The impact of ventricular morphology on midterm outcome following completion total cavopulmonary connection

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Abstract

Objective: This study was undertaken to compare the early and midterm outcome following completion total cavopulmonary connection (TCPC) in patients with a single functional ventricle of left or right morphology.

Methods: Between August 1996 and July 2001, 103 patients underwent completion TCPC following an interim superior cavopulmonary connection. The single functional ventricle was of left (\(n=44, 42\%\)) or right ventricular morphology (\(n=59, 58\%\)). The TCPC was performed using an extracardiac conduit (\(n=84, 82\%\)) or a lateral atrial tunnel (\(n=19, 18\%\)), and was fenestrated in 53 patients (51%). Outcomes studied included duration of pleural effusions and in-patient hospitalisation; early mortality, reoperation and reintervention; actuarial survival, freedom from reoperation and reintervention; and current functional status. These were assessed according to a series of preoperative, operative and postoperative variables. Follow-up was complete with a median interval of 17 months (range, 21 days–5.2 years).

Results: Early mortality was 1.9% (\(n=2\)) and one other patient required take-down of the Fontan circulation. There was one late death. Five-year survival with a Fontan circulation (± 1 SEM) was 95.6 ± 2.5%.

Forty-two patients (41%) had prolonged pleural drainage (≥14 days) and 41 patients (40%) had a prolonged hospital stay. Five-year freedom from reoperation and reintervention (± 1 SEM) were 92.2 ± 5.0 and 73.4 ± 6.0%, respectively. The Fontan procedure was associated with an improved functional class (\(P<0.005\)) and all current survivors (\(n=99\)) are in either New York Heart Association classes I or II. Multivariate analysis identified left atrial isomerism as the single risk factor for death (\(P<0.05\)). Independent risk factors for prolonged hospital stay included a morphologic right ventricle (\(P<0.05\)), increased postoperative pulmonary artery pressures (\(P<0.005\)) and an unfenestrated Fontan procedure (\(P<0.01\)).

Conclusions: In this contemporary series, the modified Fontan procedure was characterised by low early mortality, excellent midterm survival, and improved functional class independent of the morphology of the single functional ventricle. Nevertheless, a morphologic right ventricle was a risk factor for prolonged in-patient hospitalisation and may yet influence long term survival.

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1. Introduction

The management of patients with congenital cardiac abnormalities characterised by functionally single ventricle anatomy generally involves a series of palliative operations, which culminate in the Fontan procedure. Since its original description [1], the Fontan procedure has been applied to the management of virtually all forms of congenital cardiac malformations that are not suitable for biventricular repair. Increasingly, this includes patients with a single functional ventricle of right ventricular morphology. A morphologic right ventricle (mRV) may represent an additional risk factor for the successful creation of the Fontan circulation [2].

This study was undertaken to review our institutional experience with the modified Fontan procedure in the current era. It included only those patients who underwent a total cavopulmonary connection (TCPC) following an interim superior cavopulmonary (CP) shunt. We sought to compare the early and midterm outcome in patients with a single functional ventricle of either left or right ventricular morphology.
morphology and determine whether the morphology influenced outcome. In addition, we sought to identify whether other preoperative, operative and postoperative variables influenced outcome following the modified Fontan procedure.

2. Materials and methods

Between 1st August, 1996 and 31st July, 2001, 118 patients with functionally single ventricle anatomy underwent a TCPC at the Diana Princess of Wales Children’s Hospital, Birmingham, UK. One hundred and five patients (89%) had previously undergone a superior CP shunt, as part of their electively staged palliation. The majority of these patients (n = 103, 98%) had functionally single ventricle anatomy of either left or right ventricular morphology. Two patients (2%) had a dominant ventricle of indeterminate morphology and were not included in this study.

This study involved the retrospective review of all hospital records, operation notes, and echocardiographic and cardiac catheter data as well as the assessment of current clinical and functional performance. The duration of pleural drainage (until last thoracocentesis or final removal of intercostal drains) and length of in-patient hospital stay; early (in-patient or 30 day) mortality and actuarial survival; and current functional status were used as outcome measures. These were evaluated with regard a series of preoperative, operative and postoperative variables, which are summarised in the Appendix.

