Institutional report - Congenital

Do we need fenestration when performing two-staged total cavopulmonary connection using an extracardiac conduit?

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Abstract

Between August 1999 and December 2007, 72 consecutive patients with single ventricle physiology underwent a modified Fontan procedure after a bidirectional Glenn shunt using an extracardiac polytetrafluoroethylene conduit without fenestration. Nitric oxide gas inhalation was commenced just after cardiopulmonary bypass together with intravenous phosphodiesterase III inhibitor administration. After oral intake was started, pulmonary vascular dilators such as beraprost, sildenafil, bosentan were given orally according to amount of chest drainage and patient’s condition. After discharge, oxygen therapy at home was continued for three months. No hospital death occurred after surgery. All patients were followed by our institute and follow-up period was 44.2 ± 26 (36–106.8) months. One late death occurred during this follow-up period after re-operation. Cardiac catheterization after the Fontan completion showed transpulmonary gradient of 19/9 mmHg, systemic output of 3.4 ± 2.1 l/min m². Arterial oxygen saturation (SaO₂) at the latest outpatient visit was 94.4 ± 3.8%. According to our clinical experience with two-staged total cavopulmonary connection using an extracardiac conduit without fenestration, fenestration in the Fontan circuit is not necessary when performing the Fontan completion. Two-staged extracardiac total cavopulmonary connection without fenestration can be satisfactorily completed with the aid of pulmonary vasodilation therapy.

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Keywords: Bidirectional Glenn shunt; Total cavopulmonary connection; Extracardiac conduit; Fenestration; Pulmonary vasodilation therapy

1. Introduction

Fenestration in the Fontan circulation, first described in 1990 by Bridges et al. [1], allows for decrease in venous pressure in the circuit and augmentation of cardiac output, which is believed to be advantageous especially soon after the operation.

In the early 1990s, reports from Boston introduced two-staged Fontan operation in which the bidirectional Glenn shunt was added as an interim procedure to the Fontan completion [2]. This staging procedure accomplishes early reduction of the volume work of the systemic ventricle, which leads to good preparation of the patient toward the Fontan completion.

Marceletti and co-workers reported a new form of right heart bypass, by the use of an extracardiac conduit placed between the inferior vena cava and the pulmonary artery [3].

On the other hand, many pharmacological agents which reduce pulmonary vascular resistance have been developed and put into clinical use early in the postoperative period in the current era [4–6]. Furthermore, oral drugs have been also investigated and applied to the clinical use.

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In the light of the potential hemodynamic advantages of staging strategy of the Fontan completion by use of an extracardiac conduit, fenestration in the Fontan circuit in this setting might be less needed under pharmacological pulmonary vasodilation therapy. In order to evaluate our surgical strategy, we reviewed our eight-year surgical experience with the two-staged extracardiac Fontan operation without fenestration.

2. Patients and methods

2.1. Patients

Between August 1999 and December 2007, 72 patients with single ventricle physiology underwent extracardiac Fontan operation at Nagano Children’s Hospital using a polytetrafluoroethylene conduit without fenestration. All of them had a bidirectional Glenn shunt performed prior to Fontan completion. Patient characteristics are summarized in Table 1.

Mean age at bidirectional Glenn shunt was 1.8 ± 1.5 years, and mean period prior to Fontan completion was 2.0 ± 0.6 years. The additional forward blood flow from the ventricle to the pulmonary circulation was closed at bidirectional Glenn shunt. Initial palliations before bidirectional Glenn shunt are listed in Table 2. Concomitant procedures at bidirectional Glenn shunt are listed in Table 3.
Table 1
Patient profile

<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOR, double outlet right ventricle; LV, left ventricle; HLHS, hypoplastic left heart syndrome; DIV, double inlet ventricle; SV, single ventricle; TA, tricuspid atresia; PAIVS, pulmonary atresia with intact ventricular septum; AVSD, atrioventricular septal defect.</td>
<td></td>
</tr>
</tbody>
</table>

