Intracardiac Fontan procedure for heterotaxy syndrome with complex systemic and pulmonary venous anomalies

Yuji Naito*, Mitsuru Aoki, Kozo Matsuo, Hiromichi Nakajima, Hiroyuki Aotsuka, Tadashi Fujiwara

Departments of Cardiovascular Surgery and Cardiology, Chiba Children’s Hospital, Chiba, Japan

Received 1 September 2008; received in revised form 29 May 2009; accepted 12 June 2009; Available online 19 August 2009

Abstract

Objective: The extracardiac conduit procedure is widely used for patients with heterotaxy syndrome with complex systemic and pulmonary venous anomalies; however, it lacks conduit-growth potential and requires long-term anticoagulation. We present the intracardiac Fontan procedure, which eliminates the above-mentioned disadvantages.

Patients and methods: Twenty-four patients (mean age, 4.1 years; weight, 13.0 kg) with heterotaxy syndrome underwent intracardiac Fontan operations between March 1995 and March 2008. In each patient, the anomalous systemic venous return with the isolated hepatic vein was redirected to the pulmonary artery using an intra-atrial baffle without obstructing the pulmonary venous pathway; this was accomplished by anterior (n = 5), lateral (n = 15) or posterior tunnel methods (n = 4), depending on the anatomical relationship of the systemic and pulmonary venous pathways.

Results: There was one (4%) in-hospital and two (8%) late deaths in total. Five (21%) patients underwent re-operation for either pulmonary venous obstruction or supraventricular tachycardia. The actuarial 12-year survival was 86% (the Kaplan—Meier survival plot). The freedom from re-operation at 10 years was 77%. Anticoagulation was not required except for two patients (8%) who had prosthetic valves and coagulation disorder. Obstruction of the systemic venous pathway was not observed in any patient; however, five (20%) patients had clinically significant postoperative arrhythmias. At the final follow-up, all survivors were categorised as the New York Heart Association class I.

Conclusions: Aided by detailed preoperative anatomical and physiological diagnoses, intracardiac Fontan procedures were technically feasible in patients with complex systemic and pulmonary venous anomalies. The specific cardiac anatomy in these patients warranted this procedure; however, taking into consideration the improved outcomes of the modified Fontan procedure, this method should be performed with deliberation.

© 2009 European Association for Cardio-Thoracic Surgery. Published by Elsevier B.V. All rights reserved.

Keywords: Fontan; Extracardiac conduit; Lateral tunnel; Thrombosis; Arrhythmia

1. Introduction

Since first described in 1971, modifications to the Fontan operation and the introduction of a staged approach have improved the early and long-term outcomes in patients with a functional single ventricle. In order to complete the Fontan circulation, the design of both the superior and inferior cavo-pulmonary connections should be decided, and two currently favoured approaches to establish these connections are the extracardiac conduit consisting of a tube graft between the inferior vena cava and the pulmonary arteries [1] and intracardiac tunnel methods consisting of a prosthetic or autologous baffle in the intra-atrial route.

Heterotaxy syndrome is a constellation of defects characterised by the malposition of cardiac and abdominal visceral structures, and typically comprises complex systemic and pulmonary venous anomalies [2]. In patients with heterotaxy syndrome, the construction of a smooth, non-obstructive and high-energy efficient inferior cavopulmonary route is the most crucial task for surgeons. Extracardiac conduit methods have gained wide acceptance because they are relatively simple surgical procedures that provide excellent long-term results [3]; however, this method is limited by the lack of conduit-growth potential and long-term anticoagulation requirement. Since first introduced in 1987 [4], the intracardiac tunnel method has been performed on children and pregnant women because it offers the potential advantages of conduit-growth potential and no anticoagulation requirement. This study aimed to elucidate the effects of the intracardiac tunnel Fontan procedure on heterotaxy patients with complex systemic and pulmonary venous anomalies.
2. Patients and methods

2.1. Patients

Twenty-four patients (male, 12; female, 12) with heterotaxy syndrome who underwent intracardiac tunnel Fontan operations at the Chiba Children’s Hospital, Chiba, Japan, between March 1995 and March 2008 were enrolled in the study, and the cases were retrospectively reviewed. The preoperative patient demographics are summarised in Table 1.