2.1. Pre-operative variables

Of the 103 patients included in this study, 59 patients (57%) had a single functional ventricle of right ventricular morphology and 44 patients (43%) had a single functional ventricle of left ventricular morphology. Seventy-seven patients (75%) were male. The most common primary cardiac malformation was hypoplastic left heart syndrome (HLHS; n = 41, 40%). Of the remaining patients, 21 patients had tricuspid atresia (20%), 12 patients had double-inlet left ventricle (12%), ten patients had double-outlet right ventricle with mitral atresia (10%), nine patients had an unbalanced atroventricular septal defect with a dominant ventricle of either left or right ventricular morphology (9%) and ten patients had other diagnoses (10%). Twelve patients had atrial isomerism (12%), eight with right atrial isomerism and four with left atrial isomerism. Sixteen patients (16%) were originally diagnosed with abnormal pulmonary venous drainage, including patients with azygous or hemiazygous continuation of the inferior vena cava (IVC), bilateral superior vena cavae, anomalous systemic venous drainage, as well as the patients with left atrial isomerism. Thirteen patients (13%) were originally diagnosed with abnormal pulmonary venous drainage, including patients with pulmonary venous obstruction; total or partial anomalous drainage; as well as the patients with right atrial isomerism.

The majority of patients (n = 92, 89%) required initial surgical palliation either as neonates or young infants. This generally consisted of either a Norwood stage I procedure (n = 58, 63%) or a systemic-pulmonary arterial shunt (n = 26, 28%). Seven patients (8%) had pulmonary artery banding to limit pulmonary arterial flow and a further patient (1%) had required an isolated atrial septectomy. An interim superior CP shunt was created in all patients, at a median age of 7 months (range, 30 days–7 years). Universally, this involved a bidirectional Glenn procedure.

Completion TCPC was indicated in patients with progressive cyanosis or increasing dyspnoea on exertion. The median preoperative oxygen saturations in air were 82% (range, 60–91%). Preoperative clinical status has been retrospectively graded using the New York Heart Association (NYHA) classification, and the majority of patients were in NYHA functional class II (n = 68, 66%). However, 35 patients (34%) were in a poor functional condition, with 33 patients (32%) in NYHA class III and two patients (2%) in NYHA class IV.

Preoperative cardiovascular function was routinely assessed using echocardiography and elective cardiac catheterisation. Ventricular and valvular functions were primarily evaluated using echocardiography. Ventricular function was graded as good, moderate or poor. Valvular dysfunction was graded as none, mild, moderate or severe; moderate and severe valvular dysfunction was regarded as clinically important. Cardiac catheterisation defined the size and shape of the central pulmonary arteries and characterised the systemic and pulmonary venous return. In addition, the mean pulmonary arterial (PA) and common atrial pressures and the trans-pulmonary pressure gradient were routinely recorded during cardiac catheterisation.

Prior to completion TCPC, 95 patients (92%) had good ventricular function. Six patients (6%) had moderate ventricular function and only two patients (2%) had poor ventricular function. Eight patients (8%) had clinically important atrio-ventricular valve (AVV) regurgitation and one patient (1%) had clinically important sub-aortic obstruction. In addition, two patients (2%) with HLHS had clinically important native aortic valve regurgitation.

Preoperative cardiac catheterisation demonstrated 40 patients (39%) had clinically important abnormalities of the central pulmonary arteries, including relatively small pulmonary arteries (n = 21), isolated stenoses (n = 28) and distorted pulmonary arteries (n = 4). Cardiac catheterisation also identified three cases (3%) in which the superior cavopulmonary shunt was stenosed at the anastomosis, limiting flow in the superior cavopulmonary shunt. Under general anaesthesia, the median PA pressure was 12 mmHg (range, 8–17 mmHg); the median atrial pressure was 8 mmHg (range, 2–14 mmHg); and the median
transpulmonary gradient was 5 mmHg (range, 0–14 mmHg). Fourteen patients (14%) had elevated PA pressures (≥15 mmHg) and five patients (5%) had elevated atrial pressures (≥12 mmHg).

