13–1.83)
Weight (kg)	54 ± 12.3 (17–92)
Body surface area (m^2)	1.53 ± 0.22 (0.75–2.14)
Right ventricular midcavity diameter (mm)	41.8 ± 5.4 (28–55)
Pulmonary flow/systemic flow ratio	2.4 ± 0.7 (1.2–4.1)

Data are expressed as numbers or as mean ± SD (range).

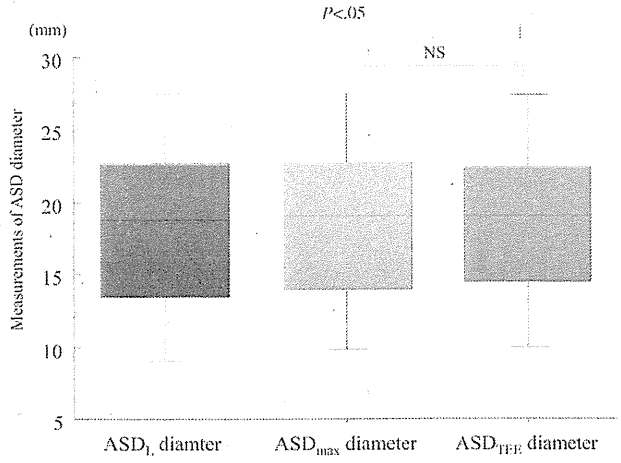

Figure 2 Box plots showing the comparison ASD_L diameter obtained with the conventional left approach (*red box*), maximal ASD diameter obtained with both the left conventional and right parasternal approaches (*orange box*), and ASD_{TEE} diameter (*blue box*).

rim were obtained in the right parasternal approach was significantly higher in those aged <40 years than in those aged ≥40 years (90.5% vs 73.5%, $P = .033$).

Data for the 88 patients in whom optimal 2D transthoracic echocardiographic images for measurements of ASD diameter and surrounding rims were obtained by both approaches were analyzed in our study.

Morphologic Evaluation with 2D TTE and TEE

Maximal ASD diameters between ASD_L diameter, maximal ASD diameter, and ASD_{TEE} diameter were compared in 88 patients with optimal images from the right parasternal approach. There was a small but significant difference between ASD_L diameter and ASD_{TEE} diameter (18.5 ± 6.9 vs 19.0 ± 6.9 mm, $P < .05$). However, when the diameter obtained with the right parasternal approach was taken into account in addition to the diameter obtained with the conventional left approach, a significant difference was not found between measurements of maximal ASD diameter and ASD_{TEE} diameter (18.8 ± 6.7 mm, $P = .18$; Figure 2). Bland-Altman analysis showed the smallest mean absolute differences and narrower limits of agreement when the measurement from the right parasternal approach was added to that from the conventional left approach (Figure 3).

TEE demonstrated that 17 patients (19.3%) had centrally positioned ASD, 55 (62.5%) had superoanterior rim deficiencies, three (3.4%) had inferoposterior deficiencies, five (5.7%) had both superoanterior and inferoposterior deficiencies, and eight (9.1%) had multiple ASDs. Although the detection of a deficient rim showed concordance in 75 patients (85.2%) between TTE with the conventional left approach and 2D TEE, diagnostic concordance was improved to 90.9% by adding the right parasternal approach. In nine patients with inferoposterior rim deficiencies, diagnostic accuracy of the rim deficiency was improved from 66.7% to 100% when the right parasternal approach was added to the conventional left approach.

Evaluation of ASDs with 3D TTE

Although 3D TTE from the left parasternal approach could visualize the 3D optimal image for understanding the shape and location of

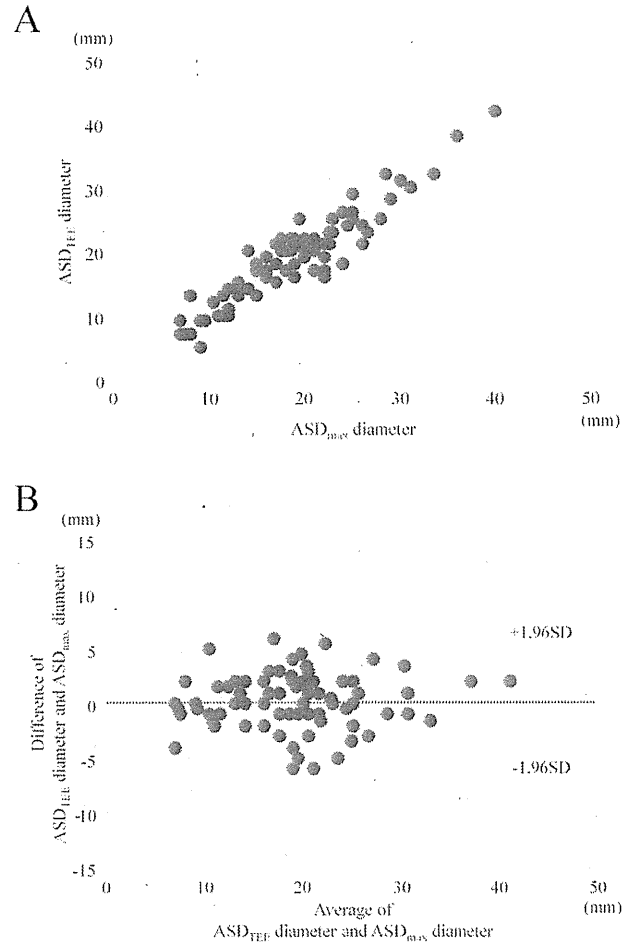

Figure 3 **(A)** Correlations of maximal ASD diameter measured by 2D TTE versus 2D TEE. **(B)** Bland-Altman plot of ASD diameter difference between the measurements on 2D TTE and those on 2D TEE as a function of the average measurements. The *thick continuous line* and *dotted line* indicate the mean ± 1.96 SD of the difference, respectively.