Table 2
Initial palliation

<table>
<thead>
<tr>
<th>Palliative procedures</th>
<th>Number of procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>BTS</td>
<td>45</td>
</tr>
<tr>
<td>PAB</td>
<td>21</td>
</tr>
<tr>
<td>Norwood operation</td>
<td>13</td>
</tr>
<tr>
<td>Arch repair</td>
<td>3</td>
</tr>
<tr>
<td>Bilateral PAB</td>
<td>2</td>
</tr>
<tr>
<td>Starnes operation</td>
<td>1</td>
</tr>
<tr>
<td>Central shunt</td>
<td>1</td>
</tr>
<tr>
<td>TAPVC repair</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>83</td>
</tr>
</tbody>
</table>

BTS, Blalock–Taussig shunt; PAB, pulmonary artery banding; TAPVC, total anomalous pulmonary venous connection.

Table 3
Concomitant procedures at bidirectional Glenn shunt

<table>
<thead>
<tr>
<th>Concomitant procedures</th>
<th>Number of procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP</td>
<td>24</td>
</tr>
<tr>
<td>DKS anastomosis</td>
<td>14</td>
</tr>
<tr>
<td>ASD enlargement</td>
<td>6</td>
</tr>
<tr>
<td>AVVP</td>
<td>4</td>
</tr>
<tr>
<td>PM implantation</td>
<td>2</td>
</tr>
<tr>
<td>Norwood operation</td>
<td>2</td>
</tr>
<tr>
<td>TAPVC repair</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>52</td>
</tr>
</tbody>
</table>

PAP, pulmonary artery plasty; DKS, Damus–Kaye–Stansel; ASD, atrioseptal defect; AVVP, atrioventricular valve plasty; PM, pacemaker; TAPVC, total anomalous pulmonary venous connection.

Cardiac catheterization before Fontan completion showed mean pulmonary artery pressure of 8.4 ± 1.9 mmHg, transpulmonary gradient of 3.9 ± 2.1 mmHg, Nakata index of 210 ± 80 mm²/m², and Rp of 2.2 ± 0.7 U × m² (Table 4).

Mean age at Fontan completion was 4.0 ± 2.0 (2.0–11.0) years. Body weight was 13.3 ± 3.1 (8.7–25.8) kg. Concomitant procedures at Fontan operation included repair of atrioventricular valve regurgitation in five patients, pulmonary artery plasty in four, Damus–Kaye–Stansel anastomosis in one, and cryoablation in one.

2.2. Surgical procedures

Fontan operation was completed by connecting the inferior vena cava to the pulmonary artery with an extracardiac conduit of an expanded polytetrafluoroethylene graft (Gore Tex vascular graft; W.L. Gore and Associates, Inc, Flagstaff, AZ, USA). The patient was placed on the conventional cardiopulmonary bypass with the heart beating. When a concomitant intracardiac procedure was planned, the aorta was cross-clamped and cold crystalloid cardioplegia was administered. No patient had fenestration in the Fontan circuit placed. Just after cardiopulmonary bypass, nitric oxide gas inhalation was started at the concentration of 10–20 ppm. Phosphodiesterase III inhibitor, amrinone or milrinone, was also administered intravenously at routine dose.

2.3. Postoperative management

The patient was extubated in the intensive care unit soon after commencement of spontaneous breathing. Until then, nitric oxide gas inhalation was continued. Upon starting oral intake, pulmonary vasodilator such as beraprost, sildenafil, bosentan was administrated orally according to the amount of the chest drainage and patient’s condition by the attending physician. The patient received oxygen inhalation through a nasal cannula, which continued until three months after discharge.

2.4. Data analysis

Data were collected retrospectively from patient records and expressed as mean ± S.D. Actuarial survival and freedom from events were estimated by Kaplan–Meier methods.

3. Results

3.1. Postoperative course

In the intensive care unit, patients required mechanical ventilation for 3–282 h. Nitric oxide gas inhalation was continued until weaning from mechanical ventilation. Two patients needed mechanical ventilation for 24 h. Mechanical ventilation time was 6.9 ± 4.5 (3–21) h except for these two patients, whereas these two patients required ventilation for 89 and 282 h, respectively.

