Efficacy of the ‘intrapulmonary-artery septation’ surgical approach for Fontan candidates with unilateral pulmonary arterial hypoplasia

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Abstract

OBJECTIVES: The bilaterally unbalanced development of pulmonary arteries (PAs), as a result of unilateral pulmonary arterial hypoplasia (PAhypo) makes patients either ineligible for the Fontan operation or candidates for the one-lung Fontan operation. In the present study, we examined the efficacy of intrapulmonary-artery septation (IPAS), a technique we reported in 2007 in which a septation is constructed within the central PA, in patients with unilateral PAhypo.

METHODS: Sixteen patients with unilateral PAhypo and an affected PA index of ≤60 mm²/m², including non-confluent PA (NCPA), underwent IPAS between January 2000 and March 2012; patients with pulmonary venous obstruction were excluded from this study. We compared the affected PA index values before and after IPAS and after the Fontan operation as well as the bilateral pulmonary blood flow ratio using pulmonary scintigraphy. The post-Fontan operation values of central venous pressure (CVP), pulmonary vascular resistance (PVR), ventricular end-diastolic pressure (VEDP), cardiac index (CI) and arterial oxygen saturation (SaO₂) at the most recent cardiac catheterization, as well as the pre-IPAS and post-Fontan New York Heart Association (NYHA) classification levels were examined.

RESULTS: One patient died after IPAS (survival rate 93.8%). Thirteen (86.7%) of the surviving 15 patients underwent the Fontan operation. The mean PA indexes were 25.5 ± 18.9 mm²/m² before IPAS and 67.9 ± 34.2 mm²/m² after IPAS (P = 0.003); the mean PA index was 71.1 ± 50.0 mm²/m² after the Fontan operation. Restenosis did not occur after the Fontan operation, and the PA diameters were maintained. The mean affected/unaffected lung blood flow ratio was 0.89 ± 0.67. The most recent cardiac catheterization after the Fontan operation indicated the following values: CVP, 11.7 ± 1.8 mmHg; PVR, 1.3 ± 0.4 U·m²; EDP, 5.7 ± 2.0 mmHg; CI, 3.1 ± 0.5 l/min/m² and SaO₂, 94.9 ± 2.0%. The mean pre-IPAS and post-Fontan NYHA levels were 2.3 ± 0.6 and 1.2 ± 0.4, respectively (P = 0.0002).

CONCLUSIONS: With IPAS, the affected PA diameters increased significantly, and were maintained after the Fontan operation, and continuity of the native PAs was achieved. IPAS is very effective for patients suffering from otherwise intractable diseases.

Keywords: Unilateral pulmonary arterial hypoplasia • Fontan • Glenn shunt • Pulmonary artery index • One-lung Fontan

INTRODUCTION

Since it was first described in 1971, the Fontan operation has been applied to patients with functional single-ventricle physiology [1]; the outcomes of the Fontan operation have markedly improved following various modifications [2, 3]. Currently, more than 400 patients/year undergo the Fontan operation in Japan [4]. However, in patients with functional single-ventricle physiology, severely unbalanced pulmonary arteries (PAs) may develop for several reasons, both intrinsic and iatrogenic in nature, thus making patients either ineligible for the Fontan operation or candidates for the one-lung Fontan operation.

The ‘Ten Commandments’ of patient selection for the Fontan operation were suggested by Choussat et al. [5]. Among these criteria, the size of the PAs has been one of the most important factors influencing the results of the Fontan operation. Several studies have shown that PA distortions and smaller PA sizes are risk factors for early and late outcomes after the Fontan operation [6–10].

We have consistently performed ‘intrapulmonary-artery septation (IPAS)’ for patients with severely unbalanced PAs to stimulate the growth of the PAs [11]. In the present study, we aimed to evaluate the efficacy of IPAS in terms of the early to mid-term outcomes.

