Systemic Atrioventricular Valve Replacement in Patients With Functional Single Ventricle

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To review the outcome after atrioventricular valve replacement in single ventricle patients. The medical records of 37 consecutive patients who underwent initial valve replacement between 2001 and 2016 were reviewed. Actuarial survival rates were 73%, 65%, and 59% at 1, 5, and 10 years, respectively. Multivariate analysis indicated body surface area <0.28 m^2 ($P = 0.007$; hazard ratio, 31.1), preoperative inotropic support ($P < 0.001$; hazard ratio, 24.5), primary valve replacement ($P = 0.044$; hazard ratio, 6.1), oversized prosthesis ($P = 0.001$; hazard ratio, 14.5), and intra- or postoperative extracorporeal membrane oxygenation support ($P < 0.001$; hazard ratio, 53.2) were the risk factors for mortality. Cumulative incidences of redo replacement were 11%, 17%, and 17% at 1, 5, and 10 years, respectively. There was no risk factor for redo replacement. Among 11 patients undergoing valve replacement before or at the time of bidirectional cavopulmonary shunt, all 4 patients who reached Fontan completion survived. Among 13 patients undergoing valve replacement after bidirectional cavopulmonary shunt, only 3 patients reached Fontan completion. Among 11 patients undergoing valve replacement after Fontan completion, there were 3 operative mortalities and 2 late mortalities. For 7 of 8 hospital survivors, cardiac index improved from 2.2 L/min/m^2 (interquartile range, 2.0–2.4) to 3.4 (2.8–3.7) ($P = 0.002$). Atrioventricular valve replacement was a reasonable choice of treatment for single ventricle patients. For small patients with impaired ventricular function who had no choice other than valve replacement, commercially available valves were oversized and outcomes remained poor.

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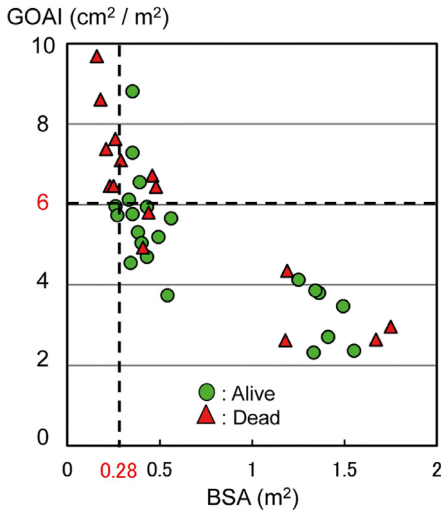

Scatterplot of geometric orifice area index (GOAI) vs body surface area (BSA).

Central Message

For small patients with impaired single ventricular function who had no other choice than atrioventricular valve replacement, commercially available valves were oversized and outcomes remained poor.

Perspective Statement

Multivariate analysis indicated body surface area <0.28 m^2, preoperative inotropic support, primary valve replacement, and geometric orifice area index >6.0 were the risk factors for mortality. These factors, however, must be linked together. For small patients with marginal preoperative conditions, atrioventricular valve replacement was challenging and commercially available valves were oversized.

Abbreviations: BCPS, bidirectional cavopulmonary shunt; BSA, body surface area; BW, body weight; BNP, brain natriuretic peptide; CI, confidence interval; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; FSV, functional single ventricle; GOAI, geometric orifice area index; HR, hazard ratio; MVR, mitral valve replacement; PT-INR, prothrombin time-international normalized ratio; SAVV, systemic atrioventricular valve; SAVVR, systemic atrioventricular valve replacement

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INTRODUCTION

Significant systemic atrioventricular valve (SAVV) regurgitation remains a risk factor affecting survival and Fontan completion in patients with functional single ventricle (FSV).[1,2] Whereas SAVV repair is the treatment of choice for SAVV regurgitation,[3–10] SAVV replacement (SAVVR) is occasionally required for patients with unrepairable SAVV. The outcomes of SAVVR, however, have not been well documented. In fact, there have been only a few reports on consecutive FSV patients undergoing SAVVR.[11,12]

This study reviewed a single institution's experiences with SAVVR in FSV patients to identify the factors associated with the outcomes.

MATERIAL AND METHODS

Patients

All 37 consecutive FSV patients who underwent initial SAVVR between January 2001 and December 2016 were enrolled in this study. All patients suffered from SAVV regurgitation without stenosis. Patient demographic and morphologic variables are provided in Table 1. The median age was 24.6 months (interquartile range, 12.3–173.6) with a median body weight (BW) of 8.1 kg (6.1–34.2). SAVV morphology involved the common atrioventricular valve in 17 patients (46%), the tricuspid valve in 15 (41%), both the tricuspid and mitral valves in 3 (8%), and the mitral valve in 2 (5%). Two of the 3 patients with both tricuspid and mitral valves underwent preceding tricuspid valve closure followed by mitral valve replacement (MVR). The other patient underwent mitral valve closure and tricuspid valve replacement simultaneously. SAVVR was performed before bidirectional cavopulmonary shunt (BCPS), at the time of BCPS, after BCPS, at the time of Fontan completion, and after Fontan completion in 7 (19%), 4 (11%), 13 (35%), 2 (5%), and 11 patients (30%), respectively.