ASDs in only 72 patients (65.5%), the use of the right parasternal approach improved the visualization of optimal 3D TTE images to 74.5% (Figures 4 and 5).

Measurement Variability

Interobserver and intraobserver variability were 1.1% and 0.6%, respectively, for ASD diameter measured by 2D TTE; 6.1% and 6.8%, respectively, for superoposterior rim measurement by 2D TTE; and 9.7% and 8.0%, respectively, for inferoposterior rim measurement by 2D TTE.

DISCUSSION

Our study demonstrated that 2D TTE with the addition of the right parasternal approach to the conventional left approach is feasible and enables evaluation of the morphology of ASDs for transcatheter closure with satisfactory accuracy compared with evaluation by 2D TEE. In particular, the right parasternal approach contributes greatly

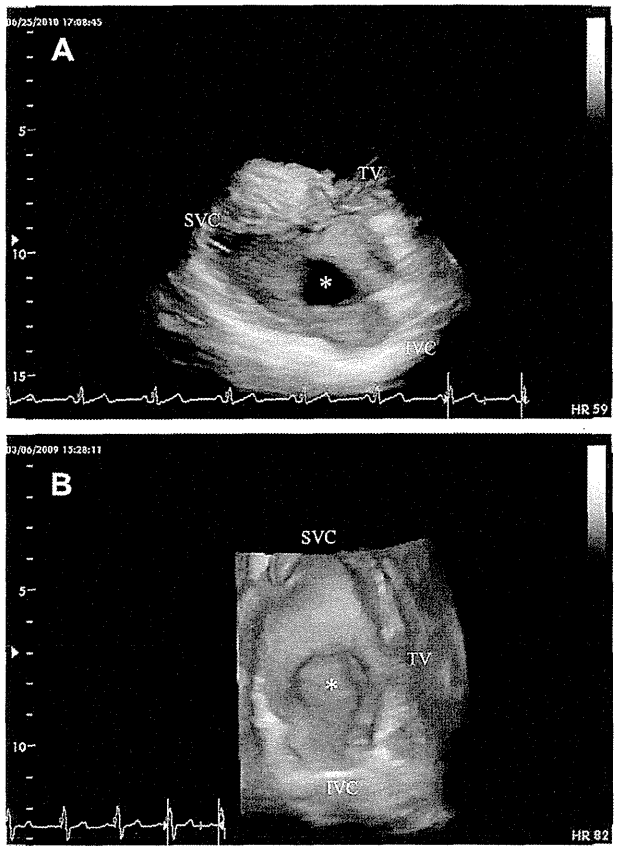

Figure 4 Three-dimensional transthoracic echocardiography of various shapes of the secundum-type ASD (*asterisk*) viewed from the right atrium. **(A)** Superoanterior rim deficient from the left parasternal approach, **(B)** inferoposterior rim deficient from the right parasternal approach. *IVC*, Inferior vena cava; *SVC*, superior vena cava; *TV*, tricuspid valve.

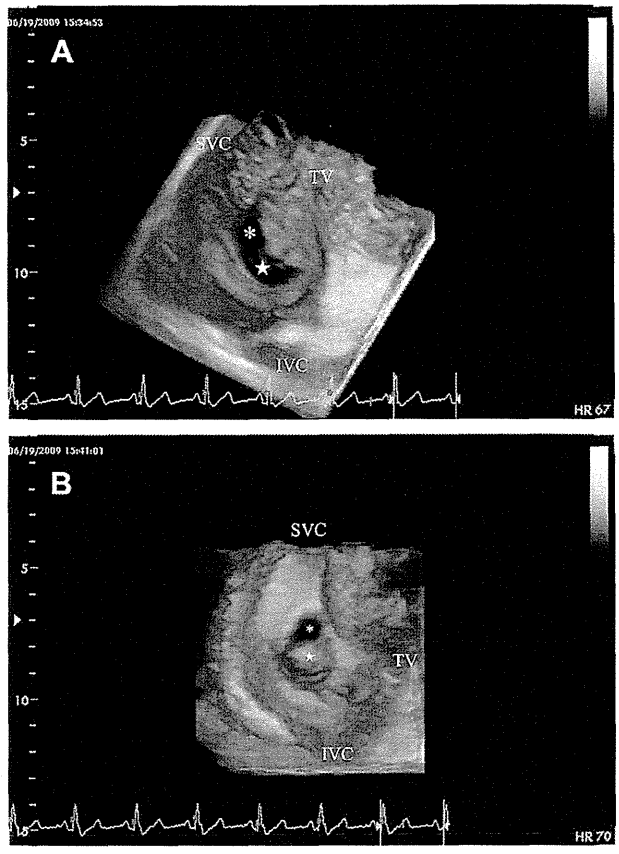

Figure 5 Three-dimensional TTE of the secundum-type ASD (*asterisk*) with an atrial septal aneurysmal (ASA) viewed from the right atrium. **(A)** The ASA (*white star*) was dropped out from the left parasternal approach **(B)** but was clearly visualized from the right parasternal approach. *IVC*, Inferior vena cava; *SVC*, superior vena cava; *TV*, tricuspid valve.

to the identification of rim deficiency, especially in patients with inferoposterior rim deficiencies. In terms of the acquisition of optimal 3D transthoracic echocardiographic images, the addition of the right parasternal approach to the conventional left approach can improve the feasibility of ASD morphologic evaluation.