MATERIALS AND METHODS

Study design

Twenty-seven patients underwent IPAS at our hospital between January 2000 and March 2012. At the time of IPAS, 16 patients...
were considered less than ideal candidates for the Fontan operation because of the presence of unilateral pulmonary arterial hypoplasia (PAhypo), and 11 patients were considered less than ideal candidates for the Fontan operation because of the presence of unilateral pulmonary venous obstruction. In this study, we targeted the 16 patients with unilateral PAhypo, excluding those with unilateral pulmonary venous obstruction. We defined PAhypo as an affected PA index of ≤60 mm²/m². Table 1 shows the characteristics of the patients who underwent IPAS; 7 (44%) patients had non-confluent PAs (NCPAs). This study was a single-centre, retrospective review, and was approved by the Mount Fuji Shizuoka Children’s Hospital Institutional Review Board. Individual patient consent was waived.

**Affected pulmonary artery index**

The candidates for IPAS had an unbalanced PA with a well-developed PA, or an unaffected PA and a hypoplastic PA, or an affected PA. The diameters of the affected PAs were measured at the hilum, immediately proximal to the origin of the first lobe branches, in the frontal view of a pulmonary angiogram. The affected PA index was calculated using the cross-sectional area of affected branches, in the frontal view of a pulmonary angiogram. The diameters of the affected PAs were measured at the hilum using standard antegrade pulmonary angiography. However, it could be confirmed in some patients using enhanced computed tomography or retrograde pulmonary angiography through the aorto-pulmonary collateral arteries (APCAs) or pulmonary veins. If the presence of an affected PA at the hilum was confirmed, we calculated the PA index by using the Nakata method. If the presence of an affected PA was not confirmed using the described modalities, we recorded the PA index as 0 mm²/m² (Fig. 1).

**Operative procedure for intrapulmonary-artery seption**

A median sternotomy was performed, and cardiopulmonary bypass was established using mild hypothermia. Direct PA-PA anastomosis of the posterior wall was performed with patch augmentation, using either autopericardium, a 0.4-mm expanded polytetrafluoroethylene patch (Gore-Tex; W. L. Gore & Assoc, Flagstaff, AZ, USA), or heterogeneous pericardium (Xenomedica; Baxter Healthcare, Horw, Switzerland). The connective tissue was used as a native PA wall in patients with NCPA in whom the PA wall was not present. A Glenn shunt and systemic-pulmonary artery shunt (SPS) were anastomosed to the unaffected PA just adjoining. Based on the concept of anastomosis just adjoining, we usually anastomosed the SPS from the innominate artery to the unaffected PA, which is the ‘modified Blalock–Taussig shunt’. Thereafter, a septation patch was placed obliquely within the central PA, between the unaffected and affected PAs, using a 0.1-mm expanded polytetrafluoroethylene membrane (Gore-Preclude; W. L. Gore & Assoc). The IPAS procedure established two separate blood flows, and achieved continuity of the PAs. A Glenn shunt was connected to the unaffected PA, and an SPS was connected to the affected PA [11] (Fig. 2).

**Evaluation of intrapulmonary-artery seption**

We compared the affected PA index, before and after the IPAS as well as after the Fontan operation, as a growth parameter of the affected PA, and measured the bilateral pulmonary blood flow ratio using lung perfusion scintigraphy after the Fontan operation.

The post-Fontan operation values of the central venous pressure (CVP), pulmonary vascular resistance (PVR), ventricular end-diastolic pressure (VEDP), cardiac index (CI) and arterial oxygen