Twenty-three patients (62%) underwent SAVV repair prior to replacement. The median interval from SAVV repair to replacement was 13.6 months (6.5–35.7). The frequency of SAVV repair was once in 19 patients, twice in 3, and 3 times in 1. Primary SAVVR (no previous SAVV repair) was performed mainly in patients before or at the time of BCPS ($P < 0.001$).

Operative Method

SAVVR was performed through a median sternotomy, under cardiopulmonary bypass with mild-to-moderate hypothermia. Cardiac arrest with antegrade cardioplegia was employed in all patients. A prosthesis was placed at the intra-annular position with pledgeted interrupted sutures. Chordal attachments were reserved as much as possible. In patients with a common atrioventricular valve, interrupted pledgeted mattress sutures were placed in the fringe of the leaflet tissue along the area beyond the rim of the ventricular septal defect to avoid conduction block. Procedures performed concomitantly are provided in Table 2.

All implanted valves were mechanical bileaflet valves. The types of implanted prostheses were St. Jude Medical Standard valve (St. Jude Medical, Inc, St. Paul, MN) in 14 patients, St. Jude Medical Masters Hemodynamics Plus valve in 4, and ATS Advanced Performance valve (ATS Medical, Inc, Minneapolis, MN) in 19. Distribution of implanted valve size is shown in Figure 1.

Anticoagulation Protocol

Once adequate hemostasis was obtained following SAVVR, all patients were administered heparin sodium intravenously to maintain an activated partial thromboplastin time between 45 and 55 seconds. All patients subsequently took oral

Table 1. Patient Characteristics

Characteristic	*N* (%)
Sex (female/male)	16/21
Age at repair	
Infant	8 (22%)
1–2 years old	9 (24%)
>2 years old	20 (54%)
Primary diagnosis	
Unbalanced atrioventricular septal defect	18 (49%)
Hypoplastic left heart syndrome	9 (24%)
Corrected transposition of the great arteries	5 (14%)
Tricuspid atresia	2 (5%)
Others	3 (8%)
Associated lesions	
Atrial isomerism	14 (38%)
Extracardiac total anomalous of pulmonary venous connection	5 (14%)
Dominant ventricle morphology	
Right	28 (76%)
Left	6 (16%)
Undetermined	3 (8%)
Systemic atrioventricular valve morphology	
Common atrioventricular valve	17 (46%)
Tricuspid valve	15 (41%)
Mitral valve	2 (5%)
Both tricuspid and mitral valve	3 (8%)
Situs	
Solitus	21 (57%)
Inversus	2 (5%)
Ambiguous	14 (38%)
Apex	
Right	6 (16%)
Left	31 (84%)
Regurgitation grade	
Moderate	6 (16%)
Moderate-to-severe	10 (27%)
Severe	21 (57%)

Table 2. Concomitant Operations

Procedure	*N*
Central shunt	2
Ventricle-to-pulmonary artery conduit	1
Pulmonary artery banding	1
Coarctation of aorta repair	1
Main pulmonary artery to descending aorta bypass	1
Norwood procedure	2
Damus-Kaye-Stansel anastomosis	1
Bidirectional cavopulmonary shunt	4
Bidirectional cavopulmonary shunt revision	1
Fontan procedure	2
Fontan revision	3
Creation of fenestration	2
Pulmonary artery plasty	8
Pulmonary venous obstruction release	3
Aortic valve plasty	1
Aortic valve replacement	1
ASD enlargement	4
Mitral valve closure	1
Arrhythmia surgery	7
Maze, PV isolation	5
AV node isolation/cryoablation	1/1
Permanent pacemaker lead ± generator implantation	8
CRT-P implantation	2

ASD, atrial septal defect; AV, atrioventricular; CRT-P, cardiac resynchronization therapy-pacemaker; PV, pulmonary vein.

warfarin potassium to maintain a prothrombin time-international normalized ratio (PT-INR) between 2.0 and 3.0. (Complications that tend to occur in Japanese patients involve bleeding rather than thrombosis.[13,14] The Japanese Circulation Society guideline for surgical and interventional treatment of valvular heart disease[15] recommends that a target PT-INR for aortic valve replacement is between 2.0 and 2.5, and a target PT-INR for mitral valve replacement is between 2.0 and 3.0. The target PT-INR is between 2.5 and 3.5 for post-thrombotic events.)