2.2. Anatomical diagnosis

Visceroatrial heterotaxy syndrome is characterised by typical cardiac, vascular and visceral malpositions associated with abnormal sidedness. The diagnoses were based on radiographic, echocardiographic and angiographic findings and direct inspection during surgery. Asplenia is not a constant feature of right atrial isomerism, as indicated by the presence of a spleen in some patients with this syndrome [5]. The terms right and left atrial isomerism are used in this study.

Ventricular morphology was classified as ‘dominant right/left ventricle’ when the two ventricles were not balanced or well developed, while balanced ventricles were referred to as ‘two ventricles’.

Atroventricular (AV) valve morphology was described as ‘two valves’ or ‘common AV valve’ when the two AV junctions were guarded by either two separate valves or a common AV valve, respectively. The absence of a unilateral AV connection and a unilateral imperforate valve was described as ‘unilateral AV valve atresia’ because of the haemodynamic identity in both the conditions.

Patients in which all four pulmonary veins drained individually to the atrium were considered to have normal drainage, while the remaining patients who underwent extracardiac connections were considered to have anomalous pulmonary venous connections.

2.3. Surgical techniques

The surgical procedures involved median sternotomy with standard extracorporeal circulation. In patients without prior cavopulmonary anastomosis, a unilateral or bilateral superior cavopulmonary anastomosis was constructed. The single-stage Fontan operation involved superior cavopulmonary anastomosis and redirection of the inferior vena caval and/or hepatic venous blood to the pulmonary artery (PA). Taking into consideration the spatial relationship between the AV valve and pulmonary vein orifices, the systemic venous return was redirected via an intra-atrial route by the anterior, lateral or posterior tunnel methods as described below:

(i) The anterior tunnel (Fig. 1A) re-routes the inferior vena caval and/or hepatic venous blood to the entrance of an atrial appendage, that is, the suture line of the intra-atrial baffle. The systemic venous pathway was created with the anterior (A), lateral (B), and posterior tunnel (C) methods. AV: atrioventricular; HV: hepatic vein; IVC: inferior vena cava; SVC: superior vena cava; L: left; R: right; and PVs: pulmonary veins.

(ii) The lateral tunnel (Fig. 1B) is the typical tunnel along the lateral atrial wall connecting the inferior vena cava and/or hepatic venous orifice with the ipsilateral or contralateral superior vena cava or atrial appendage. Indication: pulmonary venous orifices located in the vicinity of the AV valve, which facilitate the re-routing of the inferior vena caval and/or hepatic venous blood to the ipsilateral superior vena cava or atrial appendage.

(iii) The posterior tunnel (Fig. 1C) traverses the back of the atrium and the space between the pulmonary venous orifices and AV valve to connect the inferior vena cava and/or HV with the superior vena cava or atrial appendage. Indication: pulmonary venous orifices located at a more lateral site than the superior vena
cava orifice, and sufficient space between the pulmonary venous orifices and AV valve for placing the baffle to re-route the inferior vena cava and/or hepatic venous blood to the superior vena cava or appendage.

The superior vena cava or atrial appendage was then end-to-side anastomosed to the PA in each method.

2.4. Postoperative antithrombotic therapy

Acetylsalicylic acid (3–5 mg kg\(^{-1}\) per day) and warfarin sodium (target prothrombin time-international normalised ratio (PT-INR) value, 1.5–2.0) were routinely administered to all patients during the early postoperative period (3–6 months). Antithrombotic therapy was discontinued after no evidence of thrombosis was found. Antithrombotic agents were not administered to patients who underwent the intracardiac tunnel method with autologous tissues.

2.5. Postoperative arrhythmia

Postoperative cardiac rhythm was assessed by Holter electrocardiography (ECG). A heart rate that exceeded 2 standard deviations below the age-adjusted mean implied sinus node dysfunction. Supraventricular tachycardia was characterised by non-sinus, narrow, complex tachycardia, including junctional ectopic tachycardia, atrial fibrillation, atrial flutter, AV re-entrant tachycardia and AV nodal re-entrant tachycardia. Arrhythmia with clinical significance was considered as sustained tachycardia with symptoms or deterioration in haemodynamic status that warranted therapy or cardioversion.

