Results of the modified Fontan procedure are not related to age at operation

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Abstract

Objective: The modified Fontan procedure represents the final stage for the palliation of hearts with single-ventricle physiology. Different opinions exist regarding the optimal timing of the operation, with most centres advocating early intervention. By contrast, over the past decade, we have progressively increased the age at Fontan operation with the aim to potentially delay the onset of late Fontan failure, and to possibly use larger extracardiac conduits. We retrospectively reviewed our surgical experience with Fontan operation, to understand the impact of this strategy on morbidity and mortality.

Methods: Between 1990 and 2008, 65 patients underwent a modified Fontan operation at our institution (extracardiac conduit in 52 and lateral tunnel in 13). The median age at operation in our series was 7.3 years (range: 2.2–15.8 years) and this value was used to divide the study cohort into two groups. Group A (n = 28) included patients with an age at Fontan operation ≤7 years, whereas group B (n = 37) included patients who had a Fontan operation at >7 years of age. Preoperative characteristics, intra-operative data and short- and medium-term results were assessed.

Results: No differences in baseline characteristics, morbidity and mortality were evident between groups. Hospital mortality was 0% in group A and 5.4% (2/37) in group B (p = 0.5). Prolonged pleural effusions were present in eight patients in group A (29%) and seven in group B (19%, p = 0.39). After a mean follow-up of 5.7 ± 5.4 years (range: 0.3–18 years), the overall mortality of group A (1/28) was similar to that of group B (2/37) (3.6% vs 5.4%, p = 0.999). The incidence of arrhythmias, protein-losing enteropathy, Fontan take down and re-operation were not different between the two groups. Conclusions: The modified Fontan operation can be performed safely in older patients without affecting operative and medium-term follow-up results. Postponing the extracardiac Fontan operation may have the advantage of the use of a larger conduit.

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Keywords: Univentricular heart; Fontan; Outcomes

1. Introduction

After Fontan and Baudet [1] reported a new operation for tricuspid atresia in 1971, various modifications of the Fontan procedure have been used for patients with a functional univentricular heart. The original atrio-pulmonary connection has evolved to the lateral tunnel total cavo-pulmonary connection (TCPC) to improve fluid dynamics and reduce energy losses, as demonstrated by de Leval et al. [2], and towards the concept of an extracardiac inferior vena cava to pulmonary artery connection, as proposed by Marcelletti et al. in 1990 [3]. The concept of staging the Fontan operation through an intermediate procedure for partially unloading the single ventricle by means of a bidirectional cavo-pulmonary anastomosis (BCPA) connection has had a positive impact on the results of Fontan completion [4]. There is a general consensus among clinicians regarding the age at which BCPA should be performed [5]. However, unlike BCPA, no consensus exists about the optimal timing of the Fontan operation. Some centres advocate early intervention to minimise the effects of persistent cyanosis and the risk of paradoxical embolism [6]. However, very young infants have shown higher values of pulmonary vascular resistance, lower oxygen saturation and a higher prevalence of arrhythmias after TCPC than older ones [7]. Furthermore, several groups demonstrated that TCPC cannot be considered a definitive solution because of progressive, long-term attrition in terms of mortality and morbidity [8–10]. For example, a recent study has demonstrated a progressive 2.6% per year decrease in exercise capacity after Fontan operation [10]. For this reason, the policy in terms of timing of the Fontan operation has progressively changed at our institution, in an attempt to delay as much as possible the onset of systemic venous hypertension associated with the Fontan operation. To understand the impact of this strategy on the morbidity

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and mortality of TCPC, we retrospectively reviewed our surgical experience with particular emphasis on the age at operation.

2. Patients and methods

The Institutional Review Board approved the present retrospective study. Informed consent for retention and use of patient data for scientific purposes was routinely obtained at the same time as consent for the procedure.

A review of our clinical database was conducted to identify the patients who received a TCPC between 1990 and 2008. All demographic, echocardiographic, surgical, haemodynamic and follow-up data were collected.