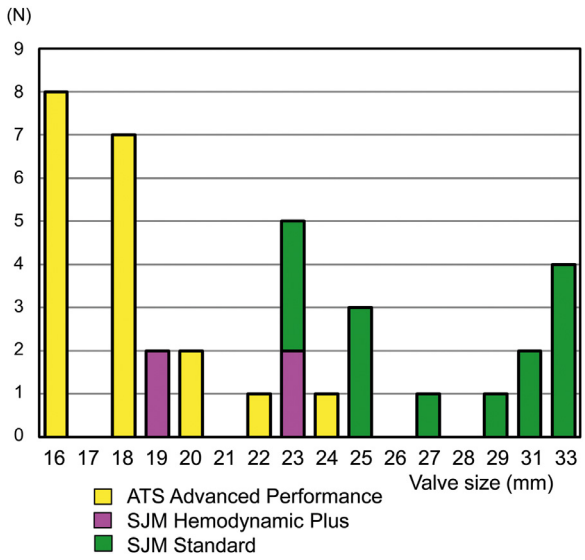


Figure 1. Distribution of size of implanted prosthetic valves. SJM, St. Jude Medical.

STUDY DESIGN AND STATISTICAL ANALYSIS

This study was approved by the institutional review board of the hospital; need for patient consent was waived. Medical, operative, angiographic, and echocardiographic data for all patients were reviewed. Information regarding their clinical status was obtained from the medical records and consultation with the referring cardiologist.

Continuous variables are presented as median values (interquartile range). Data from groups were compared with chi-square test, Fisher's exact probability test, or Wilcoxon signed-ranks test as appropriate. Actual survival rate and freedom from redo SAVVR rate were estimated by Kaplan-Meier method. Competing risk outcomes were analyzed with a cumulative incidence. Each time-to-event was defined as the time elapsed from the date of initial SAVVR to the date of death, redo SAVVR, or last known follow-up. Prognostic variables examined include continuous variables and categorical variables (listed in Appendix 1). Serum brain natriuretic peptide (BNP) has been routinely examined since 2003. BNP >400 pg/mL was tested as a possible predictor. Geometric orifice area index (GOAI) is calculated from the geometric orifice area (cm^2) divided by the body surface area (BSA; m^2). In regard to GOAI, receiver operating characteristic curve analysis suggested that the optimal cutoff value of predicting mortality within 2 years following SAVVR was 6.44 (area under curve, 0.718; $P = 0.034$; Fig. 2). Therefore, GOAI >6.0 was defined as "oversized prosthesis," and was also tested as a possible predictor. To evaluate the disproportion of implanted valves, we used a GOAI instead of using the

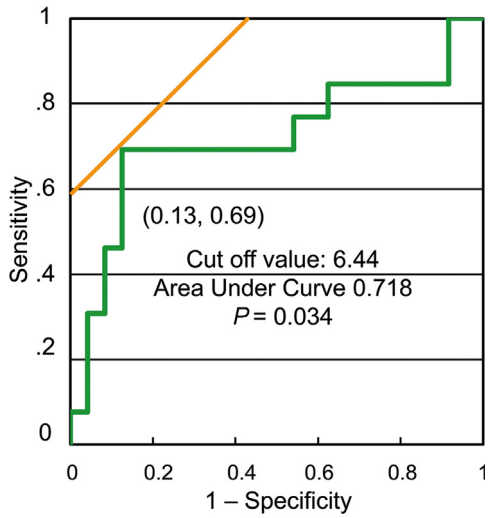


Figure 2. Receiver operating characteristic curve for GOAI and mortality within 2 years following systemic atrioventricular valve replacement. The cutoff point of GOAI was 6.44 (area under curve, 0.718; $P = 0.034$). Therefore, GOAI >6.0 was defined as "oversized prosthesis" in this study.

"labeled" size of the mechanical valve that the manufacturer provided, because it more accurately represented the physiological orifice. For example, the orifice of a 21-mm Masters Hemodynamics Plus valve made by St. Jude Medical is equal to that of a 23-mm Standard valve. Several other indicators (prosthesis size/patient weight ratio [mm/kg] or z-score difference between prosthetic valve and actual valve) were employed to identify the oversized prosthesis in MVR as a risk factor for mortality.[16–18]

Operative mortality was defined as death before hospital discharge or within 30 days of the operation. Late mortality was defined as death after discharge and more than 30 days following the operation.

These clinical variables were analyzed using the Cox regression hazard model for continuous variables and the log-rank test for categorical variables on univariate analysis. Variables with P values <0.05 on the univariate analysis were entered as candidates into the Cox proportional hazard model (stepwise) for multivariate analysis. Hazard ratios (HR) with 95% confidence intervals (CI) were constructed for the significant multivariate predictors. Statistical analyses were performed using JMP 13.2.1 software for Windows and R (version 3.5.1).

RESULTS

Overall Outcomes

Survival

The follow-up period was 4.0 years (0.4–10.7), and the follow-up rate was 100%. Heart transplantation or ventricular assist device implantation were not performed during the study period for patients with postcardiotomy heart failure due to the paucity of donors in Japan.