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**Table 1: Patient characteristics**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Age at IPAS (years)</th>
<th>Wt at IPAS (kg)</th>
<th>Affected PA</th>
<th>Timing of IPAS</th>
<th>PRHB</th>
<th>Another source</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TA</td>
<td>5.2</td>
<td>16.2</td>
<td>NCPA</td>
<td>during the Glenn</td>
<td>RSVC</td>
<td>RM8754.0</td>
<td>alive</td>
</tr>
<tr>
<td>2</td>
<td>Ebstein, PA</td>
<td>1.5</td>
<td>9.3</td>
<td>lt.PAhypo</td>
<td>after the Fontan</td>
<td>f-Fontan</td>
<td>LMB754.0</td>
<td>alive</td>
</tr>
<tr>
<td>3</td>
<td>HLHS</td>
<td>6.3</td>
<td>17.7</td>
<td>lt.PAhypo</td>
<td>after the hemi-Fontan</td>
<td>RSVC</td>
<td>RM8754.0</td>
<td>alive</td>
</tr>
<tr>
<td>4</td>
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<td>4.1</td>
<td>NCPA</td>
<td>during the Glenn</td>
<td>LSV</td>
<td>RM8753.5</td>
<td>alive</td>
</tr>
<tr>
<td>5</td>
<td>IAA, dTGA, LVOTO</td>
<td>1.4</td>
<td>10.3</td>
<td>lt.PAhypo</td>
<td>during the Glenn</td>
<td>RSVC</td>
<td>LITA</td>
<td>alive</td>
</tr>
<tr>
<td>6</td>
<td>SV</td>
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<td>12.1</td>
<td>rt.PAhypo</td>
<td>during the Glenn</td>
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</tr>
<tr>
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<td>6.3</td>
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<td>RSVC</td>
<td>RM8753.5</td>
<td>ED</td>
</tr>
<tr>
<td>8</td>
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<td>during the Glenn</td>
<td>RSVC</td>
<td>VPC5.0</td>
<td>alive</td>
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<tr>
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<td>TA</td>
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<td>5.6</td>
<td>lt.PAhypo</td>
<td>during the Glenn</td>
<td>RSVC</td>
<td>RM8753.5</td>
<td>alive</td>
</tr>
<tr>
<td>10</td>
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<td>6.5</td>
<td>NCPA</td>
<td>after the Glenn</td>
<td>RSVC</td>
<td>LM8753.5</td>
<td>alive</td>
</tr>
<tr>
<td>11</td>
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<td>1.7</td>
<td>10.2</td>
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<td>after the Glenn</td>
<td>RSVC</td>
<td>RM8754.0</td>
<td>alive</td>
</tr>
<tr>
<td>12</td>
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<td>2.4</td>
<td>10.5</td>
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<td>after the Glenn</td>
<td>RSVC</td>
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</tr>
<tr>
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<td>52.4</td>
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<td>11.1</td>
<td>NCPA</td>
<td>after the Glenn</td>
<td>RSVC</td>
<td>RM8754.0</td>
<td>alive</td>
</tr>
<tr>
<td>15</td>
<td>cTGA,PA</td>
<td>1.5</td>
<td>9.7</td>
<td>lt.PAhypo</td>
<td>during the Glenn</td>
<td>RSVC</td>
<td>RM8755.0</td>
<td>alive</td>
</tr>
<tr>
<td>16</td>
<td>HLHS</td>
<td>1.8</td>
<td>8.3</td>
<td>lt.PAhypo</td>
<td>after the Glenn</td>
<td>RSVC</td>
<td>RM8754.0</td>
<td>alive</td>
</tr>
</tbody>
</table>

IPAS: intrapulmonary-artery seption; TA: tricuspid atresia; PA: pulmonary atresia; HLHS: hypoplastic left heart syndrome; IAA: interruption of aortic arch; TGA: transposition of great arteries; LVOTO: left ventricular outflow obstruction; SV: single ventricle; VSD: ventricular septal defect; DOLV: double outlet left ventricle; cTGA: corrected transposition of great arteries; NCPA: non-confluent pulmonary artery; lt. PAhypo: left pulmonary arterial hypoplasia; PRHB: partial right heart bypass; RSVC: right superior vena cava; f-Fontan: fenestrated Fontan; LSV: left superior vena cava; MBTS: modified Blalock–Taussig shunt; CS: central shunt; VPC: ventricular pulmonary conduit; ED: early death.
saturation (SaO2) at the most recent cardiac catheterization were reviewed as the clinical parameters. The follow-up period after the Fontan operation was 8.1 ± 3.8 years (range, 1.4–13.3 years). The pre-IPAS and post-Fontan New York Heart Association (NYHA) classification values were also examined.

Statistics

The measurements are presented as means ± SD or medians (ranges), as appropriate.

Continuous variables were analysed using the Student t-test for normally distributed variables or the Wilcoxon signed-rank test for non-normally distributed variables. A two-sided P-value of < 0.05 was considered statistically significant.