The overall mortality was defined as death occurring from the time of surgery to the most recent follow-up. Early postoperative death was defined as death occurring during admission or within 30 days from the operation.

For the purpose of statistical analysis, single-ventricle morphology was defined as left in a patient with unbalanced double-outlet right ventricle with uncommitted ventricular septal defect.

2.1. Demographics

Sixty-five patients with functionally univentricular hearts were included in the study. Demographic, anatomic and haemodynamic characteristics are shown in Tables 1 and 2.

Three patients had isomerism of the left appendage, and two had isomerism of the right appendage. The single-ventricle morphology was left in 48 patients, right in 16 and indeterminate in one. Fifty-two patients received neonatal palliative procedures at a mean weight of 3.1 ± 0.6 kg: modified Blalock–Taussig shunt (MBTS) in 32 patients, pulmonary artery banding (PAB) in nine, stage 1 Norwood operation in 9 and Damus–Kaye–Stansel (DKS) in 2 patients. In five patients, an aortic arch repair was associated with the first palliative procedure. At a mean age of 14 ± 11 months, 61 patients received a BCPA and four had a Kawashima operation. A DKS operation was performed at the time of BCPA in three patients. An accessory pulsatile pulmonary blood flow was present in 25 patients: through a stenotic or banded pulmonary artery in 21 and through a partially or completely patent MBTS in 4 patients.

2.2. TCPC operation

All TCPC procedures were performed through a median sternotomy with normothermic cardio-pulmonary bypass (CPB). The mean bypass time was 110 ± 40 min. Cardioplegic arrest was used in 23 patients, with a mean duration of 72 ± 28 min.

In 52 patients, an extracardiac TCPC was performed using a polytetrafluoroethylene vascular graft (W.L. Gore and Associates, Inc., Flagstaff, AZ, USA), whereas the remaining 13 patients received a lateral tunnel intracardiac TCPC. A fenestration of approximately 4.0 mm in diameter was created in 52 patients at the time of TCPC completion (Table 3).

2.3. Group definitions

Median age at TCPC completion was 7.3 years (range 2.2—15.8 years). From the distribution of age at TCPC (Fig. 1), we used the median value of 7 years to divide the study population into two groups. Group A included patients who had received a TCPC at an age ≤7 years, whereas group B

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Preoperative diagnosis in the 65 patients undergoing modified Fontan operation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
<td>Number of patients</td>
</tr>
<tr>
<td>Tricuspid atresia</td>
<td>21</td>
</tr>
<tr>
<td>Double inlet left ventricle</td>
<td>14</td>
</tr>
<tr>
<td>Hypoplastic left heart syndrome</td>
<td>11</td>
</tr>
<tr>
<td>Mitral atresia</td>
<td>6</td>
</tr>
<tr>
<td>Pulmonary atresia-intact ventricular septum</td>
<td>7</td>
</tr>
<tr>
<td>Unbalanced atrio-ventricular septal defect</td>
<td>2</td>
</tr>
<tr>
<td>Double inlet indeterminate ventricle</td>
<td>1</td>
</tr>
<tr>
<td>Unbalanced DORV uncommitted VSD</td>
<td>3</td>
</tr>
</tbody>
</table>

DORV, double-outlet right ventricle; VSD, ventricular septal defect.

AV, arterio-venous; BCPA, bi-directional cavo-pulmonary anastomosis; TCPC, total cavo-pulmonary connection.
included patients who had received a TCPC at an age $> 7$ years.

2.4. Statistical analysis

Data are presented as mean $\pm$ standard deviation and range, unless otherwise specified. Comparison of the demographic, anatomic and haemodynamic characteristics observed in two groups was performed using the Fisher’s exact test for categoric variables and the Student’s unpaired $t$-test for continuous variables. Statistical significance was set at a $p \leq 0.05$. Survival functions were obtained by Kaplan–Meier product limit method and compared by log-rank test. SPSS 12 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

3. Results

Two patients in group A (7%) and three in group B (8%) experienced postoperative chilotorax requiring prolonged chest tube drainage and somatostatin therapy ($p = \text{NS}$).