Feasibility of the Right Parasternal Approach

Previous studies have shown that the right parasternal approach is a reliable technique for detection of ASDs.[22-26] Iliceto *et al.*[25] reported that ASDs were identified using the right parasternal approach in 13 of 17 patients (76.5%) and that the right parasternal approach improved the feasibility of 2D TTE for the detection of ASDs. In our study, we could detect ASDs on color-flow Doppler imaging by 2D TTE using the right parasternal approach with high sensitivity (92.7%). Advances in the technology of echocardiography may have greatly contributed to its high feasibility compared with previous studies. In our study, optimal images in the right parasternal approach were obtained more frequently in younger patients than in older patients, who sometimes have obesity or lung disease. A previous study also demonstrated that the right parasternal view was often easily obtainable in neonates and young children.[26] Therefore, especially in younger patients with intolerance of TEE, TTE including the right parasternal approach can contribute to evaluating ASD morphology for transcatheter closure.

Morphologic Evaluation of ASDs

Previous studies have demonstrated that appropriate patient selection is essential for successful transcatheter closure of ASDs using the Amplatzer Septal Occluder.[16,17] Two crucial parameters, maximal ASD diameter to choose an appropriately sized device and tissue rim dimensions all around the defect to optimize placement of the device, should be measured to select patients for transcatheter closure of ASDs in addition to detection of atrial shunts or echocardiographic findings of right ventricular volume overload.[12] Although TEE is considered the gold standard in evaluating ASD morphology for the suitability of transcatheter closure, TEE has a semi-invasive nature. TTE used to perform a detailed morphologic evaluation of ASDs before TEE can lead to avoiding oversight and shortening transesophageal examination time. Therefore, detailed morphologic evaluation, including evaluation of maximal ASD diameter and surrounding rims by TTE, is important. In our study, the use of the additional right parasternal approach in TTE improved measurements of maximal ASD diameter and detection of rim deficiencies and enabled morphologic evaluation comparable with that obtained by TEE. In the conventional left approach, because the

direction of the ultrasound beam is almost parallel to the interatrial septum, there is frequent dropout of interatrial septal echoes in the region of the mid portion (fossa ovalis). Previous studies have shown that echo dropout in the region of the mid portion frequently occurs and can lead to false diagnoses of large defects.[22,28,29] One of those previous studies showed that the maximal ASD diameter measured with 2D TTE was larger than that measured with 2D TEE and that there was a poor correlation between these measurements because of dropout in the region of the fossa ovalis.[29] The subcostal approach is another useful method for visualizing perpendicularly the interatrial septum.[28] Although 2D TTE from the subcostal approach enables the detection of shunt flow across ASDs easily in pediatric patients,[25,28] this approach can provide suboptimal images or incomplete clinical information with regard to morphologic evaluation for transcatheter ASDs closure, especially in adult patients, because of the limited echocardiographic window.[6-8] The right parasternal approach is a method that can provide better evaluation of the structure of the interatrial septal because the ultrasound beam passes in a plane perpendicular to the interatrial septal.[22-26] The use of the right parasternal approach provided better visualization of the superior vena cava and inferior vena cava entering into the right atrium. The right parasternal approach contributed greatly to the detection of deficient rims in the present study, particularly for the inferoposterior rim, which is sometimes difficult to visualize clearly by TEE. A previous study showed that inferior rim deficiency was a significant factor associated with unsuccessful transcatheter closure.[30] Therefore, the additional right parasternal view can contribute to appropriate patient selection and the prediction of procedural results for transcatheter ASD closure.

Considerable experience and operator skills are necessary for evaluating ASD morphology precisely using 2D TTE, equivalent to 2D TEE. There are some issues of technique and some pitfalls. The ultrasound beam should be passed as perpendicularly to the interatrial septum as possible. In addition, gain adjustment using time-gain compensation, focus position, and the use of zoom mode (high frame rate) should be set for morphologic evaluation. In addition, control of respiration and body position should be required to avoid potential artifacts such as dropout and side lobe.

Three-Dimensional Echocardiography Using the Right Parasternal Approach

ASDs are known to have complex geometry that may be elliptical, ovoid, or multiple defects or fenestrations.[20,21] Three-dimensional echocardiography provides more spatial anatomic information without the need for mental 2D reconstruction. There have been several studies on the usefulness for assessing ASDs of 3D transesophageal echocardiographic reconstruction[10-12] and real-time 3D TEE.[18-21] In addition, some previous studies have demonstrated possible usefulness of 3D TTE for evaluating ASD morphology.[18,21,22] Acar *et al.*[31] reported a high correlation between 3D transthoracic and 3D transesophageal echocardiographic measurements of maximal ASD diameter in pediatric patients. Van den Bosch *et al.*[13] demonstrated that real-time 3D TTE enabled reliable assessment of the dimensions of ASDs and the exact location and extent of the surrounding rim, and they reported an excellent correlation of real-time 3D transthoracic echocardiographic findings compared with surgical and 2D transesophageal echocardiographic measurements of ASDs in pediatric and relatively young adult patients. Chen *et al.*[14] reported that 3D TTE could provide accurate diagnosis of sinus venosus ASDs. In terms of the usefulness of 3D TTE in the right parasternal approach for evaluating ASD morphology, although there was one case report, studies with a sufficient number patients and including patients with a wide age range have been limited. In the present study, we demonstrated that the use of the right parasternal approach in addition to the conventional left approach improved the feasibility of visualization of satisfactory 3D images, even in adult patients.