RESULTS

Clinical course

Between January 2000 and March 2012, we attempted to perform IPAS for 16 patients, including the patients with NCPAs and PA indexes of 0 mm²/m². IPAS was performed at the time of the Glenn shunt procedure (n = 8, 50%), after the Glenn shunt procedure (n = 6, 38%), after the hemi-Fontan operation (n = 1, 6%) or after the Fontan operation (n = 1, 6%). The median patient age and weight when IPAS was performed were 1.6 years (range, 4 months to 23.0 years) and 10.6 kg (range, 4.1–52.4 kg). The Glenn shunt was connected to the unaffected PA as a partial right-heart bypass in 14 patients.

A modified Blalock-Taussig shunt was established as another blood source for the affected PA in 13 patients (Table 1). Among eight patients who underwent IPAS at the time of the Glenn shunt procedure, we used pre-existing shunts for IPAS in 5 patients, established new shunts in 2 patients and used the left internal mammary artery in one patient.

In 4 of 16 patients (25%), compression of the left PA by the dilated ascending aorta was caused by unilateral PAhypo. In 2 of the 4 patients, we performed ascending aorta plication to secure sufficient aortopulmonary space at the time of IPAS or the Fontan operation.

There was 1 case of early death because of low output syndrome caused by uncontrollable atrioventricular regurgitation after IPAS (Table 1, Patient 7); the post-IPAS survival rate was 93.8%. Thirteen (86.7%) of 15 patients underwent the two-lung Fontan operation at a median age of 2.5 years (range, 1.1–24.3 years), including 1 patient who was converted from the Fontan operation to IPAS (Table 1, Patient 2).

IPAS was performed on Patient 2 after the Fontan operation. The fenestrated Fontan was connected to the unaffected PA, and an SPS was connected to the affected PA. Eight months later, we converted from the IPAS to Fontan circulation without heart failure.

The mean interval from IPAS to the Fontan operation was 1.2 ± 0.5 years (range, 0.6–2.5 years). During the Fontan operation, only 3 (23%) of 13 patients needed repair for the affected PA again; thus, 10 (77%) patients completed the Fontan operation readily by removal of the septation patch. No patients needed repair for the central PA.

Two (13.3%) of 15 patients did not undergo the Fontan operation because of neurological conditions (multiple anomalies or lower body paralysis due to spinal cord infarction), and not because of their lung conditions (Table 1, Patients 8 and 14).
The affected pulmonary artery growth after intrapulmonary-artery septation

The changes in the affected PA index are shown in Fig. 3. Compared with the pre-IPAS value, the affected PA index increased significantly post-IPAS (pre-IPAS, 25.5 ± 18.9; post-IPAS, 67.9 ± 34.2 mm²/m²; \( P = 0.003 \)). The mean post-Fontan PA index was 71.1 ± 50.0 mm²/m². No restenosis occurred after the Fontan operation, and the PA diameters were maintained during the 8.1-year follow-up period. The mean affected/unaffected lung blood flow ratio was 0.89 ± 0.67.

Clinical parameters after the Fontan operation

Cardiac catheterization was performed after the Fontan operation in all 13 patients who underwent the Fontan operation. The mean interval from the Fontan operation to the last cardiac catheterization was 5.2 ± 3.8 years (range, 0.8–12.4 years). Cardiac catheterization after the Fontan operation indicated the following values: CVP, 11.7 ± 1.8 mmHg; PVR, 1.3 ± 0.4 U m²; EDP, 5.7 ± 2.0 mmHg; CI, 3.1 ± 0.5 l/min/m² and SaO₂, 94.9 ± 2.0%.

Moreover, the mean pre-IPAS and post-Fontan NYHA levels were 2.3 ± 0.6 and 1.2 ± 0.4, respectively (\( P = 0.0002 \)). None of the patients died during the 8.1-year follow-up period after the Fontan operation.

DISCUSSION

The major findings of this study were that the affected PA index increased significantly after IPAS, the majority of patients with unilateral PAhypo underwent the two-lung Fontan operation and the improved pulmonary condition and cardiac function were maintained after the Fontan operation.