Prolonged pleural effusions, defined as in-dwelling pleural drainage for more than 10 days or re-admission for significant pleural effusion requiring chest drainage, were present in eight patients in group A (29%) and seven in group B (19%) ($p = 0.39$). The overall hospital mortality was 3.1%. Both patients who died belonged to group B (2/37, 5.4%). The first one was an 8-year-old female with mitral atresia who had been palliated by BCPA. She was lost to follow-up and admitted with 70% $O_2$ saturation and severe tricuspid incompetence. Nakata index was 167 mm$^2$ m$^{-2}$. She underwent extracardiac TCPC and tricuspid valvuloplasty according to De Vega technique but she rapidly developed low cardiac output just few hours after the operation. Femoro-femoral extra-corposoral membrane oxygenation (ECMO) was instituted but the patient died 3 days later due to fatal intestinal haemorrhage. The second patient had a double-inlet left ventricle with transposed great vessel and underwent uneventful extracardiac TCPC. On postoperative day 15 he experienced a cardiac arrest, probably due to an arrhythmia. Femoro-femoral ECMO was instituted but severe brain damage was evident. ECMO was switched off 5 days later after cerebral death was diagnosed. Mortality in the two groups was not statistically different (Table 4).

3.1. Follow-up

Follow-up was complete for all 63 hospital survivors. Mean follow-up time was 5.7 $\pm$ 5.4 years (range: 0.3–18 years). As expected, length of follow-up for group A was significantly longer than that for group B (8.7 $\pm$ 6.2 vs 3.2 $\pm$ 2.9 years, $p < 0.0001$) due to the progressive change of our strategy concerning the timing of the operation. The overall survival was 96.9% at 1 year and 93.8% at 5 and 10 years. One patient in group A (1/28, 3.6%) died 55 months after Fontan operation for lung infection. He had left atrial isomerism and unbalanced atrio-ventricular septal defect with azygos continuation. Before completing total cavo-pulmonary connection, he developed arterio-venous pulmonary fistulae leading to chronic desaturation, partially reversed after hepatic veins’ redirection to the pulmonary arteries. Late mortality in group B was 0% ($p = \text{NS}$; Table 4). Survival at 10 years from the operation was 94.7% in group A and 94.6% in group B (Fig. 2). No significant differences were evident between the functional status and morbidity of the two

Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A ($n = 28$)</th>
<th>Group B ($n = 37$)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of TCPC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracardiac</td>
<td>10</td>
<td>3</td>
<td>0.01</td>
</tr>
<tr>
<td>Extracardiac</td>
<td>18</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Fenestration present, $n$</td>
<td>23</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td>Extracardiac conduit diameter (mm)</td>
<td>$16.4 \pm 2.3$, median 16 mm</td>
<td>$18.3 \pm 2.1$, median 18 mm</td>
<td>0.01</td>
</tr>
</tbody>
</table>

TCPC, total cavo-pulmonary connection.
groups (Table 4). No significant difference in the reintervention rate between the two groups was observed (Table 5). Five patients underwent re-operation during follow-up. An epicardial pacemaker was implanted in two patients with complete heart block. One patient required percutaneous enlargement of the fenestration for severe protein-losing enteropathy refractory to medical therapy. One patient received percutaneous closure of the fenestration for chronic arterial desaturation. One patient required percutaneous balloon dilatation of a pulmonary stent implanted before TCPC completion that was partially damaged at operation.

No patient underwent extracardiac conduit replacement for patient overgrowth during follow-up.

Take down of an intracardiac TCPC was undertaken in one patient, belonging to group A, 35 days after operation for massive thrombosis of the intra-atrial tunnel and pulmonary arteries. The patient survived the operation and underwent successful TCPC completion 7 years later.