2.6. Statistical analysis

Statistical analyses were performed using the SPSS version 11.5 for Windows (SPSS Inc., Chicago, IL, USA). All data are presented as frequencies, medians with ranges and means with standard deviations. The Kaplan–Meier estimates were used to plot both the survival and the re-operation-free rate curves. Cardiac death and re-operations due to Fontan failure were used as the endpoints.

3. Results

3.1. Anatomical diagnosis

The anatomical characteristics are provided in Table 2.

3.2. Surgical procedures

Twenty-one patients had previously undergone the following palliative procedures: systemic–PA shunt (19 patients), artery banding (one patient) and Norwood-type operation (one patient). The Fontan procedure was preceded by cavopulmonary anastomosis, including the Kawashima operation, for interrupted inferior vena cava in seven patients (29%), and the single-stage Fontan operation was performed in 17 patients (71%).

The lateral, anterior and posterior tunnel methods were performed in 16 (67%), five (21%) and three (12%) patients, respectively. A xenopericardial or expanded polytetrafluoroethylene (ePTFE) patch was used as the intra-atrial baffle in 22 patients, and the autologous atrial free wall was used to create an intra-atrial tunnel in two patients. Fenestration was performed in only two patients.

Five surgical corrections of anomalous pulmonary venous connections were performed during the neonatal period (one case), concomitantly with cavopulmonary anastomosis (two cases) or along with the Fontan procedure (two cases). Eighteen concomitant procedures were performed in 16 patients: aortic valve replacement (one case), AV valve plasty (11 cases) and PA angioplasty (six cases). The mean cardiopulmonary bypass and aortic cross-clamp times were 248 ± 66.1 and 34.5 ± 43.1 min, respectively.

3.3. Mortality

The follow-up was complete (7.3 ± 3.9 years (range: 1.3–13.5)) and was indicated by a closing interval (the time elapsed between the date of the Fontan operation and that of the most recent outpatient visit).

There was one (4%) early death and two (8%) late deaths in total. The former occurred in a 3-year-old girl diagnosed with right atrial isomerism with dominant right ventricle, who underwent the modified Fontan procedure with the lateral tunnel method concomitantly with AV valve plasty. She suffered a sudden cardiac collapse and died on postoperative day 1 due to bradycardia caused by breath holding. Late death occurred in a 3-year-old girl diagnosed with right atrial isomerism with dominant right ventricle and common AV valve regurgitation who underwent the modified Fontan operation with the lateral tunnel method. She underwent surgical re-intervention for pulmonary venous obstruction due to the intra-atrial prosthetic baffle. She died of congestive heart failure due to a diffusely hypokinetic heart with unknown aetiology 3 months later. Late death also occurred in a 2-year-old boy diagnosed with right atrial isomerism with dominant right ventricle, infra-cardiac total

### Table 2

<table>
<thead>
<tr>
<th>Anatomical characteristics</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visceroatrial morphology</td>
<td></td>
</tr>
<tr>
<td>Right atrial isomerism</td>
<td>20</td>
</tr>
<tr>
<td>Left atrial isomerism</td>
<td>4</td>
</tr>
<tr>
<td>Ventricle</td>
<td></td>
</tr>
<tr>
<td>Right dominant</td>
<td>20 (83%)</td>
</tr>
<tr>
<td>Left dominant</td>
<td>3 (13%)</td>
</tr>
<tr>
<td>Two ventricles</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>AV valve</td>
<td></td>
</tr>
<tr>
<td>Common AV valve</td>
<td>19 (79%)</td>
</tr>
<tr>
<td>Unilateral AV valve atresia</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Two valves</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Anomalous pulmonary venous connection</td>
<td></td>
</tr>
<tr>
<td>( I_a )</td>
<td>3</td>
</tr>
<tr>
<td>( I_b )</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>1</td>
</tr>
<tr>
<td>Abnormalities of systemic venous connections</td>
<td></td>
</tr>
<tr>
<td>Bilateral superior vena cava</td>
<td>18</td>
</tr>
<tr>
<td>Inferior vena cava interruption</td>
<td>3</td>
</tr>
<tr>
<td>Isolated hepatic vein</td>
<td>6</td>
</tr>
</tbody>
</table>

The lateral, anterior and posterior tunnel methods were performed in 16 (67%), five (21%) and three (12%) patients, respectively. A xenopericardial or expanded polytetrafluoroethylene (ePTFE) patch was used as the intra-atrial baffle in 22 patients, and the autologous atrial free wall was used to create an intra-atrial tunnel in two patients. Fenestration was performed in only two patients.