2.2. Intraoperative variables

The median age at the time of operation was 4.4 years (range, 1.9–12.9 years), and the median weight was 15.9 kg (range, 10.9–27.7 kg). During the study period, completion TCPC was performed using either a lateral atrial tunnel \((n = 19, 18\%)\) or an extracardiac conduit \((n = 84, 82\%)\), as illustrated in Fig. 1. The extracardiac conduit TCPC involved the interposition of a 20 ± 2 mm GORE-TEX® tube conduit (W.L. Gore & Associates (UK) Ltd. Livingston, Scotland) between the IVC and the right pulmonary artery with extension to the central pulmonary artery. A 3–6 mm fenestration was intentionally created in the Fontan circuit in 53 patients (51%). This involved either a single-punch fenestration in the lateral tunnel baffle or a side-to-side anastomosis between the extracardiac conduit and the lateral atrial wall. In 50 patients (49%), concomitant surgical procedures were performed, as summarised in Table 1.

For patients undergoing lateral tunnel TCPC, the median cardiopulmonary bypass time was 59 min (range, 31–118 min). The median aortic cross clamp time of 54 min (range, 29–69 min), during which time myocardial protection was afforded by intermittent cold crystalloid cardioplegia. Seventeen patients also required a period of deep hypothermic circulatory arrest with a median duration of 16 min (range, 1–74 min).

The extracardiac conduit TCPC was generally accomplished using bicaval cardiopulmonary bypass only, with a median cardiopulmonary bypass time was 66.5 min (range, 39–132 min). Twenty-four patients required a period of aortic cross clamping, with a median duration of 37 min (range, 3–103 min). In these patients, myocardial protection was afforded by intermittent cold crystalloid cardioplegia. Forty-nine patients required a period of deep hypothermic circulatory arrest, with a median duration of 29 min (range, 5–57 min).

2.3. Postoperative variables

Postoperative ventricular and valvular functions were evaluated by serial echocardiography, using the same grading system. During the initial postoperative period, mean PA and common atrial pressures and the transpulmonary pressure gradient were routinely recorded, using invasive monitoring lines inserted at operation. Cardiac catheterisation was not routinely performed following completion TCPC. In select patients, it was performed either as a diagnostic tool, when more precise haemodynamic or angiographic information was required, or to enable therapeutic reintervention.

Echocardiography was performed on all patients within 24 h following completion TCPC. Ninety-five patients (92%) had good ventricular function and eight patients (8%) had moderate ventricular function. Six patients (6%) had clinically important AVV regurgitation and two patients (2%) had clinically important aortic valve regurgitation. Postoperatively, the median PA pressure was 14 mmHg (range, 10–22 mmHg); the median atrial pressure was 7 mmHg (range, 2–10 mmHg) and the median transpulmonary gradient was 7 mmHg (range, 2–18 mmHg). Thirty-eight patients (37%) had elevated PA pressures and no patients had elevated atrial pressures. The median postoperative oxygen saturations were 96% (range, 75–100%).

Following completion TCPC, all of the patients were anticoagulated with a lifelong warfarin regimen. The warfarin dose was adjusted to maintain an international

Table 1

| Concomitant surgical procedures for fifty patients who underwent completion TCPC |
|---------------------------------|---|
| Pulmonary artery augmentation   | 39 |
| Atrio-ventricular valve annuloplasty | 4 |
| Atrial septectomy               | 3 |
| Resection of subaortic muscle   | 3 |
| Enlargement of ventricular septal defect | 2 |
| Surgical occlusion of native aortic valve | 2 |
| Interruption of modified Blalock-Taussig shunt | 1 |
| Insertion of permanent pacemaker | 2 |
| Total procedures                | 56 |
normalised ratio of 2.0–3.0. All patients have been followed up since discharge from hospital by a paediatric cardiologist either in our own unit or in the patients’ referring hospital. Current clinical status was graded using the NYHA functional classification. Follow-up was complete with a median interval of 17 months (range, 21 days–5.2 years).