One patient in group A and one patient in group B developed protein-losing enteropathy refractory to conventional medical management. In both patients symptoms have improved after administration of oral sildenafil.

No difference in ventricular systolic function, as assessed semi-quantitatively, could be observed between the two groups. In group A, 71% of patients had a normal systolic ventricular function compared with 80% in group B. A similar proportion of patients had mildly or moderately impaired ventricular systolic function in the two groups (p = NS). Moreover, objective exercise capacity was measured in 25 patients (10 from group A and 15 from group B) at 2 years from TCPC completion and no difference in peak exercise oxygen uptake was detectable in the two groups (Table 5).

4. Discussion

The Fontan operation, which places the systemic and pulmonary circulations in series and is driven by a single-ventricular chamber, is the treatment of choice for patients with underlying single-ventricle physiology. A large number of children have benefited and continue to benefit from the Fontan operation, but there is still a genuine concern that, despite the refinement of the surgical procedures in the past 20 years, continuing attrition might be inevitable. One of the main concerns is related to the fact that Fontan operation, besides separating the pulmonary and systemic circulations, imposes caval hypertension, particularly in the splanchnic area. Such haemodynamic abnormality is not compatible with a normal life expectancy and exercise capacity in the long term, and leads in a time-related manner to failure of the Fontan circulation and onset of its typical complications.

Given the limited duration and sustainability of Fontan circulation in the long term, it appears clear to us that postponing the age of TCPC operation can potentially delay the age of late Fontan failure. Our experience and current practice are in disagreement with what has been recommended by some large-volume centres, which have advocated reducing the age of TCPC to avoid the deleterious effects of cyanosis on patient growth, and those of volume overload on the single-ventricle function. This potential advantage of early Fontan completion should however translate into improved mortality and morbidity and improved functional outcomes. We could not observe any clear advantage of earlier Fontan completion on hospital and long-term mortality. It is theoretically possible that if a larger cohort had been examined, differences in outcomes between the two groups might have been appreciated. However, the 95% confidence intervals do not appear to be clinically
relevant and suggest no real difference in early and total mortality between the two groups.

As far as functional status is concerned, we could not observe any difference between the two groups in pre- and postoperative ventricular systolic function (Tables 2 and 5). Furthermore, no significant difference in exercise capacity between the two groups could be observed in the older subset of patients in which peak oxygen uptake could be measured (Table 5).

Another reason frequently used to justify early intervention is that early TCPC completion avoids the effects of prolonged cyanosis. However, delaying TCPC completion does not necessarily translate into accepting long-standing suboptimal arterial saturation levels. Indeed, as institutional policy, all patients in whom arterial oxygen saturation dropped below 80% and had no treatable cause of cyanosis (such as venous–venous collaterals) were immediately considered for TCPC completion. Moreover, all patients reported normal social life and attended school without gross neurodevelopmental limitations at follow-up.

On the other hand, the interpretation of the effect of progressively reducing the age at Fontan operation based on the available evidence is not straightforward. For example, Francois and colleagues [11] retrospectively analysed the impact of the reduction of the intervals between BCPA and TCPC completion on morbidity and mortality in 32 children. The age at operation decreased progressively during the 10 years considered in the analysis, and this was associated with a reduction in the operative mortality and morbidity. The authors suggested that improved results were related to a progressive reduction of the age at TCPC completion. However, the fact that a progressive significant reduction of CPB and aortic cross-clamping time was reported in that study may explain, by itself, the reported improved outcome [11].