Five surgical corrections of anomalous pulmonary venous connections were performed during the neonatal period (one case), concomitantly with cavopulmonary anastomosis (two cases) or along with the Fontan procedure (two cases). Eighteen concomitant procedures were performed in 16 patients: aortic valve replacement (one case), AV valve plasty (11 cases) and PA angioplasty (six cases). The mean cardiopulmonary bypass and aortic cross-clamp times were 248 ± 66.1 and 34.5 ± 43.1 min, respectively.

3.3. Mortality

The follow-up was complete (7.3 ± 3.9 years (range: 1.3–13.5)) and was indicated by a closing interval (the time elapsed between the date of the Fontan operation and that of the most recent outpatient visit).

There was one (4%) early death and two (8%) late deaths in total. The former occurred in a 3-year-old girl diagnosed with right atrial isomerism with dominant right ventricle, who underwent the modified Fontan procedure with the lateral tunnel method concomitantly with AV valve plasty. She suffered a sudden cardiac collapse and died on postoperative day 1 due to bradycardia caused by breath holding. Late death occurred in a 3-year-old girl diagnosed with right atrial isomerism with dominant right ventricle and common AV valve regurgitation who underwent the modified Fontan operation with the lateral tunnel method. She underwent surgical re-intervention for pulmonary venous obstruction due to the intra-atrial prosthetic baffle. She died of congestive heart failure due to a diffusely hypokinetic heart with unknown aetiology 3 months later. Late death also occurred in a 2-year-old boy diagnosed with right atrial isomerism with dominant right ventricle, infra-cardiac total
an anomalous pulmonary venous connection and mild common AV valve regurgitation. He underwent the modified Fontan operation with the anterior tunnel method concomitantly with AV valve plasty. He died of sudden cardiac collapse possibly due to arrhythmia after surgical re-intervention for pulmonary venous obstruction. The actuarial 12-year survival rate was 86%, as determined by the Kaplan—Meier survival plot (Fig. 2).

3.4 Re-operations

There were five re-operations in total. They were performed for pulmonary venous obstruction in four patients and supraventricular tachyarrhythmia in one. Three patients underwent the takedown of Fontan circulation by bidirectional superior cavopulmonary anastomosis to alleviate the elevated central venous pressure due to pulmonary venous obstruction. Extracardiac total cavopulmonary connection conversion was performed in one patient to release pulmonary venous obstruction possibly caused by the proximity of the intra-atrial baffle to the pulmonary venous orifice. Postoperative extracardiac total cavopulmonary connection conversion with arrhythmia surgery and pacemaker implantation was performed on a paroxysmal supraventricular tachycardia patient.

Three patients with postoperative pulmonary venous obstruction had normal pulmonary venous return without surgical intervention on the pulmonary vein; therefore, the occurrence of postoperative pulmonary venous obstruction was considered to be idiopathic and did not result because of the intimal hyperplasia of the surgical suture line. The pulmonary venous obstructions were relatively distal from the orifice and the atrial wall. The actuarial 10-year re-operation-free rate was 77%, as determined by the Kaplan—Meier survival plot (Fig. 3).

3.5 Late catheterisation study

All patients who survived the Fontan operation were included in the postoperative cardiac catheterisation study, the mean duration of which was 2.6 ± 2.9 years. The data are summarised in Table 3. A non-obstructive systemic venous pathway to the PA was created in each method. There was no significant pressure gradient between the inferior vena cava and the PA.

3.6 Late angiography

3.6.1 Anterior tunnel (Fig. 4A)

We present the case of a 4-year-old boy diagnosed with right atrial isomerism with dominant right ventricle and mild common AV valve regurgitation, who underwent bilateral superior cavopulmonary anastomosis and the creation of an inferior cavopulmonary connection with the anterior tunnel method. A widely opened inferior cavopulmonary pathway with a bulgy configuration and a somewhat pulsatile flow to both pulmonary arteries were observed on postoperative angiography.