The actuarial survival rates were 73% (95% CI, 57–85), 65% (95% CI, 48–78), and 59% (95% CI, 41–75) at 1, 5, and 10 years, respectively (Fig. 3A). There were 11 operative mortalities and 4 late mortalities. Univariate analysis indicated age <1 year (P = 0.009), BSA <0.28 m^2 (approximately equal to BW <5 kg) (P = 0.02), primary SAVVR (P = 0.02), preoperative inotropic support (P = 0.02), preoperative ventilator support (P < 0.001), oversized prosthesis (P = 0.002), and intra- or postoperative extracorporeal membrane oxygenation (ECMO) support (P < 0.001) were the risk factors for mortality. Multivariate analysis indicated BSA <0.28 m^2 (P = 0.007; HR, 31.1; 95% CI, 1.9–502.6), preoperative inotropic support (P < 0.001; HR, 24.5; 95% CI, 3.8–158.6), primary SAVVR (P = 0.044; HR, 6.1; 95% CI, 1.0–36.9), oversized prosthesis (P = 0.001; HR, 14.5; 95% CI, 2.3–91.1), and intra- or postoperative ECMO support (P < 0.001; HR, 53.2; 95% CI, 6.0–474.2) were the risk factors of mortality. Figure 4A shows individual prognostic outcomes characterized by GOAI and BSA at the time of SAVVR. In detail, in patients whose GOAI was between 2 and 4, the actuarial survival rates were 90% (95% CI, 53–99), 80% (95% CI, 46–95), and 60% (95% CI, 23–88) at 1, 5, and 10 years, respectively. In patients whose GOAI was between 4 and 6, the actuarial survival rates were 93% (95% CI, 63–99), 86% (95% CI, 57–96), and 86% (95% CI, 57–96) at 1, 5, and 10 years, respectively. In patients whose GOAI was more than 6, the actuarial survival rates were 38% (95% CI, 17–66), 31% (95% CI, 12–59), and 31% (95% CI, 12–59) at 1, 5, and 10 years, respectively (P = 0.009).

Redo SAVVR

Cumulative incidences of redo SAVVR were 11% (95% CI, 3–23), 17% (95% CI, 7–32), and 17% (95% CI, 7–32) at 1, 5, and 10 years, respectively (Fig. 3B). There was no risk factor for redo SAVVR. Eight patients underwent redo SAVVR. The interval from initial SAVVR to redo was 14.7 months (2.2–76.9).

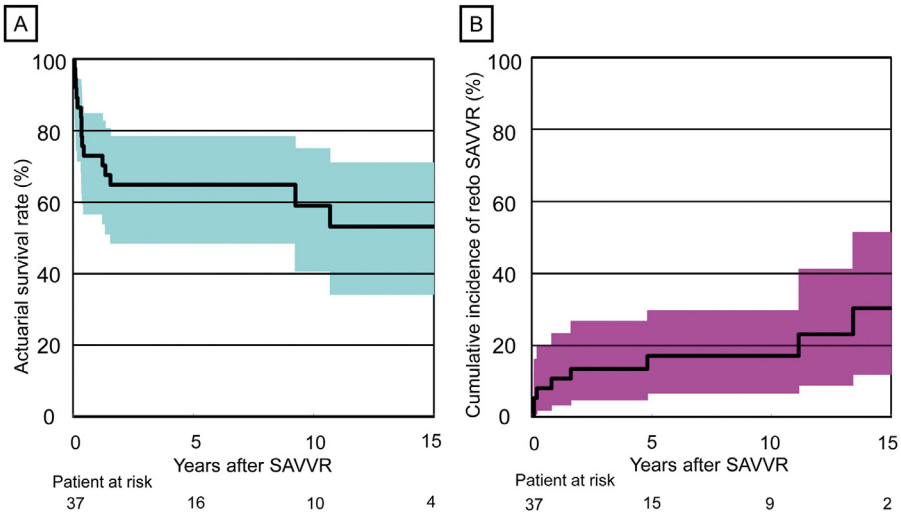


Figure 3. Kaplan-Meier estimated actuarial survival rate (A), and cumulative incidence of redo systemic atrioventricular valve replacement (B). Numbers of patients at risk at 0, 5, 10, and 15 years are shown.
SAVVR, systemic atrioventricular valve replacement.