Limitations

This study had some limitations. First, the number of patients in this study was relatively small to conclude whether the extent of variation in ASD type was taken into account. Second, almost all patients in the present study were referred from other hospitals to our institution for transcatheter closure of ASDs. Therefore, patient selection bias could have existed before enrollment. Third, visualizing ASDs and surrounding rims using the right parasternal approach requires a learning curve. In this study, interobserver variability and intraobserver variability were quantitatively evaluated by two skilled operators. Finally, evaluation in the subcostal view may improve the feasibility and accuracy of TTE.

CONCLUSIONS

The use of the right parasternal approach enables detailed morphologic evaluation, especially for longitudinal ASD diameter, superoanterior rim diameter, and inferoposterior rim diameter of ASDs in a longitudinal vena cava superior-inferior plane of the interatrial septum. In patients with suboptimal images with the conventional left approach, additional 3D TTE in the right parasternal approach can improve the feasibility of obtaining optimal 3D images to evaluate the shapes and locations of ASDs.

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Outcomes of One-Lung Fontan Operation: A Retrospective Multicenter Study in Japan

Yasuhiro Fujii, MD, Shunji Sano, MD, Toshihide Asou, MD, Yutaka Imoto, MD, Yoshihiro Oshima, MD, Shiori Kawasaki, MD, Hidefumi Kishimoto, MD, Kisaburo Sakamoto, MD, Masanobu Maeda, MD, Masaaki Yamagishi, MD, and Kozo Matsuo, MD

Department of Cardiovascular Surgery, Okayama University Hospital, Okayama; Department of Cardiovascular Surgery, Kanagawa Children's Medical Center, Kanagawa; Department of Cardiovascular Surgery, Kyushu Kouseinenkin Hospital, Fukuoka; Department of Cardiovascular Surgery, Kobe Children's Hospital, Hyogo; Department of Cardiovascular Surgery, Juntendo University School of Medicine, Tokyo; Department of Cardiovascular Surgery, Osaka Medical Center and Research Institute for Maternal and Child Health, Osaka; Department of Cardiovascular Surgery, Mt. Fuji Shizuoka Children's Hospital, Shizuoka; Department of Cardiovascular Surgery, Aichi Children's Health and Medical Center, Aichi; Department of Pediatric Cardiovascular Surgery, Kyoto Prefectual University of Medicine, Kyoto; and Department of Cardiovascular Surgery, Chiba Cardiovascular Center, Chiba, Japan

Background. The Fontan operation for patients with one available lung is an extremely challenging situation. However, few reports are available on this procedure. The purpose of this study was to describe outcomes of one-lung Fontan operation.

Methods. A retrospective multicenter study was performed. Twelve of 1,142 patients whose data were recorded here underwent one-lung Fontan operation between September 1989 and October 2009. Preoperative, operative, and postoperative data were reviewed.

Results. Median age at operation was 3.5 years (range, 1.0 to 22.8), the preoperative mean pulmonary pressure was 11.5 ± 3.3 mm Hg (range, 7.0 to 18.0), the ventricular ejection fraction was 58% ± 13% (range, 39 to 76), and end-diastolic ventricular pressure was 7.5 ± 3.5 mm Hg (range, 1.0 to 12.0). The available lung was right in 9 patients and left in 3 patients. Eleven patients underwent a two-staged Fontan completion. Extracardiac conduit total cavopulmonary connection, intraatrial extracardiac conduit total cavopulmonary connection, and atriopulmonary connection were performed in 10 patients, 1 patient, and 1 patient, respectively. The estimated actuarial survival was 83% at 1year, 73% at 5 years, and 73% at 10 years. Impaired ventricular function was found to be a significant risk factor for mortality by univariate analysis (43.0% ± 9.5% versus 64.0% ± 9.5%, $p < 0.01$), but not by multivariate analysis.

Conclusions. One-lung Fontan operation can be performed with an acceptable midterm to long-term mortality rate in patients without impaired ventricular function. Thus, absence of one lung itself is not a contraindication to the Fontan operation.

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Since Fontan and Baudet first described their procedure for the correction of tricuspid atresia in 1971, its principles have been applied to all forms of functional single ventricle [1]. Having made several modifications, the total cavopulmonary connection (TCPC) that was first reported by de Leval and coworkers [2] became a standard method for the Fontan operation because of its better venous hemodynamics [3] and because it is less arrhythmogenic [4] than the others. In addition, several management strategies have been incorporated to achieve a low mortality rate: the adoption of universal risk factors that have resulted in better patient selection [5], a "staged" approach [6], fenestration [7], and modified ultrafiltration [8]. With these modifications, the indications for the Fontan operation have gradually extended. One of the most challenging situations is a patient with a single ventricle who has only one available lung. A one-lung Fontan operation seems possible if the patient's pulmonary arterial resistance is low. However, very few reports are available on this procedure because it is an extremely rare situation. Therefore, we conducted a retrospective multicenter study to describe the early to late outcomes for one-lung Fontan operation.