3.6.2 Lateral tunnel (Fig. 4B)

This is the case of a 5-year-old girl diagnosed with right atrial isomerism with dominant left ventricle, common AV valve and isolated HV, who underwent bilateral superior cavopulmonary anastomosis and the creation of an inferior cavopulmonary connection with the lateral tunnel method using the autologous atrial free wall. A smooth, non-obstructive, inferior cavopulmonary route comprising the isolated HV was achieved.
3.6.3. Posterior tunnel (Fig. 4C)

This is the case of a 2-year-old girl diagnosed with right atrial isomerism with dominant right ventricle, supracardiac total anomalous pulmonary venous connection and non-confluent PA, who previously underwent PA reconstruction with bilateral superior cavopulmonary anastomosis. An inferior cavopulmonary connection was created with the posterior tunnel method. A non-obstructive inferior cavo-pulmonary pathway with balanced lung perfusion was achieved.

3.7. Late arrhythmia

Holter ECG was performed for all patients at 3.4 ± 3.6 years after the Fontan operation. Clinically significant postoperative arrhythmias developed in five (21%) patients at 2—10 years after the Fontan operation. Four patients had AV nodal re-entrant tachycardia, and one had atrial fibrillation. Postoperative sinus node dysfunction was not observed in any patient.

3.8. Medication

Seven patients received angiotensin-converting enzyme (ACE) inhibitor treatment, while two received both ACE inhibitor and beta-blocker treatment. Two patients required anticoagulant therapy. A prosthetic valve had to be inserted in one patient, while another suffered a brain infarction possibly due to coagulation 1 year after the operation.

3.9. Late functional status

At the last follow-up, all the patients who survived the Fontan operation and re-operation were categorised as the New York Heart Association class I. The plasma atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) concentrations at the most recent outpatient visit were 40.2 ± 24.4 and 33.4 ± 20.0 pg ml⁻¹, respectively. The peripheral oxygen saturation was 93.3% ± 3.1% while breathing in room air.

4. Discussion

4.1. Fontan operation for patients with heterotaxy syndrome

This study showed the effects of the intracardiac Fontan procedure on heterotaxy syndrome patients with complex systemic and pulmonary venous anomalies; the anatomically atypical systemic and/or pulmonary venous configurations observed in this syndrome are technical hazards during the determination of a reliable Fontan pathway. We did not obtain comprehensive long-term data using this study group.

Initial reports on the modified Fontan operation outcomes in heterotaxy syndrome revealed early mortality rates of 41—80% [6,7]. After the recent procedural improvements, the actuarial 10-year survival was reported to be 63—93% [8,9]. Improvements in the long-term survival outcome could not be achieved merely by procedural improvements and are a result of many contributing factors such as improved patient selection, staged surgical procedure, younger age at the time of the Fontan operation, refinements in surgical techniques and advancements in postoperative care.

Although the extracardiac conduit Fontan procedure provides excellent long-term results, several studies have shown that the outcomes of intracardiac tunnel methods are better. Giannico and colleagues [10] reported in their review of 193 cases, for which the extracardiac conduit Fontan procedure was performed, that the Kaplan—Meier estimate of the freedom from arrhythmias was 83% at 15 years. Another study revealed that the incidence of postoperative arrhythmia in heterotaxy syndrome patients who underwent the extracardiac conduit Fontan procedure was 25% in 8 years [11]. These rates are acceptably low as compared to the incidence of arrhythmias after atrio pulmonary connection; however, the incidence of postoperative arrhythmia was similar to that determined in our study (20%). A longer follow-up may reveal a higher risk of sudden death and arrhythmias in patients with heterotaxy syndrome than in patients with less complex functional single-ventricular defects. Therefore, detailed and aggressive investigations on preventing arrhythmia are more essential than predicting the occurrence of arrhythmia merely based on the operative procedure.