2.4. Statistical analysis

Data have been examined by analysis of variance using a commercial statistical software package (SPSS for Windows, version 10, SPSS Inc, Chicago, IL, USA). Continuous variables are expressed as median and range and comparative univariate analyses have been made using the Mann–Whitney U-test or Wilcoxon signed rank test. Binomial or ordinal data are expressed as percentage and comparative univariate analyses have been made using the $x^2$ test, two-sided Fisher exact test or binomial logistic regression, as appropriate. A probability value, $P < 0.05$, was taken to represent a statistically significant difference between groups.

The effect of the preoperative, operative and postoperative variables on outcome was tested by univariate and multivariate analyses. Univariate analyses of early outcome measures have been made using the $x^2$ test, two-sided Fisher exact test and binomial logistic regression. Variables with a probability value, $P \leq 0.1$, were included in a stepwise logistic regression model. Results of these multivariate analyses have been expressed as odds ratios (OR) with 95% confidence intervals (CI) for variables with a probability value, $P < 0.05$.

Actuarial survival, freedom from reoperation and freedom from reintervention were estimated using the Kaplan–Meier product limit method. These results have been expressed as probability estimate $\pm$ 1 standard error of the mean (SEM). Univariate analyses of actuarial outcome measures have been made using the log-rank test. Variables with a probability value, $P \leq 0.1$ were included in a stepwise Cox regression analysis. Results of these multivariate analyses have been expressed as likelihood-ratios (LR) with 95% CI for variables with a probability value, $P < 0.05$.

3. Results

3.1. Duration of pleural drainage

The median duration of pleural drainage for the entire cohort was 12 days (range, 3–83 days). Forty-two patients (41%) had prolonged pleural drainage, with persistent drainage for 14 days or more. On univariate analysis, the morphology of the single functional ventricle did not influence either the period of pleural drainage ($P = 0.15$) or the proportion of patients with prolonged pleural drainage ($P = 0.54$, Table 2).

Multivariate analysis identified two variables that were associated with prolonged pleural drainage. Abnormal pulmonary venous drainage (OR, 10.1; 95% CI, 2.2–46.1; $P < 0.005$) and increased postoperative PA pressure (OR, 2.4 per quartile increase; 95% CI, 1.2–4.6; $P < 0.05$) each independently increased the risk of prolonged pleural drainage.

3.2. Duration of in-patient hospital stay

The median length of in-patient hospital stay for the entire cohort was 16 days (range, 6–104 days). Forty-one patients (40%) required prolonged hospital stay, defined as a period $\geq$21 days post-operation. On univariate analysis, the morphology of the single functional ventricle did not influence either the length of hospital stay ($P = 0.08$) or the proportion of patients requiring prolonged hospital stay ($P = 0.07$, Table 2). However, an mRV was associated with an increased risk of prolonged hospital stay on multivariate analysis (OR, 3.5; 95% CI, 1.3–9.7; $P < 0.05$).

Multivariate analysis identified four other variables associated with prolonged hospital stay. The risk of prolonged hospital stay was increased by prolonged cardiopulmonary bypass (OR, 2.0 per quartile increase; 95% CI, 1.3–3.3; $P < 0.005$) and aortic cross clamp times (OR, 2.4 per quartile increase; 95% CI, 1.4–4.1; $P < 0.005$) and increased postoperative PA pressure (OR, 1.9 per quartile increase; 95% CI, 1.0–3.7; $P < 0.05$). The risk of prolonged hospital stay was decreased by fenestration of the Fontan circuit (OR, 0.24; 95% CI, 0.1–0.7; $P < 0.01$).

3.3. Early mortality and actuarial survival

In-patient or 30 day mortality was 1.9% ($n = 2$). One further patient required acute takedown of the Fontan circulation and restitution of the superior cavopulmonary shunt for Fontan failure. The early survival with a Fontan circulation was 97.1% ($n = 100$). On univariate analysis, the morphology of the single functional ventricle did not influence the risk of either early mortality ($P = 0.67$) or early survival with a Fontan circulation ($P = 0.61$, Table 2). Multivariate analysis did not identify any variables that were associated with early survival with a Fontan circulation.