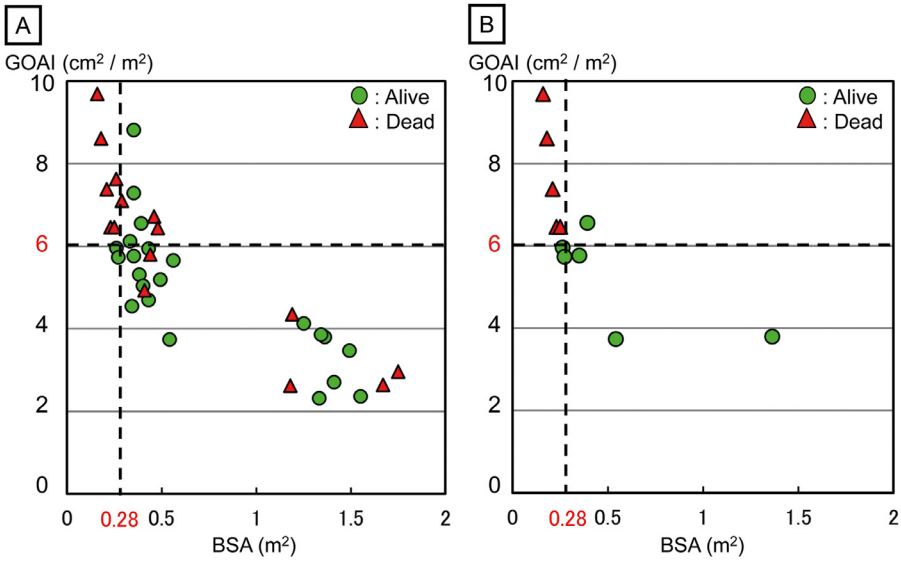


Figure 4. Scatterplot of GOAI vs BSA. Open green circles represent living patients, and open red triangles represent dead patients. All patients (A) and patients who underwent systemic atrioventricular valve replacement before or at the time of bidirectional cavopulmonary shunt (B). Multivariate analysis indicated both GOAI >6.0 (oversized prosthesis) and BSA <0.28 were risk factors for mortality.
BSA, body surface area; GOAI: geometric orifice area index.

All 4 patients underwent early redo SAVVR (<1 year after SAVVR) because of stuck valve due to thrombus. Two underwent redo SAVVR using a downsized prosthesis (from 24-mm ATS [after Fontan completion] to 22-mm [from a GOAI of 2.72 to 2.25] [BSA 1.41] and from 20-mm ATS [after BCPS] to 18-mm [from a GOAI of 5.95 to 4.70] [BSA 0.43]) and were free from valve thrombosis thereafter. However, the 2 other patients (from 33-mm St. Jude Medical Standard [after BCPS] to 29-mm [from a GOAI of 4.35 to 3.71] [BSA 1.19] and from 16-mm ATS [at the time of BCPS] to 17-mm St. Jude Medical Standard [from a GOAI of 6.46 to 6.79] [BSA 0.24]) required ECMO support, and subsequently expired. There was no risk factor for thrombosed stuck valve.

Four other patients underwent late redo SAVVR (>1 year after SAVVR) due to prosthesis-patient mismatch by somatic outgrowth in 2 patients, stuck valve caused by pannus and thrombus in 1, and opening restriction caused by pannus in 1. No patient died after late redo SAVVR. Preoperative peak flow velocity through the prosthetic valve exceeded 2.0 m/s in 2 patients with prosthesis-patient mismatch. (One patient [BW 11.3 kg] with a 16-mm ATS underwent redo SAVVR at the time of Fontan completion, and the other patient after Fontan completion with a 23-mm St. Jude Medical Standard underwent redo SAVVR at a BW of 52.5 kg.) For another patient with a 16-mm ATS after Fontan completion, redo SAVVR was scheduled because peak flow velocity was beyond 2.0 m/s and his BW was over 30 kg.

The most recent peak velocities of all remaining patients were below 2.0 m/s (median 1.7 m/s [1.4—1.8]). (Three of 8 patients with a 16-mm ATS survived after SAVVR. Besides the 2 mentioned in the previous paragraph, the recent BW of the other patient is around 15 kg. Six of 7 patients with an 18-mm ATS survived after SAVVR. Their latest BW measurements range from 12 to 25 kg.) No redo SAVVR was required due to perivalvular leakage, hemolysis, or prosthetic valve endocarditis.

Cardiac Function After SAVVR

Preoperative and postoperative (1 month following SAVVR) systemic ventricular ejection fraction (EF) data of 35 patients (95%) were evaluated and analyzed using 2D echocardiography. EF decreased from 59% (50—70) prior to SAVVR to 46% (33—55) at 1 month following SAVVR ($P < 0.001$). For hospital survivors after SAVVR in particular, follow-up EF data at 6 and 12 months following SAVVR were also evaluated. (These serial EF data were available in 20 patients including 2 late mortalities.) EF also decreased from 58% (47—71) prior to SAVVR to 48% (40—54) at 1 month following SAVVR ($P = 0.006$); EF however improved to 55% (47—70) at 6 months ($P = 0.032$) and remained at 12 months (60% [48—64]). The serum BNP improved from 203 pg/mL (93—317) at preoperative examination to 81 pg/mL (31—151) in recent outpatient follow-up examinations ($P = 0.034$; $N = 22$).

