Long-Term Results of Modified Fontan Operation for Single-Ventricle Patients Associated With Atrioventricular Valve Regurgitation

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Background. The long-term outcome of modified Fontan operation concomitant with a valve operation for atrioventricular valve (AVV) regurgitation is not well described.

Methods. Between 1977 and 2003, 500 children who underwent modified Fontan operation were subdivided into 192 with AVV plasty (group P) and 308 without AVV plasty (group N). Factors associated with patient outcome were investigated retrospectively.

Results. Surgical techniques to correct valve incompetence included circular annuloplasty, partial annuloplasty with Kaye-Reed methods, edge-to-edge repair methods, and valvoplasty, which were combined according to the etiology of the valve lesion. The estimated actuarial survival rates at 10 and 20 years were, respectively, 82.0% and 76.6% in group P (hazard ratio, 0.921; 95% confidence interval, 0.873 to 0.972; p < 0.05) and 90.8% and 86.8% in group N (p = 0.001). The estimated actuarial survival rates at 10 years among patients with AVV plasty did not show a statistically significant difference (circular annuloplasty, 79.0%; partial annuloplasty, 81.6%; edge-to-edge, 83.3%; valvoplasty, 82.6%; p = 0.90). A Cox regression model revealed that a higher preoperative ventricular ejection fraction was associated with a significant reduction in long-term mortality in group P (hazard ratio, 0.921; 95% confidence interval, 0.873 to 0.972; p < 0.05). Each repair method showed acceptable durability at medium-term follow-up, without progression of lesions.

Conclusions. Given worse results with poor ventricular function, early intervention against valve pathology before development of ventricular failure may improve long-term outcomes. Multiple methods are appropriate for a variety of valve lesions; however, circular annuloplasty remains a reliable repair option due to its technical simplicity.


Atrioventricular valve (AVV) regurgitation (AVVR) has a severe impact on the outcome of the modified Fontan operation, despite improved perioperative care. Earlier reports demonstrate 10-year survival of patients with AVVR of 36% compared with 62.5% in those without it [1].

Our previous report showed the short-term results of patients with AVVR repaired predominantly using circular annuloplasty [2]. Most studies, including ours, were conducted during the short-term or medium-term follow-up phase [3]; therefore, information available regarding the long-term outcome of patients with AVVR corrected at modified Fontan operation is scarce. Here we describe the long-term outcome of patients with AVVR repaired at modified Fontan operation and analyze several repair techniques.

Patients and Methods

This retrospective study was conducted with the approval of the Tokyo Women’s Medical University Institutional Review Board under a waiver of individual patient consent. The study enrolled 500 patients who underwent a modified Fontan operation between 1977 and 2003. They were subdivided into group N, comprising 308 patients with a modified Fontan operation without AVV plasty, and group P, comprising 192 patients who underwent a modified Fontan operation with concomitant AVV plasty.

Each patient’s diagnosis was based on the report of The Society of Thoracic Surgeons Nomenclature and Database Project. Double-inlet left ventricle (DILV) and tricuspid atresia were classified as left dominant, whereas double-inlet right ventricle (DIRV) and mitral atresia were classified as right dominant. In other ventricular morphology, the diagnosis was classified as biventricular if both ventricles had more than 50% of normal value; otherwise, ventricular dominance was determined by the relative size of each ventricle. Patient preoperative characteristics, diagnosis, ventricular morphology, and AVV characteristics are reported in Table 1.

Early death was defined as 30-day mortality and death at same admission after Fontan operation.