One patient developed protein-losing enteropathy and died late following completion TCPC. The actuarial survival with a Fontan circulation for the entire cohort was 95.6 ± 2.5% at 1 and 5 years postoperatively. When the patients with a systemic ventricle of either right ventricular morphology or left ventricular morphology were analysed separately, survival was similar ($P = 0.51$, Fig. 2).

Multivariate analysis identified left atrial isomerism as the only variable that independently increased risk of mortality or takedown of the Fontan circulation (LR, 95.1; 95% CI, 1.8–4958.9; $P < 0.05$). By comparison, right atrial isomerism was not associated with an increased risk (LR, 0.3; 95% CI, 0.1–2.1; $P = 0.87$).
3.4. Early and actuarial freedom from reoperation and cardiac catheter reintervention

Seven patients (6.8%) required early reoperation (n = 3, 2.9%) or early reintervention (n = 5, 4.9%) following completion TCPC. In addition, 17 patients required either reoperation (n = 1) or reintervention (n = 16) during the follow-up period. These procedures are summarised in Table 3. The most common reason for reoperation or reintervention was to reduce or close the fenestration (n = 12, 48%). The actuarial freedom from reoperation was 97.0 ± 1.7% at 1 year and 92.2 ± 5.0% at 5 years postoperatively and the actuarial freedom from reintervention was 88.8 ± 3.4% at 1 year and 73.4 ± 6.0% at 5 years postoperatively.

On univariate analysis, the morphology of the single functional ventricle did not influence the risk of early reoperation or early reintervention (P = 0.61 and P = 0.39, respectively, Table 2) or the actuarial freedom from reoperation or reintervention (P = 0.48 and P = 0.12, respectively), as illustrated in Figs. 3 and 4, respectively.

Multivariate analysis did not identify any variables that were associated with either early reoperation or reintervention. Multivariate analysis did identify two variables, abnormal pulmonary venous return and postoperative oxygen saturations, which were independently associated with the actuarial risk of reoperation and reintervention, respectively. Abnormal pulmonary venous return increased the actuarial risk of reoperation (LR, 7.6; 95% CI, 1.0–55.8; P < 0.05) and increased postoperative oxygen saturations reduced the actuarial risk of reintervention (LR, 0.5 per quartile increase; 95% CI, 0.3–0.8; P < 0.05).

3.5. Functional status

Of the current 99 survivors with a Fontan circulation, all are in a satisfactory functional condition. Fifty-seven patients (58%) are in NYHA class I and 42 patients (42%) are in NYHA class II. The creation of the Fontan circulation was associated with an overall improvement in functional class (P < 0.005). For all remaining patients, functional class was either improved (n = 72, 73%) or remained unchanged (n = 27, 27%).

On univariate analysis, the morphology of the single functional ventricle did not influence the preoperative functional status (P = 0.11), current functional status (P = 0.19) or change in functional status (P = 0.47). Multivariate analysis did not identify any variables that were associated with current functional status.

4. Discussion

The management of patients with congenital cardiac malformations characterised by a single functional ventricle generally involves a series of palliative operations, which culminate in the Fontan procedure. A variety of technical modifications have been made to the Fontan procedure, including notably the development of the TCPC [3], either...
as a lateral atrial tunnel or an extracardiac conduit; the fenestration of the Fontan circuit [4]; and the introduction of the staged Fontan procedure [5]. These technical modifications, in conjunction with advances in the general management of these patients, have been associated with a marked improvement in early outcome following the Fontan procedure [6]. Operative mortality has decreased despite the application of the Fontan procedure to an increasing proportion of patients with anatomic and haemodynamic characteristics, which were originally considered to carry higher risk [7]. In particular, this includes patients with a single functional ventricle of right ventricular morphology (mRV).

The mRV may represent a risk factor for a successful Fontan procedure because of intrinsic geometric, functional and pathophysiologic differences between the mRV and the morphologic left ventricle (mLV) [2]. The mRV has a tripartite crescentic shape, which may be less suited to sustained, high pressure contractile function than the prolate spheroid mLV. The mRV has a relatively low ejection fraction and reduced myocardial functional reserve compared to the mLV [8] and the mRV is associated with a relatively poor functional adaptation to pressure and volume overload [9]. At present, however, the clinical importance of these differences remains essentially speculative.