Postoperative Complications

Excluding 3 patients who underwent pacemaker implantation preoperatively, cumulative incidences of pacemaker implantation ($N = 34$) were 21% (95% CI, 9—36), 28% (95% CI, 13—44), and 34% (95% CI, 16—52) at 1, 5, and 10 years, respectively. Advanced or complete atrioventricular block developed in 6 patients, which necessitated pacemaker implantation following initial SAVVR in 3 patients, redo SAVVR in 2, and 4.7 years after initial SAVVR in 1. Three patients developed sick

sinus syndrome, which necessitated pacemaker implantation following initial SAVVR in 2 patients and 1.7 years after initial SAVVR in 1. Six patients underwent cardiac resynchronization therapy—pacemaker implantation concomitant with initial SAVVR in 2 patients and after discharge in 4 patients. (Median interval from initial SAVVR to cardiac resynchronization therapy—pacemaker implantation was 7.9 years [5.6—8.8].)

Cumulative incidences of cerebral infarction/hemorrhage were 8% (95% CI, 2—20), 11% (95% CI, 3—24), and 11% (95% CI, 3—24) at 1, 5, and 10 years, respectively. Cerebral infarction occurred in 2 patients. One patient recovered without any sequelae, and the other one resulted in mild hemiparesis. Cerebral bleeding occurred in 2 patients. One patient with subdural hematoma expired due to cardiac dysfunction, and another patient expired after a small cerebral hemorrhage spread to the brainstem.

Specific Impact of SAVVR on FSV Surgical Stage

Before or at the Time of BCPS

Among the 11 patients who underwent SAVVR before or at the time of BCPS, all 4 patients who reached Fontan completion survived (Fig. 5A). BCPS was not indicated for 2 patients (21 trisomy and palliative surgery for adult patient [late referral]). All 5 mortalities had GOAI >6.0 and BSA <0.28 m^2 (Fig. 4B).

After BCPS or at the Time of Fontan Completion

Among the 15 patients who underwent SAVVR after BCPS or at the time of Fontan, all 5 patients who reached Fontan completion were survived (Fig. 5B). Concomitant Fontan completion was not indicated for 13 patients due to marginal cardiopulmonary conditions; SAVVR was therefore performed prior to Fontan completion. Of these 13 patients, only 3 (23%) reached Fontan completion. Three hypoplastic left heart syndrome patients are still awaiting Fontan completion, and they all show signs of marginal cardiopulmonary function: a 12-year-old patient with Turner syndrome, a 5-year-old patient after cardiac resynchronization therapy—pacemaker implantation, and a 6-year-old patient with hypoxia due to pulmonary arteriovenous malformation and veno-venous collateral proliferation. For the other 2 patients, Fontan completion was not indicated due to protein-losing enteropathy and pulmonary venous obstruction.

After Fontan Completion

Among the 11 patients who underwent SAVVR after Fontan completion, there were 3 operative mortalities and 2 late mortalities (Fontan failure 9 and 10 years following SAVVR; Fig. 5C). Univariate analysis showed high BNP (>400 pg/mL; $P = 0.018$) was a risk factor for mortality. For 7 of 8 hospital survivors, cardiac index improved from 2.2 L/min/m^2 (2.0—2.4) before SAVVR to 3.4 (2.8—3.7) after SAVVR ($P = 0.002$). However, central venous pressure (15 mm Hg [11—16] to 14 [11—16]), pulmonary capillary wedge pressure (10 mm Hg [8—13] to 12 [7—13]), and EF (48% [37—53] to 46 [38—51]) showed no improvement.

DISCUSSION

This study yielded acceptable SAVVR outcomes in terms of survival rate, morbidity rate, and Fontan completion.