Patients and Methods

Study Subjects

The data were collected retrospectively by filling out questionnaires by doctors of each institute. Ten institutes in Japan participated in this study and reported a total of 1,142 Fontan operations performed from September 1989 to October 2009. Four institutions supplied 12 one-lung Fontan operations (1.1%) and six did not. Ethical Committee approval was obtained for each institution. The

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Address correspondence to Dr Fujii, Department of Cardiovascular Surgery, Okayama University Hospital, 2-5-1 Shikata-cho, Kita-ku, Okayama City, Okayama 700-8558, Japan; e-mail: yasuhiro-f@live.jp.

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variables examined included demographic data, cardiac diagnosis, date of surgery, details of operative procedure, echocardiographic data, catheterization data, laboratory data, the length of postoperative hospital stay, duration of mechanical ventilation, duration of chest tube drainage, and outcomes. The inclusion criteria for "one lung" in this study is 100% occlusion of either the right or left pulmonary artery (PA).

Data Analysis

Data are expressed as the mean (SD) or median and range, as appropriate. To determine the risk factors for mortality, univariate and multivariate analyses were performed. Binary data and continuous data were analyzed using Fisher's exact test and the unpaired *t* test, respectively. Calculation of survival was performed by the Kaplan-Meier method. Cox proportional hazard analysis was used for multivariate analysis. A *p* value less than 0.05 was considered statistically significant.

Results

Patient Characteristics and Pre-Fontan Data

The detailed characteristics of each patient are provided in Table 1. The median age at the time of one-lung Fontan operation was 3.5 years (range, 1.0 to 22.8). The median height was 89 cm (range, 66 to 171) and the median body weight was 11.0 kg (range, 6.3 to 45.4). All these patients had previously undergone numerous cardiac operations, with a median of 4 (range, 2 to 5) per patient. Eleven of the 12 patients (92%) had undergone a bidirectional Glenn operation previously. The available lung was right in 9 patients (75%) and left in 3 patients (25%). Potential causes of unilateral obstruction of the PA were pulmonary venous obstruction (PVO) in 8 patients and PA thromboembolism in 4 patients. These pulmonary obstructions were caused before Fontan operation in 11 patients and early after Fontan operation in 1 patient.

Blood examination revealed the hemoglobin concentration, hematocrit, and platelet count were 16.9 ± 2.8 g/dL (range, 12.4 to 22.5), 51.7% ± 2.8% (range, 39.7 to 63.1), and 272 ± 74 × 10^3/μL (158 to 366), respectively. The total protein and albumin was 7.4 ± 0.7 mg/dL (range, 6.2 to 9.0) and 4.5 ± 0.5 mg/dL (range, 3.8 to 5.1), respectively. The aspartate transaminase and alanine transaminase concentrations were 36 ± 20 IU/L (range, 17 to 91) and 21 ± 14 U/L (range, 8 to 90), respectively. The total bilirubin concentration was 0.7 ± 0.4 mg/dL (range, 0.3 to 1.5). The creatinine concentration was 0.49 ± 0.28 mg/dL (range, 0.28 to 1.10). The arterial oxygen saturation was 83% ± 7% (range, 69 to 92). The mean available pulmonary arterial pressure (mPAP), atrial pressure, and ventricular end-diastolic pressure were 11.5 ± 3.3 mm Hg (range, 7.0 to 18.0), 5.9 ± 2.9 mm Hg (range, 2.0 to 12.0), and 7.5 ± 3.5 mm Hg (range, 1.0 to 12.0), respectively. The ventricular ejection fraction was 58% ± 13% (range, 39 to 76). The grade of atrioventricular valve regurgitation (AVVR) was none in 3 patients, trivial in 6 patients, and mild in 2 patients. The grade of AVVR was not recorded clearly in 1 patient: however, it was mild or lower.

Surgical Data

The technique used for the one-lung Fontan operation was extracardiac TCPC in 10 patients, intraatrial extracardiac TCPC in 1 patient, and an atriopulmonary connection in 1 patient. Associated procedures included creation of a fenestration in 7 patients, pulmonary arterial plasty in 2 patients, release of the PVO in 1 patient, and plication of the left diaphragm in 1 patient. The cardiopulmonary bypass time was 151 ± 64 minutes (range, 60 to 243). An aortic cross-clamp was performed in 7 patients, with duration of 46 ± 25 minutes (range, 11 to 84). Modified ultrafiltration was used in 10 patients.

Early Outcomes

No patient died within 30 days after the operation. There was 1 in-hospital death (patient no. 5 in Table 1). This patient had a cerebral infarction at an extracardiac TCPC, complicated by severe right-side pneumonia, and she died 85 days after the operation. For the hospital survivors, the median duration of mechanical ventilator support was 14 hours (range, 0 to 768). The median duration of the requirement for chest drainage was 8 days (range, 5 to 78). One patient required bilateral chemical pleural adhesion therapy owing to persistent pleural effusion (patient no. 11 in Table 1). This patient could be weaned off chest drainage on postoperative day 78 and required home oxygenation therapy after discharge. The median postoperative hospital stay was 72 days (interquartile range, 40 to 122). The median maximum postoperative serum creatinine concentration was 0.71 mg/dL (range, 0.41 to 6.70). The grade of AVVR at the time of discharge was none in 3 patients, trivial in 6 patients, and mild in 2 patients. The other major early postoperative complications were pneumonia of unavailable lung in 2 patients, mediastinitis with left pyothorax (the available lung is right) in 1 patient, renal dysfunction requiring dialysis in 2 patients, bradycardia with junctional rhythm in 1 patient, and paroxysmal supraventricular tachyarrhythmia in 1 patient.