The unsuitability of the mRV to support the systemic circulation has been reported both in congenitally corrected transposition and in simple transposition following the atrial switch procedure [10,11]. It seems plausible that that a single functional mRV may be unable to support the entire circulation following the Fontan procedure. Julsrud et al reported the Mayo Clinic experience of outcomes following a non-fenestrated, modified Fontan procedure in 500 patients operated between 1973 and 1987 [12]. The authors identified ventricular morphology to be a significant predictor of early (<6 months) survival on univariate and multivariate analysis. Survival for patients with an mRV was significantly worse than for those with an mLV with a relative risk ratio of 1.7. In a comparable series of 500 patients operated at Boston Children’s Hospital between 1973 and 1991 [13], a single right ventricle and a tricuspid valve as the systemic atrioventricular valve (i.e. mRV) were each identified as risk factors for early failure following a modified Fontan procedure. On multivariate analysis, a tricuspid valve as the systemic atrioventricular valve was a significant risk factor (OR, 3.5). These two series report the results of the Fontan procedure during a period that encompassed marked changes in patient selection and management as well as modifications to the Fontan procedure. Furthermore, the patients with an mRV represent a small proportion of each series, 16 and 17%, respectively. These two studies may partly reflect the evolution of the Fontan procedure.

The current study has reported a contemporary series of 103 patients following a modified Fontan procedure. In this study, there were a comparable number of patients with a single functional ventricle of right ventricular or left ventricular morphology. Ventricular morphology was not associated with an increased mortality, either early or during the follow-up period. Ventricular morphology was also not associated with either an increased risk of reoperation or cardiac catheter reintervention. However, ventricular morphology was independently associated with an increased risk of certain postoperative morbidity, with more than a threefold increase in risk of prolonged in-patient hospitalisation ($P < 0.05$).

The findings of the current study are consistent with another contemporary study [14]. In a series of 332 consecutive patients who had a modified Fontan procedure at the Children’s Hospital of Philadelphia, Gaynor et al.

Table 3
Surgical reoperations and cardiac catheter reinterventions performed following completion TCPC

<table>
<thead>
<tr>
<th>Surgical reoperations</th>
<th>Early ($n = 3$)</th>
<th>Late ($n = 1$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction of fenestration size</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Creation of fenestration</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary artery augmentation</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Augmentation of pulmonary venous confluence</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Plication of hemidiaphragm</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Total number of reoperations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cardiac catheter reinterventions</th>
<th>Early ($n = 5$)</th>
<th>Late ($n = 16$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device closure of fenestration</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Dilatation of fenestration and stent insertion</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary artery dilatation ± stent insertion</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Occlusion of main pulmonary artery</td>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td>Aortic arch dilatation</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>IVC dilatation</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Occlusion of systemic-pulmonary collaterals</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total number of reinterventions</td>
<td>6</td>
<td>18</td>
</tr>
</tbody>
</table>
reported that ventricular morphology was not associated with an increased early mortality. HLHS, the principle diagnosis amongst patients with an mRV, was associated with an increased period of postoperative hospitalisation. In contrast to the current study, HLHS was also associated with more prolonged pleural effusions. This study was reported to demonstrate that the modified Fontan procedure could be successfully applied to high-risk patients, such as those with HLHS. The basis for the relatively higher morbidity was, however, not discussed.

The current study sought to identify other preoperative, operative and postoperative characteristics that influence outcome following completion TCPC. Prolonged pleural effusions represent a clinically important cause of morbidity, occurring in up to 45% of patients [15]. Despite their relative frequency, the basis for the development of pleural effusions following the Fontan procedure remains unexplained [16]. Many factors have been proposed, including elevated central venous pressure, absence of a fenestration, aorto-pulmonary collaterals, the type of Fontan procedure as well as the presence of an intercurrent respiratory tract infection. In the current study, 41% of patients had prolonged pleural drainage. Multivariate analysis identified increased postoperative PA pressure and abnormal pulmonary venous drainage as independent risk factors for prolonged pleural drainage. Both factors are associated with increased pulmonary vascular impedance and raised pulmonary lymphatic pressure, which can produce interstitial pulmonary oedema [17]. It seems likely that these associated haemodynamic abnormalities may account for the increased risk attributable to both increased PA pressure and abnormal pulmonary venous drainage.