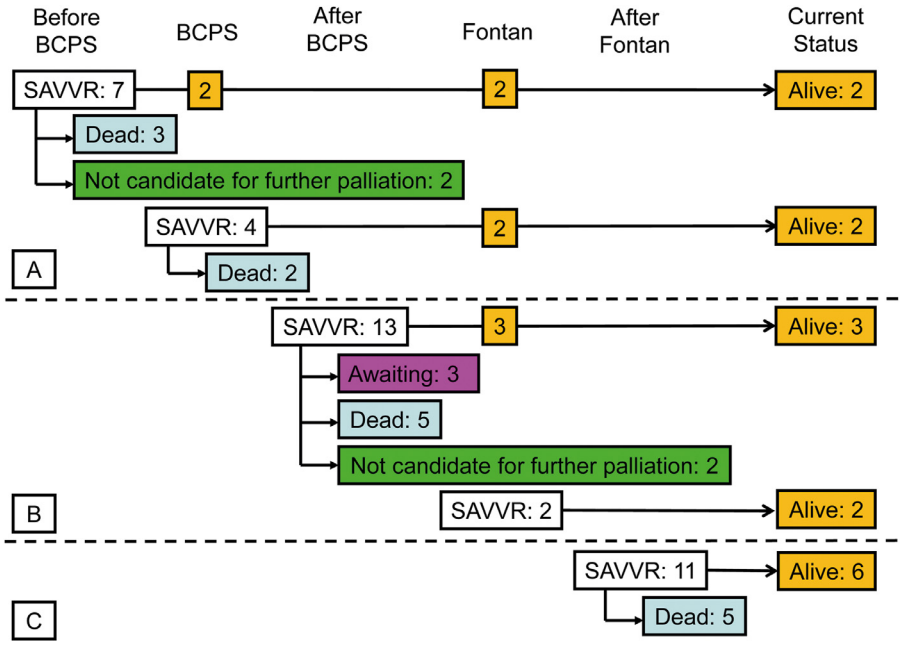


Figure 5. Individual clinical courses of patients undergoing systemic atrioventricular valve replacement before or at the time of bidirectional cavopulmonary shunt (A), after bidirectional cavopulmonary shunt or at the time of Fontan (B) and after Fontan (C). BCPS, bidirectional cavopulmonary shunt; SAVVR, systemic atrioventricular valve replacement.

Hemodynamic variables were satisfactory considering the disease severity in our patient population. Indeed, among patients who survived SAVVR, transiently decreased EF recovered within 6 months. (It is well known in patients after MVR that the percent decrease in end-diastolic diameter was more marked than that in end-systolic diameter, resulting in a significant decrease in postoperative EF.[19] The reason for improvement of EF afterward might be a better ventricular function reserve at the time of SAVVR in our cohort.[20]) Thus, SAVVR could be considered a reasonable surgical option for FSV patients with unrepairable SAVV regurgitation.

Multivariate analysis indicated BSA <0.28 m^2, preoperative inotropic support, primary SAVVR, oversized prosthesis, and intra- or postoperative ECMO were the significant risk factors of mortality. These 4 factors, excluding ECMO, must be linked together, and comparison of their HR showed that the patient size had the most significant impact on the outcomes. For small patients with unrepairable SAVV regurgitation and marginal cardiac condition, SAVVR was still challenging, and the smallest commercially available valve (a 16-mm Medtronic open pivot heart valve [Medtronic Inc., Minneapolis, MN]) was oversized (Fig. 4A).

In a report of consecutive FSV patients undergoing SAVVR, Mahle et al[11] indicated that all 6 patients aged less than 2 years died within 6 months following SAVVR. Sughimoto et al[12] also reported that younger age at the time of SAVVR was a risk factor of mortality. In relatively large series reports of SAVV repair,[3,4] smaller and younger patients were also at increased risk of mortality. FSV surgical stage was not a risk factor for mortality in this study. Therefore, if patients survive after BCPS and still fail to thrive, small-size patients receive hardly any benefit from SAVVR. They must suffer from significant heart failure (preoperative inotropic support was performed mainly for patients with BSA <0.28 m^2 [$P = 0.001$]) probably derived from longstanding SAVV regurgitation. The therapeutic effect of SAVVR, therefore, was limited.

The unfavorable effect of implanted "rigid" and "oversized" prostheses could contribute to the high mortality rate. Other reports have identified oversized prosthesis as a significant risk factor for mortality in MVR in patients with 2 ventricles.[16–18] An excessively large and rigid prosthesis could impair the motion of the heart, especially at the base. In MVR, left ventricular outflow tract obstruction, restriction of prosthetic leaflet motility, coronary injury, conduction block, and progressive ventricular dysfunction are likely to occur with oversized prosthesis,[16–18] even if the valve was implanted in the supra-annular position.[21] In fact, 4 of 9 causes of death in our cohorts whose GOAI was over 6.0 were low output syndrome.

Do smaller and flexible valve prostheses improve the outcomes? They might improve survival, yet it would depend on the hemodynamics and thrombotic characteristics of the valve. Recently, mitral valve implantation with the Melody valve (Medtronic Inc., Minneapolis, MN) or the inverted Contegra bovine jugular vein conduit (Medtronic Inc., Minneapolis, MN) have been reported as an alternative to mechanical MVR.[22,23] While this could be a good alternative to the existing mechanical valve prostheses, long-term outcomes were unclear.

In our treatment strategy, additional pulmonary blood flow was not employed at the time of BCPS to maximize the ventricular volume unloading effect, in anticipation of an improvement in SAVV regurgitation.[24] In some patients, however, SAVV regurgitation has progressed after BCPS, even if concomitant SAVV repair was performed at the time of BCPS.[25,26] For such patients, their cardiopulmonary condition was usually marginal for performing SAVVR concomitant with Fontan completion, so SAVVR was performed prior to Fontan completion. Unfortunately, the therapeutic effect of SAVVR before Fontan completion was found to be limited.

In contrast, SAVVR after Fontan completion successfully improved Fontan circulation. The cardiac index was observed to increase significantly without elevating systemic venous pressure. Since preoperative inotropic support in the total cohort and the high serum BNP level in patients after Fontan completion were significant risk factors for mortality, earlier surgical intervention should be performed regardless of the FSV surgical stage before systemic ventricular dysfunction becomes obvious.