Midterm to Long-Term Outcomes

There were 2 late deaths among the 11 hospital survivors with the mean follow-up period of 8.1 ± 6.5 years (range, 0.5 to 21.3). One patient was a 2-year-old boy (patient no. 6 in Table 1) who underwent an extracardiac TCPC. He had pneumonia 2 years after the operation and died. The other patient was a 21-year-old man (patient no. 11 in Table 1) who underwent an extracardiac TCPC and required pleural adhesion therapy as described above. He had protein-losing enteropathy 2 years after the operation and was managed with steroid, albumin, and gamma-globulin. But his course was complicated by severe fungal pneumonia, and he died 3 years after the operation. The estimated overall survival was 83%, 73%, and 73% at 1, 5, 10 years after the operation, respectively (Fig 1).

Regarding the present level of activity of the 4 adult survivors, 1 patient is working as an officer, 1 is a

Table 1. Patient Characteristics and Final Outcomes

Pt. No.	Age, Years	Sex	HT, cm	BW, kg	Main Diagnosis	Previous Operations (Age at Operation)	Available Lung	Cause of One Lung	Final Outcome
1	14.4	M	159	43	PAIVS	Lt mBTS (1 mon) BDG+ASD creation (3 y), re-Lt mBTS (8 y) IPAS+CS+PAP+Lt PVO release (13 y)	Right	Lt PVO	Alive
2	3.3	M	88	11	MA, DORV, CoA	CoA repair (EEA)+PAB (2 mon) DKS+mBTS (2 mon), BDG (8 mon) Lt PVO release+TVP+CS+IPAS (2 y) Lt PVO release (3 y)	Right	Lt PVO	Alive
3	22.8	F	151	43	CAVC, DORV, PS, asplenia	Lt mBTS (14 mon), CS (4 y), Lt BDG	Left	Rt PAO	Alive
4	1.0	F	66	6	SLV, CAVC, PA	Rt mBTS (2 mon), Lt mBTS (3 mon) Lt PVO release+PAP (5 mon) BDG+Lt mBTS+PAP (7 mon)	Right	Lt PVO	Alive
5	2.0	F	86	11	SA, SRV, PA, TGA, TAPVC(2b), asplenia	PVO release+RVPAS (2 mon) IPAS+BDG+Rt shunt with ITA (13 mon) Rt PVO release (17 mon)	Left	Rt PVO	Dead
6	2.2	M	80	9	HLHS	Norwood (RVPAS) (7 days) BDG+ASD creation+RV aneurysmectomy (6 mon) IPAS+Lt mBTS+PAP+Lt PVO release (15 mon) Lt PVO release (22 mon)	Right	Lt PVO	Dead
7	3.7	M	84	9	CAVC, DORV, SA, TAPVC(1b)	TAPVC repair+PAB (8 days) BDG+IPAS+re-PAB, PVO release+CAVVP (6 mon) CS(4)+CAVVP (16 mon) Lt PVO release+CAVVP (2 y)	Right	Lt PVO	Alive
8	5.4	M	108	16	TA(Ib)	Rt oBTS (12 mon), Lt mBTS (20 mon)	Left	Rt PA stenosis	Alive
9	2.2	M	70	7	DORV, SAS, CoA	CoA repair+PAB (11 days), Re-CoA repair+ASD creation (2 mon), VSD enlargement+PAP+RVPAS (7 mon) BDG+DKS (14 mon)	Right	Lt PVO	Alive
10	17.9	F	150	35	TA(IIA), PA	Lt mBTS(2 y), CS (9 y), CS (13 y) BDG (18 y)	Right	Lt lower PVO Lt PAO	Alive
11	21.3	M	171	45	SRV	Lt mBTS (2 mon), BDG (3 y)	Right	Lt PAO	Dead
12	2.2	M	89	10	SLV	PAB (2 mon) BDG+DKS+CAVVP+PAP (12 mon)	Right	Paralysis of Lt diaphragm	Alive

ASD = atrial septal defect; BDG = bidirectional Glenn operation; BW = body weight; CAVC = common atrioventricular septal defect; CAVVP = common atrioventricular valve plasty; CoA = coarctation of aorta; CS = central shunt; DKS = Damus-Kaye-Stansel anastomosis; DORV = double outlet right ventricle; EEA = end-to-end anastomosis; F = female; HLHS = hypoplastic left heart syndrome; HT = height; IPAS = intrapulmonary artery septation; ITA = internal thoracic artery; Lt = left; M = male; MA = mitral atresia; mBTS = modified Blalock-Taussig shunt; mon = months; oBTS = original Blalock-Taussig shunt; PA = pulmonary atresia; PAB = pulmonary arterial banding; PAIVS = pulmonary atresia with intact ventricular septum; PAO = pulmonary arterial obstruction; PAP = pulmonary arterial plasty; PS = pulmonary stenosis; PVO = pulmonary venous obstruction; Rt = right; RV = right ventricle; RVPAS = right ventricle–pulmonary artery shunt; SA = single atrium; SAS = subaortic stenosis; SLV = single left ventricle; SRV = single right ventricle; TA = tricuspid atresia; TAPVC = total anomalous pulmonary venous connection; TGA = transposition of the great arteries; TVP = tricuspid valve plasty; VSD = ventricular septal defect; y = years.

university student, and 2 other patients are at home under treatment without working or attending school. Five patients are still of the pediatric age and are under treatment in an outpatient clinic. The New York Heart Association functional class was grade 1 in 4 patients, grade 2 in 3 patients, grade 3 in 2 patients, and unknown in 1 patient (the latter patient is being followed up by a local outpatient clinic now, but there is no exact information about New York Heart Association class on the questionnaire).