Measurements of AVVR and Ventricular Function

The degree of AVVR was evaluated by retrograde cineventriculography and graded 1 to 4 with Sellars classification at preoperative catheterization in all patients.
Table 1. Patient Demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group P</th>
<th>Group N</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at repair, y</td>
<td>8.1 ± 5.9</td>
<td>8.0 ± 6.2</td>
<td>0.37</td>
</tr>
<tr>
<td>Weight at repair, kg</td>
<td>22.3 ± 14.3</td>
<td>20.8 ± 13.2</td>
<td>0.25</td>
</tr>
<tr>
<td>AVVR grade (Seller’s classification)</td>
<td>1.71 ± 0.8</td>
<td>0.15 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Preoperative hemodynamic data
- PA pressure, mm Hg: 15.5 ± 4.3 vs. 15.2 ± 4.3, p = 0.56
- PVR, Wood units: 1.7 ± 0.7 vs. 1.82 ± 0.72, p < 0.05
- Qp/Qs: 1.4 ± 0.6 vs. 1.3 ± 0.7, p = 0.29
- Nakata index: 355 ± 118 vs. 357 ± 114, p = 0.91
- VEDP, mm Hg: 9.7 ± 3.0 vs. 9.3 ± 2.8, p = 0.10
- VEDV, % of normal: 251 ± 80.0 vs. 220 ± 62.7, p < 0.001
- VEF, %: 54.1 ± 6.7 vs. 55.9 ± 6.9, p < 0.05
- Room air saturation, %: 79.5 ± 7.6 vs. 77.2 ± 8.5, p = 0.67
- Cardiothoracic ratio, %: 57.7 ± 6.9 vs. 54.0 ± 7.1, p < 0.001

Palliative operation
- Blalock-Taussig shunt: 108 (56) vs. 185 (61), p = 0.34
- PA banding: 23 (12) vs. 34 (11)
- BCPS: 45 (23) vs. 23 (8), p < 0.001

AVV characteristics
- Common AVV: 103 (50) vs. 46 (15), p < 0.001
- Unilateral AVV atresia: 35 (18) vs. 114 (37)
- Two competent valves: 54 (28) vs. 148 (48), p = 0.90

Arterial oxygen saturation was performed during the operation showed significant regurgitation.

CIRCULAR ANNULOPLASTY. Circular annuloplasty was used in patients with annular dilatation and failure of coaptation of several leaflets resulting in generalized central regurgitation. In circular annuloplasty, 2-0 or 3-0 polytetrafluoroethylene suture was used to reduce the size of the annulus. To avoid conduction impairment, the suture was placed away from the vicinity of the atrioventricular node determined by AV relationship and ventricular morphology [2].

PARTIAL ANNULOPLASTY. Partial annuloplasty was used for patients with prolapse of 1 or 2 leaflets resulting in failure of coaptation of the leaflets. The technique involves running parallel mattress sutures along the annulus supporting the redundant leaflets between their zones of apposition with intact leaflets.

AVF REPAIR. Edge-to-edge (EtE) repair was used in larger patients with failure of coaptation between 2 opposing leaflets and resultant regurgitation. EtE repair was performed by suturing the free-floating segments of the opposing leaflets to create double orifices. In a common AVV, the superior and inferior bridging leaflets were sutured together; whereas, in the tricuspid valve, the anterior and septal leaflets were sutured together.

VALVOPLASTY. If a single cleft or dehiscence was the main etiology of regurgitation, it was closed with single monofilament sutures.

Statistical Methods
Statistical analyses were performed by using SPSS 11.5 software (SPSS Inc, Chicago, IL). All data are presented as expressed as a percentage of the expected normal ventricular volume per body surface area (BSA) according to the formulas of Nakazawa and associates [5].

The total ventricular ejection fraction (VEF) was calculated using the formula: VEF = (LVEDV × LVEF + RVEDV × RVEF)/(LVEDV + RVEDV), where LVEDV is LV end-diastolic volume, RVEDV is RV end-diastolic volume, LVEF is left ventricular ejection fraction, and RVEF is right ventricular ejection fraction. The total ventricular end-diastolic volume (VEDV) was the sum of LVEDV and RVEDV.

**Operative Technique**
The operative technique is illustrated in Figure 1. Standard cardiopulmonary bypass was established with mild to moderate hypothermia. A modified Fontan procedure was performed with an atriopulmonary connection, the lateral tunnel method, or an extracardiac total cavopulmonary connection. Surgical techniques were individualized to the patient’s valve pathology on the basis of the operating surgeon’s opinion. Initial examination of the AVV was performed by filling the ventricle with saline. Our criteria for AVV repair were based on preoperative cineventriculography and echocardiography. Inspection of the AVV was performed during the Fontan operation if the patient exceeded grade 1 in the Sellars classification or had more than mild regurgitation in the echocardiogram. The final decision to proceed with AVV plasty was made if the AVVR test during the operation showed significant regurgitation.
mean ± standard deviation (SD). Continuous normally distributed data were compared between the groups with the Student t test. Categoric data were compared using a Wilcoxon signed rank test. Frequencies of events were compared with a χ² test. The time-dependent outcomes were estimated using Kaplan-Meier analysis with a log-rank test to evaluate group difference. Risk factors with p values of less than 0.1 after univariate analysis were considered eligible for entering multivariate analysis. Cox regression models were used to determine the time-related predictors for the outcomes.