In spite of rigorous anticoagulation therapy, a thrombosed stuck valve was occasionally observed during the early postoperative period. No significant risk factor for thrombosed stuck valve was identified. Although 2 patients expired postoperatively, 2 survivors undergoing redo SAVVR using downsized prosthesis were free from recurrent valve thrombosis. This suggests that selection of the appropriate-sized prosthesis may be of significance in preventing thrombosed stuck valves. It might be better to perform more aggressive anticoagulation during early postoperative period for FSV patients, paying attention to bleeding complications, especially in BCPS or Fontan circulation.

Whereas the criteria for prosthesis-patient mismatch was well established for mitral valves in adolescence and adult patients,[27,28] it is not likely that this criteria would be adopted to decide the timing of redo SAVVR for FSV patients. Especially in Fontan or BCPS circulation, elevated systemic atrial pressure by prosthesis-patient mismatch directly results in the elevation of systemic (or superior systemic) venous pressure. Although statistical analysis was not sufficient, peak flow velocity across implanted prosthesis in excess of 2.0 m/s would be an indicator for redo SAVVR. In practice, cardiac catheterization results determine the timing of redo SAVVR. A pressure gradient between a ventricular end-diastolic pressure and a pulmonary capillary wedge pressure exceeding 10 mm Hg is the absolute indication for redo SAVVR. When a 5- to 10-mm Hg pressure gradient is observed, redo SAVVR is indicated if Fontan pressure exceeds 15 mm Hg. In our opinion, prosthesis-patient mismatch might not become obvious until the BW of patients with a 16-mm ATS reaches 16–20 kg, or until the BW of patients with an 18-mm ATS reaches 30 kg. A larger number of patients and longer follow-up period are required to determine optimal timing of redo SAVVR.

STUDY LIMITATIONS

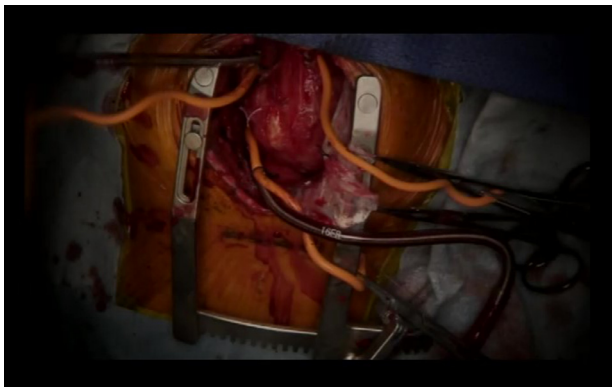
This study has several limitations. First, it is a retrospective and nonrandomized study with a relatively small number of patients, and the follow-up period is not long enough to be conclusive. Second, our study cohort was heterogeneous, yet detected risk factors for mortality seem to be clinically consistent.

CONCLUSIONS

SAVVR could be a reasonable choice of treatment for unrepairable SAVV in FSV patients. Whereas SAVVR successfully improved Fontan circulation, the therapeutic effect of SAVVR before Fontan completion was found to be limited. For small patients with impaired ventricular function who had no choice other than SAVVR, commercially available valves were oversized and outcomes remained poor.

SUPPLEMENTARY MATERIAL

The following is the supplementary data to this article:



Video 1. Operation video shows common atrioventricular valve replacement for a 10-month-old boy with right atrial isomerism in 2017 (after the study period). The patient underwent common atrioventricular valve repair and repair of supracardiac total anomalous pulmonary venous connection at the time of bidirectional cavopulmonary shunt. Common atrioventricular valve regurgitation was however not significantly reduced. The valve was therefore subsequently replaced with ATS 18-mm Advanced Performance valve 17 days after the prior valve repair.

Systemic Atrioventricular Valve Replacement in Patients with Functional Single Ventricle

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Video 2.

APPENDIX 1. VARIABLES FOR RISK FACTOR ANALYSIS

Continuous Variables

1. Total cardiopulmonary bypass time (minutes)
2. Aortic cross clamping time (minutes)

Categorical Variables

1. Gender
2. Age <1 year
3. Body surface area <0.28 m^2 (approximately equal to body weight <5 kg)
4. Primary diagnosis
5. Associated lesions
6. Systemic atrioventricular valve morphology
7. Dominant ventricle morphology
8. Situs
9. Apex
10. Preoperative degree of systemic atrioventricular valve regurgitation
11. Ejection fraction <50%
12. Without previous systemic atrioventricular valve repair
13. Surgical stage leading to Fontan completion
14. Preoperative inotropic support
15. Preoperative ventilator support
16. Intra- or postoperative extracorporeal membrane oxygenation support
17. Brain natriuretic peptide >400 pg/mL
18. Oversized prosthesis (Geometric orifice area index >6)

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