Surgical intervention was required in 1 patient. The patient underwent ligation or division of well-developed arteriopulmonary collateral arteries (patient no. 7 in Table 1). In addition, 2 patients underwent a catheter-based intervention: 1 who had undergone an atriopulmonary connection was treated with percutaneous release of a stenosis of atriopulmonary connection (patient no. 8 in Table 1); the other required coil embolization of the bronchial, intercostal, and inferior diaphragmatic arteries for the treatment of hemoptysis (patient no. 12 in Table 1). One patient required home oxygenation therapy (patient no. 9 in Table 1). One patient had paroxysmal atrial fibrillation (patient no. 8 in Table 1). One patient had repeated bronchitis (patient no. 2 in Table 1).

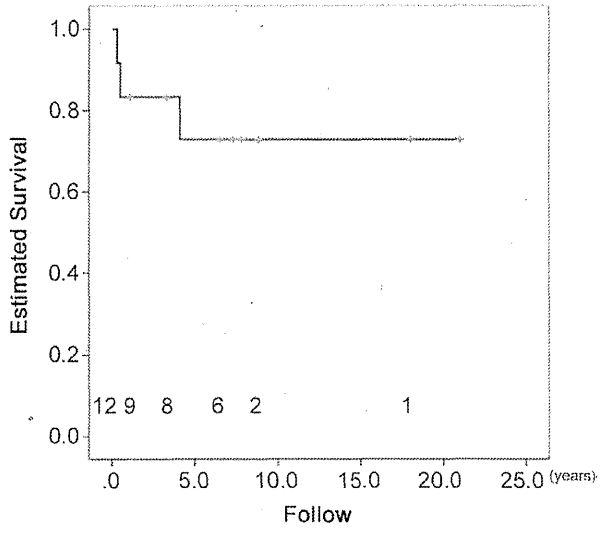

Fig 1. Estimated actuarial survival in patients who underwent one-lung Fontan operation. Actuarial survival was 83% at 1 year, 73% at 5 years, and 73% at 10 years after operation.

On blood examination in the late survivors, the hemoglobin concentration, hematocrit, and platelet count were 14.7 ± 3.3 g/dL (range, 10.5 to 18.9), 43.8% ± 8.7% (range, 31.5 to 54.2), and 165 ± 120 × $10^3/\mu L$ (range, 143 to 356), respectively. The total protein and albumin was 7.1 ± 0.5 mg/dL (range, 6.2 to 8.0) and 4.2 ± 0.8 mg/dL (range, 2.7 to 5.1), respectively. The aspartate transaminase and alanine transaminase concentrations were 27 ± 8 IU/L (range, 21 to 43) and 14 ± 6 U/L (range, 7 to 21), respectively. The total bilirubin concentration was 0.7 ± 0.4 mg/dL (range, 0.3 to 1.4). The creatinine concentration was 0.52 ± 0.32 mg/dL (range, 0.18 to 1.00).

Postoperative cardiac catheterization was performed in 7 patients. The arterial oxygen saturation was 90% ± 9% (range, 71 to 97). The average mPAP, ventricular end-diastolic pressure, and ventricular ejection fraction were 11.1 ± 0.9 mm Hg (range, 10.0 to 12.0), 9.5 ± 3.3 mm Hg (range, 6.0 to 14.0), and 63% ± 12% (range, 48 to 86), respectively.

The grade of the AVVR in the late survivors was mild or lower in 8 patients, and moderate in 1 patient.

Risk Analysis of Overall Mortality

By univariate analysis, impaired ventricular function was a significant risk factor for mortality (43.0% ± 9.5% in dead cases versus 64.0% ± 9.5% in living cases, $p < 0.01$). There was no significant association with differences in the availability of the right lung, sex, presence of a fenestration, use of aortic cross-clamp, use of modified ultrafiltration, age, body weight, hemoglobin, hematocrit, platelet count, total protein, albumin, aspartate transaminase, alanine transaminase, serum total bilirubin, arterial oxygen saturation, mPAP, ventricular end-diastolic pressure, cardiopulmonary bypass time, aortic cross-clamp time, duration of chest drainage, duration of the hospital stay, and maximum creatinine level after operation. By multivariate analysis, there was no significant risk factor for mortality.