Results

Patient Characteristics

Patient characteristics are presented in Table 1. Age and weight at repair were almost identical between groups. The mean AVVR grade in group P was 1.71 ± 0.8, which was significantly higher than in group N. The two groups had similar values related to pulmonary artery (PA) maturity, except pulmonary vascular resistance and pulmonary-to-systemic flow ratio. Pulmonary vascular resistance was significantly lower in group P (1.7 vs 1.82), with a resultant increased pulmonary-to-systemic flow ratio. The VEDV was significantly higher and the VEF significantly lower in group P. The cardiothoracic ratio was significantly higher in group P (57.7% vs 54.0%). Most patients in both groups received Blalock-Taussig shunts, and one-tenth underwent PA banding. A bidirectional cavopulmonary shunt (BCPS), as staged palliation for the Fontan pathway, was applied in less than 10% of patients in our series.

When we look at the morphology of the heart, a higher proportion of patients had isomerism in group P (52%) and a higher prevalence of left dominant heart in group N (38%). A common AVV was present in 50% of the patients in group P, whereas two competent valves were seen 48% of the patients in group N. Most patients underwent a modified Fontan procedure with atriopulmonary anastomosis. More fenestrations were used in patients in group P. Group P had significantly higher cardiopulmonary bypass time and aortic cross-clamp time were significantly higher in group P (154 and 69.8 vs 125 and 37.1 minutes).

AVV Repair Surgical Technique

The surgical technique for AVV repair is illustrated in Figure 1. Circular annuloplasty was used most frequently for all valve morphology, accounting for 84% in common AV valve, 65% in two AV valves, and 57% in unilateral AV atresia.
Patient Outcomes and Risk Factors for Death

There were 22 early deaths in group P and 14 in group N (Fig 2). Cause of death in group P was cardiac in 20 patients and noncardiac in 2 patients; whereas, cause of death in group N was cardiac in 10 patients and noncardiac in 4 patients. Late deaths were noted in 12 group P patients and in 19 group N patients. The late deaths in group P were attributed to cardiac in 7 and noncardiac in 5 patients; whereas, deaths in group N were related to cardiac in 12, noncardiac in 2, and unknown in 5 patients.

The estimated 10-year and 20-year survival rates were 82.0% and 76.6% in group P and 90.8% and 86.8% in group N (log-rank \( p < 0.05 \)). The estimated survival rates among patients with valve plasty did not show a statistically significant difference between methods at 10 years (circular annuloplasty, 79.0%; partial annuloplasty, 81.6%; EtE, 83.3%; valvoplasty, 82.6%; log-rank \( p = 0.90 \)). Cox regression model revealed that higher preoperative VEF was associated with a significant reduction in long-term mortality in group P (hazard ratio, 0.921; 95% confidence interval, 0.873 to 0.972).

Reoperation

In group P, 14 patients underwent reoperation for recurrent AVVR (Fig 2). The regurgitation was fixed with surgical plasty in 10 patients and replaced with a prosthetic valve in 4. Three late deaths were reported, all with cardiac causes. Recurrent AVVR required 3 reoperations in group N, and they were all fixed with surgical plasty. One late death was noted and had a cardiac origin. Freedom from reoperation for recurrent AVVR at 10 and 20 years was, respectively, 93.0% and 84.9% in group P and 99.7% and 98.6% in group N (log-rank \( p < 0.05 \)).

Other reoperations were performed in 12 patients in group P and in 24 patients in group N. Among those, 1 late death occurred in group P and 4 in group N.