Prolonged in-patient hospitalisation has been reported to occur in up to 45% of patients following the Fontan procedure [15]. In the current study, 40% of patients required a hospital stay of 21 days or more. The length of hospital stay was primarily related to the duration of pleural drainage (correlation coefficient 0.91, \( P < 0.01 \)). Increased postoperative PA pressure was identified as an independent risk factor for both prolonged pleural effusions and prolonged in-patient hospitalisation. Four other factors were also independently associated with prolonged hospital stay, including an unfenestrated Fontan procedure and, importantly, right ventricular morphology. Prolonged cardiopulmonary bypass and aortic cross clamp times were also identified, and probably reflect the increased risk associated with longer and more complex procedures [6,13].

The fenestrated Fontan procedure was originally introduced in order to improve cardiac output, albeit at the expense of oxygenation; reduce the systemic venous pressure; and thus improve survival and morbidity following the Fontan procedure [4]. The introduction of this modification into clinical practice has been associated with an improved outcome following the Fontan procedure [13, 14]. In the current study, the major advantage of the fenestrated Fontan procedure related to the reduction of early postoperative morbidity, as reflected by prolonged in-patient hospitalisation. However, there was no improvement in either survival or risk of prolonged pleural drainage. Furthermore, the fenestrated Fontan procedure was associated with an increased risk of expected reintervention, in order to close the fenestration.

Over the past 10 years, there has been a significant decline in the reported early postoperative mortality following the Fontan procedure and early mortality in contemporary series range between 4.5 and 7% [13–15]. The early mortality rate in the current study was less than 2%, which compares favourably with these published results. In this study, there were no variables associated with early survival. Left atrial isomerism was independently associated with actuarial survival, with an increased risk of
mortality or takedown of the Fontan circulation. There is limited information regarding the mortality following the Fontan procedure in patients with atrial isomerism. Nevertheless, the mortality is higher amongst these patients and has been reported to range between 13 and 43% [18,19]. Patients with right atrial isomerism are generally regarded as having a comparable or worse outlook than patients with left atrial isomerism [19], although this was not supported by the current study. The reason why left atrial isomerism is associated with an increased risk remains uncertain but probably reflects the presence of associated cardiovascular abnormalities, notably abnormal or anomalous systemic and pulmonary venous return, which may adversely affect the performance of the Fontan circulation [18]. Nevertheless, encouraging results have been achieved in patients with atrial isomerism as well as isolated abnormal pulmonary and systemic venous drainage and their presence should not necessarily be used as a contraindication to the Fontan procedure [20].

Previous series have reported that reoperation, including cardiac catheter reintervention, has been required in up to 29% of patients following the Fontan procedure [21]. In addition, the freedom from reoperation gradually declined with an increasing period of follow-up. In a series of 517 patients at the Toronto Hospital for Sick Children, Freedom et al reported that the freedom from reoperation or reintervention was 88% at 5 years, 77% at 10 years and 54% at 15 years post-operation [22]. In the current study, 23 patients (22%) required reoperation or cardiac catheter reintervention following the Fontan procedure. Analysed separately, the actuarial freedom from reoperation was 97% at 1 year and 92% at 5 years post-operation; and the actuarial freedom from reintervention was 89% at 1 year and 73% at 5 years post-operation.

Multivariate analysis did not identify any factors that were associated with either early reoperation or reintervention following the Fontan procedure. Abnormal pulmonary venous drainage was independently associated with the overall risk of reoperation. Abnormal pulmonary venous drainage, with or without atrial isomerism, has previously been identified as an independent risk factor for survival following the Fontan procedure [19]. The finding of this study may represent an additional risk for these patients. However, it is more likely that this finding reflects the need to clearly delineate the pulmonary venous drainage and tailor the surgical approach according to the findings [6]. In the current study, two of the five patients who required reoperation had evidence of obstructed pulmonary venous drainage, which was not diagnosed with either preoperative echocardiography or cardiac catheterisation.