Comment

Sade and associates [9] first described a one-lung Fontan operation. They reported a 10-year-old patient who successfully underwent right-side one-lung Fontan operation using a Dacron conduit between the right atrium and the right PA [9] and clinically doing well 9 years after the operation [10]. In addition, Zachary and colleagues [11] reported 7 cases of one-lung Fontan operation in 1998. They investigated the postoperative differences between patients with one lung and two lungs and reported that only difference between these two groups was noted in the postoperative arterial oxygen saturation (87% in the one-lung group versus 91% in the two-lungs group) [11]. Then, their group described the results of 5 long-term survivors of these 7 cases and their additional 5 cases of one-lung Fontan operation in 2004 [12]. The total number of reported one-lung Fontan operations including this study was 28 [9–15]. There was 1 hospital death (3.6%) and 5 late deaths (17.9%). Three of the 6 deaths were from this report. The other 3 late deaths were reported by the group of Zachary and coworkers [11, 14]. The overall mortality was 21.4%. The mortality in this report seems to be worse than overall mortality of the Fontan operation reported from Japan [16, 17]. However, it is notable that the mortality was 0% in one-lung Fontan patients with ventricular ejection fraction more than 50% with a follow-up period of 9.2 ± 6.9 years (range, 1.1 to 21.0). Considering the recent survival of pediatric heart transplantation is less than 70% at 10 years and less than 50% at 20 years [18], one-lung Fontan operation could be better option in selected patients. Conversely, patients with either impaired ventricular or pulmonary condition might be contraindicated for one-lung Fontan operation.

One case of PLE was diagnosed in this study. All of the other late survivors had no symptoms indicating PLE. However, 1 patient had serum albumin concentration of 2.7 mg/dL. This finding is very suspect for PLE; unfortunately, however, there is no information about stool alpha-1-antitrypsin level. No other patients had serum albumin concentration of less than 3.5 mg/dL. The incidence of the PLE in this study was 8.3% (16.7% if including 1 suspected case); however, Jacobs and colleagues [11] reported that 50% of the one-lung Fontan patients had PLE. To know the reason why this difference occurred is difficult. However, judging from the data of their first 7 cases (mean pulmonary arterial pressure 11.7 ± 2.7 mm Hg, mean atrial pressure 6.0 ± 3.6 mm Hg, and mean ventricular end-diastolic pressure 7.9 ± 2.7 mm Hg) [11] and the data of their additional 5 cases that they described [12], the preoperative pulmonary and cardiac condition for one-lung Fontan operation seems to be comparable between their report and this report. The follow-up period of their cases seems not to be extremely different from that of this report, although we could not know the exact follow-up period of their report. Concerning the method of Fontan procedure, 11 of 12 patients underwent a lateral tunnel

type of TCPC with or without partial hepatic vein exclusion or fenestration in their study. In this study, 11 of 12 patients underwent extracardiac or intraatrial extracardiac conduit TCPC with or without fenestration. Although the selection of the procedures may affect the incidence of the PLE, there has been no way to elucidate it. Further investigation should be required to determine the optimal surgical method for one-lung Fontan operation.

Pulmonary condition of the available lung is obviously crucial for one-lung Fontan operation. In this report, all patients except for 1 who underwent one-staged Fontan completion had mPAP of 15 mm Hg or less. Although mPAP in this patient was 18 mm Hg, the pulmonary arterial resistance was 1.4 Woods unit · m^2. We could not reach any conclusion about the borderline of pulmonary arterial resistance for one-lung Fontan operation in this study.

In this study, there is no true unilateral pulmonary atresia or hypoplasia. All unilateral pulmonary obstructions were caused by thromboembolism secondary to PVO or severe PA stenosis. Although one-lung Fontan operation seems to be a viable option, efforts to reconstruct the occluded PA should be challenged in such cases. Increasing available pulmonary vascular bed would be beneficial for the patient. Schmauss and coworkers [19] reported a case of successful reconstruction of an occluded right PA due to thromboembolism. The right PA was reconstructed with catheter intervention in this patient before the Fontan operation and was patent 3 years after the operation [19]. Tchervenkov and associates [20] described a successful case of intrapulmonary reconstruction of the left PA. Jacobs and associates [12] also said that PA reconstruction with homograft vascular patch could be successful in a few patients. They also said Blalock pulmonary shunt and PA reconstruction using cryopreserved saphenous vein and transcatheter stent could be a possible option for the PA reconstruction [12]. Reconstruction of PVO should also be tried using the same reasoning [19]; however, the recurrence rate will be high in such cases.

Cardiac function is an important factor for deciding the indication for Fontan operation [21, 22]. Although recent improvement of management strategy for Fontan operation have improved clinical outcomes [23], ventricular dysfunction and AVVR should affect the early or late outcomes, especially in patients with impaired pulmonary function. In this report, both of 2 patients with late deaths after the discharge had low systemic ejection fractions, 39% and 40%, respectively. One of them had postoperative PLE. The causes of both deaths were pneumonia; however, low output state in the background may have affected their outcome. Lower preoperative ventricular ejection fraction was a significant risk factor in univariate analysis, but not in multivariate analysis in this study. Although we could not reach any conclusion about this issue, normal ventricular function is believed to be desirable for successful one-lung Fontan operation. Regarding AVVR, all of the patients had competent atrioventricular valve function before Fontan operation in this report. One patient had moderate AVVR postoperatively probably due to increased arteriopulmonary collateral flow after one-lung Fontan operation. However, this patient did clinically well with serum B-type natriuretic peptide level of 44 pg/mL after coil embolizations of arteriopulmonary collateral arteries.

A major limitation of this study is the small number of patients. Further accumulation of data of one-lung Fontan circulation should be required to reach true conclusions to determine the boundary of one-lung Fontan operations.

In conclusion, absence of one lung itself is not a contraindication for the Fontan operation. No mortality from one-lung Fontan operation was observed among patients with both good available lung and ventricular functions. However, moderately and severely impaired ventricular function may be contraindications for one-lung Fontan operation.

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