Central venous pressure was 13.1 ± 2.0 (8–17) mmHg in the operation room, and 12.2 ± 1.9 (9–15) mmHg when the patient left the intensive care unit.

Arterial oxygen pressure (PaO₂) measured when the patient left the operation room, was 313 ± 119 (57–477) mmHg at FiO₂ = 1.0. PaO₂ below 100 mmHg was found in
five patients, all of whom had pulmonary atroventricular fistula. Arterial oxygen saturation (\(\text{SaO}_2\)) showed
95.3 ± 3.6% (81–100%) when the patient discharged under oxygen inhalation via a nasal tube. Four patients still
showed low \(\text{SaO}_2\), below 90%, because of pulmonary atroventricular fistula.

Postoperatively, chest drainage was needed for 11 ± 6 days, and hospital stay was 25 ± 19 days. Eleven
patients required chest drainage for two weeks, three patients because of infection in the thoracic cavity and
four because of chylothorax. Oral administration of beraprost was started in 43 patients. In recent cases, sildenafil
was also administrated in three patients.

There was no hospital death after extracardiac Fontan operation without fenestration.

3.2. Follow-up

Follow-up period until latest outpatient visit ranged from 3.6 to 106.8 months (44.2 ± 26.9 months), while percuta-
neous \(\text{SaO}_2\) measured by a pulse oxymeter ranged from 74 to 99% (94.4 ± 3.8%).

During this follow-up period, two patients required re-opera-
tion after the Fontan completion.

Kaplan–Meier survival curve is depicted in Fig. 1. There
have been no late deaths except in one patient which resulted from re-operation, and survival at 60 months
showed 96%. Thirteen patients have survived 60 months.

Cardiac catheterization 1–2 years after the Fontan com-
pletion showed central venous pressure of 10.9 ± 2.7 mmHg, transpulmonary gradient of 5.9 ± 2.4 mmHg,
 systemic output of 3.4 ± 2.1 l/min m². \(\text{SaO}_2\) at catheteriza-
tion was 94.4 ± 2.9% (Table 5).

As for oral pulmonary vasodilator, 23 patients still required
oral administration of beraprost, five patients needed sildenafil.

Two patients, both with hypoplastic left heart syndrome,
developed protein-losing enteropathy. One patient also
developed plastic bronchitis, which was controlled success-
fully by administration of sildenafil. The other patient has
been under good control by sildenafil and bosentan.

The majority of the patients have been on the regimen of low dose warfarin sodium with the target of international
normalized ratio ranging from 1.5 to 2.0. Oral administra-
tion of aspirin was also performed at 5 mg/kg/day. Two
patients developed intracranial hemorrhage which required surgical drainage. We have had no thromboembolic events
resulting from the extracardiac conduit.

Arrhythmia, which is still a clinical problem at out patient
clinic, exists in one patient who underwent catheter abla-
tion before the Fontan completion.

Freedom from Fontan-related events including death, re-
operation, and postoperative complications such as arrhyth-
mas, protein-losing enteropathy, thromboembolism, and
bleeding complication is depicted in Fig. 2. Freedom from
events after the Fontan completion is 89% at 60 months.

4. Discussion

Since the first description by Fontan and Baudet in 1971
[7], various types of modifications of right heart bypass
have been developed and applied to clinical use regarding
management of patients with single ventricle physiology.
Among these modifications, extracardiac total cavo-pulmo-

nary connection under staged strategy and fenestration are
most commonly adopted in many centers [8].