Ventricular Function Over Time

Two catheterization studies were performed postoperatively on 390 (78.0%) and 131 patients (26.2%) at a mean 0.7 \( \pm \) 1.0 (Post-1) and 6.7 \( \pm \) 4.6 (Post-2) years, respectively (Fig 3). After the Fontan operation, a significant decrease of VEDV was observed in both groups, and there

Fig 2. (A) Flow chart shows outcomes for patients who did (group P) and did not (group N) have atrioventricular valve plasty. (B) Actuarial survival rate and (C) freedom from reoperation against AVVR are shown for patients in group N and group P. (D) Actuarial survival rate is shown according to valve plasty method. (AVVR = atrioventricular valve regurgitation; cAP = circular annuloplasty; EtE = edge to edge repair; mFontan = modified Fontan; pAP = partial annuloplasty; VP = valvoplasty.)
was no increase in VEDV over time. A significant VEF decline was noted in both groups after the Fontan operation, but VEF in group N increased over time, unlike in group P. In both groups, VEDP decreased significantly after the Fontan operation and remained at the same value over time. Long-term ventricular function was potentially lower in group P considering its higher average VEDV and lower VEF.

Latest AVVR Degree Obtained by Echocardiography
Postoperative echocardiography was performed at mean 8.5 ± 5.5 years (Fig 4). Each plasty method showed acceptable durability of the repaired valve.

Comment
Although the outcomes of patients with functional single ventricle have improved dramatically, the treatment of patients with functional single ventricle and concomitant systemic AVVR remains a challenge. In this study, we examined long-term outcomes after the modified Fontan operation concomitant with systemic AVV repair. Our findings can be summarized as follows:

1. The valve-repaired group had a worse outcome, and a lower preoperative VEF is a mortality risk factor.
2. Valve plasty was performed using circular annuloplasty in most patients in the valve-repaired group.
3. In each repair method, there was a reduction in regurgitation and no difference in long-term survival.

Timing of Fontan Completion, Maturity of Pulmonary Vasculature, and Ventricular Function in Patients With AVVR
Relatively higher age at primary Fontan completion without staging in our series is explained by our policy that the best possible pulmonary vascular bed before modified Fontan procedure is achieved by relatively high pulmonary blood flow controlled by systemic-to-pulmonary shunt or PA banding procedures. That might be contradictory to a contemporary trend to favor a staged approach with early placement of BCPS as early as possible to limit ventricular volume load and preserve ventricular function [6]. In addition, most patients underwent an atriopulmonary connection-type Fontan because this series comprised patients operated on early in Fontan history. However, that policy was abandoned, and our current strategy is to follow standard staged extracardiac Fontan intervention by bidirectional Glenn procedure. Our statistical analysis revealed that one risk factor for death was lower preoperative VEF, suggesting that the outcome of patients might have been better if we had applied a staged approach or performed the Fontan procedure on younger patients than the present patient cohort.

There is still controversy whether AVVR would need to be repaired at the time of BCPS. Mahle and colleagues [7] concluded that AVV repair is not justified in all patients with moderate AVVR undergoing the BCPS. They showed that 6 of 27 patients (22%) who had moderate or severe AV insufficiency at the time of BCPS had improved AV insufficiency grade without AV repair. Hancock Friesen and associates [8] suggested that if the degree of regurgitation is mild before the BCPC, some improvement can be expected secondary to the reduced volume loading after the BCPC. The Toronto group concluded that lower grade ventricular function and ventricular dilation correlated with death and repair failure, suggesting early intervention before impairment of ventricular function.

Avoiding overload of the ventricle is important; however, there is a concern that excessive protection from
volume overload may result in PA hypoplasia, which in turn will severely affect the Fontan circuit [9]. The growth of the PA after a Fontan operation is reported to be decreased despite somatic growth [10]. Considering that clinical outcomes after a Fontan operation are affected by PA growth [10], there still seems to be room for debate over balancing PA growth and preservation of ventricular function from volume loading.

Mechanisms of AVVR and Treatment Options

The mechanisms of AV insufficiency in a single-ventricle physiology are complex and multifactorial [11, 12]. The postulated mechanisms include chronic volume overload, structural AVV abnormalities, and impaired ventricular functions (myocardial damage/ischemia) [13].