Early completion of Fontan operation can also be associated with high risk of early failure and increased risk of atrial arrhythmias. Pizarro and colleagues [6] discussed 107 patients who underwent TCPC at a median age of 13 months. The study cohort comprised 61 patients suffering from hypoplastic left heart syndrome, whereas only 27% of the population had a morphologically left single ventricle. All patients received a lateral-tunnel Fontan and the overall mortality was 4.5%. Two groups were identified according to an age at TCPC under or over 18 months. No difference in terms of mortality, duration of intensive care or hospital stay or prolonged chest drainage was identified between the two groups. However, five out of the six patients who received Fontan take down were less than 18 months of age at the time of the operation [6]. Alphonso and colleagues [8] reported on 122 patients who received Fontan operation with an overall mortality of 5%. In 91 patients, a lateral tunnel technique was used and six of them were re-operated for arrhythmias secondary to right atrial wall dilatation. The remaining patients received an atrio-pulmonary Fontan operation or a Kawashima operation. An age at surgery superior to 4 years was identified as a predictor of poor outcome. Twenty-six of the survivors (21%) developed supraventricular arrhythmias during a mean follow-up of 54 months. Sixteen of them had had a lateral tunnel TCPC [8]. It is important to note that, in the above-mentioned articles, the reduction of age at operation seems to have caused a parallel increase in the percentage of patients treated by lateral tunnel technique.

The extracardiac conduit has some theoretical advantages over the lateral tunnel like reduction or avoidance of atrial suture lines and atrial distension. Furthermore, fluid dynamics and clinical studies have consistently showed reduced power losses when the extracardiac conduit was compared with the lateral and extracardiac tunnel configurations [12,13]. These theoretical advantages are confirmed by numerous studies which have demonstrated a reduction in the risk of early and mid-term atrial arrhythmias and better outcome of extracardiac TCPC when compared with intra-cardiac lateral tunnel Fontan [14—18]. The only drawback of this technique is the absence of growth potential of the conduit. To obviate this problem, it is possible to oversize the conduit or to perform the operation at an older age. The upper critical conduit to inferior vena cava diameter ratio that is not associated with a negative hydrodynamic effect is approximately 1.5 [13]. Moreover, in a series reported by Alexi-Meskishvili and colleagues [19], two out of the 20 patients treated by extracardiac conduit who received a tube with a conduit to inferior vena cava ratio superior to 1.8 both experienced conduit thrombosis during follow-up. The authors concluded that implantation of extracardiac conduits which oversize the diameter of the inferior vena cava by less than 20% should be preferred [19].

For this limitation, deferring TCPC operation later in life allowed also to use larger extracardiac conduits potentially suitable for adult size. Accordingly, group B patients received an extracardiac conduit with a diameter significantly larger than group A patients (18.3 ± 2.1 mm vs 16.4 ± 2.3 mm, p = 0.01; Table 3). Even though it is currently unknown whether the use of larger conduit in a larger child could lead to a clinical benefit in adulthood, it is unlikely to turn out to be disadvantageous with extended follow-up length.

If we analyse our experience independently from the age at operation, the overall hospital mortality was 3.1% and the failure rate was 1.5%. These results are comparable with those recently reported by other centres. For example, Giannico and colleagues [20] analysed their experience on 221 patients, who received extracardiac TCPC operation a mean age of 6 years (range: 1—10 years). They reported a hospital mortality of 10% and a failure rate of 14.8% in the first 10 years of experience, decreasing to 4.7% in the past 5 years. The failure rate was 11% at 5 years, and 15% at 10 and 15 years. Kim and colleagues [21] reported on 200 patients operated in a 10-year time interval, with a hospital mortality of 3% and a 10-year mortality rate of 7.6%.

5. Limitation

This study shares all the limitations of retrospective, single-centre studies. The number of patients reported is smaller than in other series, which have described improved outcomes with early TCPC completion. Therefore, the results of the present study have to be interpreted in the light of the study and patients’ characteristics.
6. Conclusion

In conclusion, we have progressively shifted from the lateral tunnel to the extracardiac conduit-modified Fontan operation, and we have gradually increased the age at operation, to use larger and potentially definitive conduits. From the revision of our experience this trend does not affect the results, in term of both morbidity and mortality. These are comparable to the latest and largest experience published in the literature.

References