![Fig. 1. Kaplan–Meier survival curve. Number of patients at risk (N) and its percentage are shown.](https://academic.oup.com/icvts/article-abstract/9/1/50/721420/b accelerometer.png)

![Fig. 2. Kaplan–Meier overall freedom from Fontan related events, which include death, re-operation, and postoperative complications such as arrhythmias, protein-losing enteropathy, thromboembolism, and bleeding. Number of patients at risk (N) and its percentage are shown.](https://academic.oup.com/icvts/article-abstract/9/1/50/721420/b accelerometer.png)

### Table 5

Postoperative cardiac catheterization data

<table>
<thead>
<tr>
<th>Number available</th>
<th>56</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval from Fontan completion (months)</td>
<td>19 ± 12</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>10.9 ± 2.7</td>
</tr>
<tr>
<td>VEDP (mmHg)</td>
<td>5.4 ± 2.6</td>
</tr>
<tr>
<td>TPG (mmHg)</td>
<td>5.9 ± 2.4</td>
</tr>
<tr>
<td>VEDV (% normal)</td>
<td>115 ± 34</td>
</tr>
<tr>
<td>VEF (%)</td>
<td>59 ± 10</td>
</tr>
<tr>
<td>CI (l/min/m²)</td>
<td>3.4 ± 2.1</td>
</tr>
<tr>
<td>(\text{SaO}_2) (%)</td>
<td>94.4 ± 2.9</td>
</tr>
</tbody>
</table>

CVP, central venous pressure; VEDP, ventricular end diastolic pressure; TPG, transpulmonary gradient; VEDV, ventricular end diastolic volume; VEF, ventricular ejection fraction; CI, cardiac index; \(\text{SaO}_2\), arterial oxygen saturation.
Although fenestration was initially introduced to high-risk patients when completing the Fontan operation, it became routine procedure in some centers [9]. However, some authors demonstrated that routine fenestration in the Fontan circuit should be avoided [10–12]. Thompson and his associates advocated that fenestration was not necessary in most Fontan patients with an extracardiac conduit technique and that the need for fenestration should be assessed after cardiopulmonary bypass when hemodynamics can be evaluated accurately [11]. Right to left shunting produced by fenestration increases the ventricular filling volume and augments cardiac output, which is most important in the early postoperative period. On the contrary, left to right shunting produced by fenestration induces suboptimal oxygen saturation, reduced exercise capacity, liability to paradoxical embolization and stroke as well as subsequent need for closure by catheter intervention.

In recent years, a number of pharmacological agents which are useful in reducing pulmonary vascular resistance have evolved and applied to clinical use. Inhaled nitric oxide has been found to reduce pulmonary artery pressure as well as pulmonary vascular resistance without affecting systemic circulation [4].

Phosphodiesterase III inhibitor, such as amrinone or milrinone, increases intracellular concentration of cyclic adenosine monophosphate (cAMP) in the vascular smooth muscle. Intravenous administration of these drugs induces pulmonary vasodilatation, systemic vasodilatation, and improvement in cardiac function [6].

Beraprost sodium, an oral PGI2 analog, has been applied in the treatment of patients with pulmonary hypertension. Takahashi and his associates reported the effect of beraprost sodium on pulmonary vascular resistance in a candidate for the Fontan procedure and they suggested that administration of beraprost sodium could lead to reduction in the risks associated with the Fontan procedure and also improvement of its outcome [13].

Sildenafil citrate, also acting as phosphodiesterase V inhibitor, has been clinically used in the treatment of patients after the Fontan operation. Haseyama and his associates reported that pulmonary vasodilator therapy with sildenafil citrate associated with epoprostenol effectively treated steroid-resistant plastic bronchitis after the Fontan procedure [14].

The effect of bosentan as an oral endothelin antagonist has been widely admitted in the treatment of patients with pulmonary hypertension. Recently, the effect of bosentan was shown in a patient with failing Fontan circulation [15].

It is our surgical strategy of choice in the treatment of patients with single ventricle physiology who are to follow the road to Fontan to perform the bidirectional Glenn shunt prior to the Fontan completion. We believe that it is most important to complete preconditioning the patients before the Fontan completion. In order to complete preconditioning of the patients, we have performed concomitant procedures upon the bidirectional Glenn shunt and could obtain good Fontan candidates. When doing the Fontan completion, we have never placed fenestration in the Fontan circulation despite the fact that many centers recommend fenestration. Instead of fenestration, we have adopted several types of pharmacological assists which are deemed to act as a pulmonary vasodilator. Pulmonary vasodilator was useful not only in the treatment of post-operative Fontan patients in the operating room and intensive care unit, but in the treatment of various complications after the Fontan operation, such as sustained chest drainage, and protein-losing enteropathy.