In our series of high-risk patients, only seven patients (29%) underwent staged superior cavopulmonary anastomosis (bidirectional Glenn or Kawashima operation) at the risk of the pulmonary flow status being high for a relatively longer period. In the past, high pulmonary flow strategies were chosen to develop the well-formed pulmonary arteries; this was believed to improve the long-term outcomes. In fact, the staged Glenn operation approach has been shown to improve the feasibility of the high-risk Fontan operation. There have been detailed discussions on whether preoperative small PA development affects the functional status after the Fontan
Adach and colleagues [12] reported that preoperative small PA development might result in protein-losing enteropathy in the long term. Four patients underwent re-operations for pulmonary venous obstruction, depending on the nature of the obstruction in heterotaxic patients. Jenkins and colleagues [13] reported that the mean pulmonary vein sum index is significantly smaller in patients with heterotaxy syndrome than in patients without heterotaxy syndrome.

4.2 Factors that favour the intracardiac tunnel method

The three following anatomical traits favour the intracardiac tunnel Fontan procedure: (i) the separation of the HV from the inferior vena cava, which was observed in six patients in this series. Surgeons might prefer performing the extracardiac conduit after approximation of the distance between the separated HV and the inferior vena cava; however, there are cases in which the approximation is impossible, and the procedure could result in distortion of the veins. (ii) Possible pulmonary venous obstruction caused by extracardiac conduit placement, which has not been clearly documented in the literature so far. We speculated that the overhanging extracardiac conduit might press the pulmonary veins opening at the superior vena cava junction, resulting in various pulmonary venous anomalies inherent to the heterotaxic heart. (iii) The presence of an offset the model due to the extracardiac conduit procedure, which directs the majority of the inferior vena caval blood flow to the lung on the side of the offset. The creation of a T-shape configuration in the inferior cavopulmonary route is reported to evenly distribute the hepatic venous blood to both lungs [14]. If the inferior vena cava opens at the middle position (Fig. 4C), the flow could be directed to the PA via a relatively straight route using the resultant T-shaped configuration.

In most patients with surgically corrected congenital heart diseases, the speculated cause of late atrial arrhythmia is a macro re-entrant mechanism that involves the dilated atrial tissue or slow conduction tissue in the surgically created scar or intra-atrial suture line [15]. Thus, early and late atrial tachycardia can develop after the intracardiac tunnel procedure, and theoretically, the extracardiac conduit Fontan procedure is more beneficial in this regard [3]. However, this is debatable because of the following reasons: (i) several reports state that the incidence of late atrial tachycardia after intracardiac tunnel Fontan procedures was comparable to that after extracardiac conduit Fontan procedures. Furthermore, Stamm and colleagues [16] reported that freedom from the development of supraventricular tachyarrhythmia after the lateral tunnel Fontan operation was 96% and 91% at 5 and 10 years, respectively. (ii) Late morbidity due to pulmonary venous stenosis and recurrent atrial tachycardia observed in heterotaxic patients [16] could be prevented by catheter-based interventions involving fenestration or penetration of the atrial septum during the intracardiac tunnel Fontan procedure. (iii) Extracardiac conduit patients had a higher incidence of sinus node dysfunction early after the operation, and the condition persisted for several years thereafter [17], possibly owing to the damage to the sinus node at the distal portion of the right coronary artery or compression of the abnormally located sinus node at the intercaval position [18].

Our results indicate a trend favouring the extracardiac conduit Fontan procedure for any category of cardiac morphology. However, our study had several limitations. The long-term outcomes of the Fontan procedure should be taken into consideration while selecting optimal surgical methods that would most benefit the patient. Research on improved surgical methods for patients with functional single ventricles should continue because the Fontan procedure serves only as a palliative therapy that results in future complications rather than a definitive therapy.

5. Limitation

The validity of our study is clearly limited by its retrospective nature. The detectable incidence of sinus node dysfunction and transient supraventricular tachycardia was possibly underestimated because of the transient and intermittent nature of these conditions and the limited availability of serial ECG and Holter data. The growth potential of the intracardiac tunnel route was not confirmed.

6. Conclusion

Along with detailed preoperative anatomical and physiological diagnoses, intracardiac tunnel Fontan procedures were found to be technically feasible in patients with complex systemic and pulmonary venous anomalies. The specific cardiac anatomy warranted the application of this method for creating an efficient inferior cavopulmonary route in atypical configurations of systemic and pulmonary venous anomalies; however, considering the improved outcomes of the modified Fontan procedure, this method should be performed with deliberation.

References