Stein and colleagues [14] reported the morphology of common AVVs observed in angiography/echocardiography or autopsy cases. Unlike the common AVV seen with AV septal defects, they did not consist of 5 separate leaflets, but usually possessed 4 leaflets: 2 located superiorly and inferiorly, flanked by 1 leaflet on each side. The leaflets were dysplastic in 55% of patients and attached with abnormal chordae extending to the papillary muscle or occasionally the ventricular wall.

Kawahira and colleagues [15] reported 7 deaths in patients with common AVVs, and they consisted of 4 leaflets in 5 patients and 3 leaflets in 2 [15]. Considering these reports, the cause of AVVR with a common AVV is still hard to systematize.

The mechanism of systemic tricuspid valve insufficiency is also complex and results from the combination of pressure or volume overload with other factors, such as ventricular and annular dilatation, ventricular septal geometry, ventricular function, and structural abnormalities of the valve leaflets [13]. Kanter and colleagues reported 12 patients who underwent De Vega annuloplasty at the median age of 2.2, and only one patient presented with worsening of tricuspid regurgitation at mean follow-up of 2.0 years [16].

In our previous report, we used circular annuloplasty as a first option for AVV repair, and significant reduction of AVVR was observed in most patients in the short-term postoperative period [2]. Our follow-up echocardiography showed durability of the repaired valve at medium-term was acceptable. Because most of our patient cohort includes a primary Fontan procedure, which potentially causes volume overload to the ventricles for a longer period, the reduction of AVVR was
partially attributed to volume unloading. However, considering our long-term result, circular annuloplasty might be beneficial to prevent recurrence of valve regurgitation for complex AVV pathology, especially if it is caused by pure annular dilatation.

Partial annuloplasty is, however, frequently used in our patient cohort with unilateral AVV atresia. This maneuver is essentially a functional commissuroplasty plus partial annuloplasty on the zone of apposition with localized prolapse to form a bicuspid valve. This technique was reported to be the most frequently used technique in the treatment of tricuspid regurgitation in hypoplastic left heart syndrome [11]. Although the number of patients was limited in our cohort, this technique was applied in the setting of 2 AVV or unilateral AVV atresia, and effective in preventing recurrence of AVVR.

Ando and colleagues [17] reported the use of EtE in children with a functional single ventricle and showed its significance in growing children. Application of this technique to growing children may be problematic due to its potential to cause stenosis; however, no patients with stenotic valves have been reported in their series. The actuarial percentage of patients having mild AVVR or less was 57% at 5 years after repair, which may provoke controversy whether EtE itself is sufficient to prevent long-term recurrence of regurgitation. However, it is hard to make that conclusion because of the heterogeneity of their patient population.

**Future AVVR Strategies**

Real-time 3-dimensional echocardiography provides more specific and accurate information about the mechanism and site of regurgitation [12]. This imaging technique permits same-view display of the entire circumference of the AVV annulus, which is easily measured [18].

Another potential mechanism contributes to the development of AVVR in competent 2 ventricles. Several studies have demonstrated a reduction in extent of functional mitral regurgitation after cardiac resynchronization therapy in patients with dilated cardiomyopathy [19] and even with a failing Fontan [20]. These mechanisms should play an important role in reduction of AVVR in single-ventricle patients with dyssynchronous ventricles.

**Study Limitations**

This is a retrospective study. Not all patients were followed up with a catheterization study. Because not all the patients did not undergo volume unloading before Fontan, which is atypical when compared with contemporary experiences in most places, the Fontan procedures all included volume unloading in addition to valve repair. The improvement in postoperative AVVR in group P could have been due to the unloading rather than or in addition to the valve repair. In this study, most of the patients underwent an atrio pulmonary connection type Fontan operation with a two-staged manner at an older age (mean age, 8 years old). That policy was abandoned, and our current strategy is to follow standard staged extracardiac Fontan intervened by a bidirectional Glenn procedure.

**Conclusion**

Operative strategies for single-ventricle patients with AVVR are still evolving. Considering they have lower survival rates compared with those without AVVR, early intervention against valve pathology before development of ventricular failure may improve long-term outcomes. In our study, each repair method showed acceptable durability at medium-term follow-up without progression of lesions. Circular annuloplasty still stands as a reliable repair option due to its simplicity of technique.

**References**


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