Carrying out our surgical strategy, we completed a the Fontan operation in 72 patients with no hospital mortality. Although the duration of chest drainage in our series was long when comparing to other reports and more medical resources might be consumed by using pulmonary vasodilator, our surgical results revealed the possibility of completion of the Fontan operation without fenestration with the aid of pulmonary vasodilator in view of early results.

As for late results of the Fontan completion in our series, two patients with polysplenia who developed severe atrioventricular regurgitation required re-operation, one of which led to late death. Other late complications such as protein-losing enteropathy and intracranial bleeding occurred and required medical or surgical therapy, however, we did not encounter arrhythmias, thromboembolism which needed medical therapy.

Owing to the hemodynamic advantages brought by the extracardiac total cavopulmonary connection with the staging strategy, the fenestration in the Fontan circuit may not play so important a role as it formally performed by following other surgical strategy of the Fontan operation.

Now that a number of pharmacological agents are available to reduce pulmonary resistance especially soon after the Fontan completion, it is possible to conduct the two-staged extracardiac Fontan operation without fenestration using such pharmacological agents. Two-staged extracardiac Fontan operation combined with pharmacological assist may exclude the need for the placement of fenestration in the Fontan circuit.

Although follow-up period of the patients after the Fontan operation is relatively short, our clinical results are compatible with those in other centers. In conclusion, fenestration in the Fontan circuit is not necessary in the current era, when extracardiac Fontan operation is performed with staging strategy and appropriate pharmacological assist as described in this paper.

Acknowledgments

We deeply thank Ms. Yuka Sakurai and her team for their secretarial assistance.

References

pulmonary stasis in case of transient ventricular dysfunction or AV valve bypass of the pulmonary circulation, fenestration may limit the degree of setting might include benefits provided by a fenestration in combination with a shunt, the hemodynamics mimicking that in fenestrated Fontan patients.

ovenous fistulae, by definition, determines an intrapulmonary right-to-left in your cohort of patients. Furthermore, the presence of pulmonary arterio-\ldots mean pulmonary arterial pressure and pulmonary vascular resistance postoperatively.

those with poor hemodynamics, systemic venous pressure exceeding 15 mmHg, and transpulmonary pressure gradient above 10 mmHg early postoperatively.

I have a few questions. I think that inclusion of the five patients with pulmonary arteriovenous fistulae might alter the analysis of variance concerning mean pulmonary arterial pressure and pulmonary vascular resistance in your cohort of patients. Furthermore, the presence of pulmonary arteriovenous fistulae, by definition, determines an intrapulmonary right-to-left shunt, at least early postoperatively, even in the absence of intracardiac shunt, the hemodynamics mimicking that in fenestrated Fontan patients. Can you comment on this?

Aggressive pulmonary vasodilation by inhaled nitric oxide in unfenestrated setting might include benefits provided by a fenestration in combination with those provided by a fully septated heart. However, by allowing a partial bypass of the pulmonary circulation, fenestration may limit the degree of pulmonary stasis in case of transient ventricular dysfunction or AV valve incompetence which pulmonary vasodilation in an in-series setting does not and might even increase. Did you ever experience impairment of oxygenation index after inhaled nitric oxide was started in patients with unfenestrated Fontan and elevated systemic atrial pressure at the end of the operation? And if so, how did you manage it?

Finally, the incidence of protein-losing enteropathy (2 cases, one of which in association with plastic bronchitis) is quite high in your cohort of patients during a relatively short follow-up period. The observation that oral pulmonary vasodilation is capable of controlling this complication might suggest its pulmonary pathogenesis. Hence, could you postulate that fenestration at the time of the initial Fontan would have either avoided or delayed its occurrence?