Low postoperative saturations were independently associated with the risk of cardiac catheter reintervention. Each quartile increase in the postoperative saturations halved the risk of reintervention. Persistent or progressive cyanosis after the modified Fontan procedure can occur for a variety of reasons, including increased pulmonary vascular impedance, ventricular dysfunction, and pulmonary arteriovenous malformations [23]. An increasingly important cause of postoperative cyanosis and cardiac catheter reintervention relates to the use of a fenestrated Fontan procedure. In the current study, almost half of all reinterventions were potentially expected, being performed specifically to close the surgical fenestration. Delayed closure of the surgical fenestration is a generally safe procedure, which results in the abolition of the right-to-left shunt and concomitant improvement in peripheral saturations [24]. Nevertheless, closure of the fenestration is associated with significant haemodynamic changes, which may potentially influence the long-term function of the Fontan circulation [25]. The indications, optimal timing and acceptable haemodynamic sequelae of delayed closure of the fenestration have yet to be adequately defined.

This study has certain limitations. It was a retrospective study, which included only those patients who underwent a staged TCPC and who had a single functional ventricle of either left or right ventricular morphology. It is not possible to determine whether similar results can be achieved in other patient cohorts or with alternative management strategies. We also identified a high level of correlation between some of the variables. This may have confounded the multivariate analysis and prevented us from identifying independent associations between variables and the outcome measures. Finally, it is important to emphasise that the duration of follow-up is limited.

For the purposes of this study, we chose a series of conventional, clinically appropriate end-points, which reflected the spectrum of early and late outcome following the Fontan procedure. However, the overall success of the modified Fontan procedure may warrant the introduction of additional end-points in future studies, which may enable clinically and functionally important differences to be identified. The investigation of the functional importance of ventricular morphology, for example, might be assisted by investigating the impact of the Fontan procedure with independent indices of cardiovascular performance, such as ventriculo-vascular coupling analyses.

5. Conclusion

This study has demonstrated that the modified Fontan procedure is associated with low early morbidity and mortality, excellent midterm survival, and improved functional class. Furthermore, these results can be achieved in virtually all patients, including those with a single functional ventricle of right ventricular morphology. Nevertheless, a morphologic right ventricle was a risk factor for prolonged in-patient hospitalisation. It remains to be seen whether these encouraging results are reflected in improved longer-term outcome and whether ventricular morphology will influence the long-term outcome following the modified Fontan procedure.
Appendix A. Variables tested as possible predictors or early and actuarial outcome

A.1. Preoperative variables

Gender
Male or female

Ventricular morphology
Left or right

Diagnosis
Hypoplastic left heart syndrome
Tricuspid atresia
Double-inlet left ventricle
Double-outlet right ventricle with mitral atresia
Unbalanced atroventricular septal defect
Other diagnoses

Atrial isomerism
Left or right

Abnormal systemic venous drainage

Abnormal pulmonary venous drainage

Initial palliation
None
Atrial septectomy
Pulmonary artery band
Systemic-pulmonary arterial shunt
Norwood stage I

Echocardiographic findings
Ventricular function
Atrioventricular valve dysfunction
Outflow tract dysfunction

Haemodynamics
Pulmonary arterial abnormalities
Systemic venous abnormalities
Pulmonary venous abnormalities
Mean pulmonary arterial pressure
Common atrial pressure
Preoperative oxygen saturations

Functional class (NYHA)
1–IV

A.2. Operative variables

Demographics
Year of operation
Age at operation
Weight

Type of Fontan
Lateral atrial tunnel
Extracardiac conduit
Fenestration

Concomitant surgical procedures
Cardiopulmonary bypass time
Aortic cross-clamp time
Deep hypothermic circulatory arrest time

A.3. Postoperative variables

Echocardiographic findings
Ventricular function
Atrioventricular valve dysfunction
Outflow tract dysfunction

Haemodynamics
Mean pulmonary arterial pressure
Common atrial pressure
Postoperative oxygen saturations

Functional class (NYHA)
1–IV

References