The criteria for the Fontan operation, suggested by Choussat et al. [5], have been re-evaluated, and many studies have reported that PA distortions and smaller PA sizes are risk factors for the Fontan operation [6–10]. However, we have consistently performed IPAS for patients with unilateral PAhypo, including those with NCPAs [11]. IPAS comprises a Glenn shunt, another blood source and a septation patch. IPAS can yield two benefits as a result of separating the two blood sources: (i) the Glenn shunt reduces the excessive systemic ventricular volume overloading, and (ii) another blood source, such as the SPS, serves as a reliable antegrade blood source to the affected PA. After IPAS, we aggressively perform APCA interventions to prevent occlusion of the affected PA and stimulate the growth of the affected PAs. As a result, despite one early death, 13 (86.7%) of the 15 patients underwent the two-lung Fontan operation; 2 patients did not undergo the operation due to neurological problems. In these 13 patients, the affected PA diameters and good Fontan circulation were maintained after the Fontan operation. The another blood source supplying the affected PA led to PA growth without PVR elevation.
Stamm et al. [13] reported reconstruction of discontinuous PAs. They found that direct PA-PA anastomosis and control of all APCAs may further improve outcomes following discontinuous PA reconstruction. In the expectation of the growth of the native PA, we also performed direct PA-PA anastomosis of the posterior wall, with patch augmentation, to ensure continuity of the native PA. In patients with NCPA, when they had no posterior PA wall, we used even the connective tissue as the native posterior PA wall. In addition, we aggressively performed APCA interventions before and after IPAS.

Bacha et al. [14] reported on the connection of discontinuous PAs in 40 patients with functional single-ventricle physiology; they connected discontinuous PAs during or after a Glenn shunt procedure or the Fontan operation. In 10 of 29 patients wherein a Glenn shunt procedure was performed at the time of PA reconstruction, an SPS was inserted or an existing shunt was left patent. In 3 of the 4 patients with a Glenn shunt and an SPS, the patients developed central or peripheral branch PA stenosis, or both, resulting in effective unilateral flow through the Glenn shunt. The authors reported that the presence of a sole supply to one lung via APCAs was a risk factor associated with PA occlusion or reinsertion after PA connection. We had similar experiences, and, therefore, we agree with their opinion. Under these conditions, we aggressively perform APCA interventions after IPAS, or before IPAS for patients who have massive APCAs with acceptable SaO2. Our IPAS strategy involves separating the unaffected and affected PAs with a septation patch and performing aggressive APCA interventions before and after IPAS. We believe that this strategy can prevent post-IPAS occlusion of the affected PA.

A one-lung Fontan operation can be performed for patients with a hypoplastic and discontinuous PA. However, the one-lung Fontan operation is not our final target. Zachay et al. [15] reported 7 cases of one-lung Fontan operations, and indicated that only the postoperative SaO2 values were different between patients who underwent one-lung (87%) and two-lung (91%) procedures. However, Fujii et al. [16] summarized prior reports of one-lung Fontan operations, and noted that the overall mortality associated with the one-lung Fontan operation seemed to be worse than that associated with the two-lung operation [17, 18]. Jacobs et al. [19] reported a higher incidence of protein-losing enteropathy in Fontan patients undergoing one-lung surgeries than in those undergoing two-lung surgeries. Although the one-lung Fontan operation is an option for patients with unilateral PA hypoplasia, we confirmed that IPAS stimulated the growth of the affected PA and reduced the excessive volume overload, thus enabling the patients to undergo the two-lung Fontan and improve their overall prognoses.

This study was limited by its small patient population and its retrospective design. We previously reported the indications for and timing of the Fontan operation after IPAS [11], although we still need to reassess these factors after a mid-term follow-up. Hence, further studies, involving a larger group of patients and a longer follow-up period, are needed to clarify the clinical course of IPAS and the indications and timing of the subsequent Fontan operation after IPAS.

In conclusion, with IPAS, the affected PA diameters increased significantly, and were maintained after the Fontan operation. IPAS was shown to be very effective for patients suffering from otherwise intractable disease. In particular, with this procedure, the patients could avoid undergoing the one-lung Fontan operation and they also demonstrated improved prognoses and quality of life.

Conflict of interest: none declared.

REFERENCES