Dr. Harada: Regarding your first question, arteriovenous fistula, we have observed that central venous pressure after the Fontan operation in the patients with pulmonary AV fistula is not always so low comparing with that in patients without pulmonary arteriovenous fistula. Patients with pulmonary AV fistula were not excluded, because we believe that pulmonary vasodilation therapy for these patients are also effective.

As for the second question, we don’t think our pulmonary vasodilation therapy itself is effective for the patients with elevated systemic atrial pressure. It is true that systemic vasodilation is more effective in such patients. However, we think it important to keep pulmonary vasodilation, as well as systemic vasodilation, even in these patients in order to obtain good surgical results.

And as for the last question regarding protein-losing enteropathy, well, as you say, it is a very difficult question to answer because I have performed fenestrated Fontan in only one case in my life. The cause of the PLE still remains to be seen. So my preference is to keep adequate oxygen saturation in the Fontan circulation.

Dr. T. Spray (Philadelphia, Pennsylvania, USA): One of the benefits of fenestration that has been suggested is a decrease in duration of pleural effusions. And in every study of the Fontan in the very long-term that has looked at protein-losing enteropathy, the only thing that has correlated with developing protein-losing enteropathy late is the presence of a prolonged effusion at the time of the Fontan. So the benefits of the fenestration are not necessarily hemodynamic, but they may be decreasing the incidence of prolonged effusions which might decrease the incidence of late protein-losing enteropathy. So I wonder how many of your patients have we would call ‘prolonged’ pleural drainage, defined as lasting over two weeks? I noticed the mean time was 11 days, which is fairly long, and so you might see a benefit of fenestration just in decreasing the duration and magnitude of effusions, which is what most of us use fenestration for, not for hemodynamic reasons.

About one-half of your patients after surgery were put on pulmonary vasodilators. Is that now your routine approach? You said that the patients ‘required’ it, and I’m wondering what were your indications for using vasodilators. Is that now your routine approach? You said that the patients ‘required’ it, and I’m wondering what were your indications for using pulmonary vasodilation therapy? Is it everyone now and it’s just that you’re ‘required’ it, and I’m wondering what were your indications for using pulmonary vasodilation therapy? Is it everyone now and it’s just that you’re using it in the later part of the series in everyone, or are there specific indications that you use for that therapy?

Dr. Harada: As for the first question you gave me, putting a fenestration for the Fontan circuit is maybe useful to reduce duration of the chest drainage, I have to admit. But by use of our strategy using active vasodilator therapy, we can manage duration of the chest drainage. But 11 days, I have to admit, little bit long.

And as for the second question, half of the patients required pulmonary vasodilator drugs. As to whether the patient is necessary for vasodilator drug, our cardiologists determine which patient is necessary for the drugs. So it depends on the condition after the surgery. For example, if the chest drainage is very large, attending cardiologist started all vasodilator therapy.

Dr. S. Sano (Okayama, Japan): Do you continue to use nitric oxide and also these vasodilators until you remove the chest tube?

Dr. Harada: No, no.

Dr. Sano: Or just after the operation?

Dr. Harada: Just in the intensive care. So as soon as mechanical ventilation stopped, we stop the administration of nitric oxide gas.

Dr. Sano: And also many papers said they use systemic vasodilators effective, especially to the right ventricle morphology. Is that the indication of the postoperative use of vasodilators?

Dr. Harada: Yes, we think so.
eComment: Re: Do we need fenestration when performing two-staged total cavopulmonary connection using an extracardiac conduit?

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The results of the Fontan operation depend on initial hemodynamic. In our opinion fenestration in Fontan circuit should not be a routine procedure. Some pharmacological agents reduce pulmonary vascular resistance thus decreasing venous pressure \(^1\). We agree with the necessity of fenestration after cardiopulmonary bypass in high-risk patients \(^2\). We believe that Fontan operation with complex concomitant intracardiac procedures and venous pressure higher than 18 mmHg in the postoperative period are indications for fenestration. Given results are based on a perfect surgical and pharmacological strategy and optimal indications to Fontan operation.

References
