Factors influencing early and late outcome following the Fontan procedure in the current era. The ‘Two Commandments’?∗

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Abstract

Objective: This study was undertaken to identify the factors affecting early and late outcome following the Fontan procedure in the current era. We have examined whether conventional selection criteria, the ‘Ten Commandments’, are still applicable in the current era. Materials and methods: Between January 1988 and July 2004, 406 patients underwent a modified Fontan procedure at a median age of 4.7 years (IQR, 3.8–7.1 years). The single functional ventricle was of left (n = 241, 59%) or right ventricular morphology (n = 163, 40%). The modified Fontan procedure was performed using an atrio pulmonary connection (n = 162, 40%) or total cavopulmonary connection (TCPC) involving a lateral atrial tunnel (n = 50, 12%) or extracardiac conduit (n = 194, 48%). They were fenestrated in 216 patients (53%). Results: The early mortality was 4.4% (n = 18) and four other patients required takedown of the Fontan circulation. On multivariable analysis, early outcome was adversely influenced by two factors (p < 0.05): preoperative impaired ventricular function and elevated pulmonary artery pressures. Two risk models were constructed for early outcome based on preoperative and predictable operative variables (Model 1) and all preoperative and operative data (Model 2). Both models were calibrated across all deciles (p = 0.83, p = 0.25) and discriminated well. The area under the ROC curve was 0.85 and 0.89, respectively. There were 21 late deaths, 1 patient required late takedown of the Fontan circulation and 3 required orthotopic cardiac transplantation. Actuarial survival was 90 ± 2%, 86 ± 2% and 82 ± 3% at 5, 10 and 15 years, respectively. Multivariable analysis identified that outcome was influenced by preoperatively impaired ventricular function, elevated preoperative pulmonary artery pressures and an earlier year of operation. The freedom from reintervention was 83 ± 4%, 76 ± 4% and 74 ± 8% at 5, 10 and 15 years, respectively. Additional risk factors for reintervention were right atrial isomerism and preoperative small pulmonary artery size. Conclusions: Late outcome of the Fontan circulation is encouraging. Ventricular morphology, surgical technique and fenestration do not appear to influence early or late outcome. Preoperatively impaired ventricular function and elevated pulmonary artery pressures have an adverse influence on both early and late outcome. Reintervention is common, with small preoperative pulmonary artery size being an additional risk factor.

Keywords: Heart defects; Congenital; Paediatrics; Fontan procedure; Total cavopulmonary connection; Risk factors

1. Introduction

Since its first description in 1971, the Fontan procedure [1] has provided an effective method of palliating patients who are unable to undergo biventricular repair for a range of congenital heart diseases, characterised by a functionally uni-ventricular circulation. Midterm outcomes from early series have identified significant morbidity related to supraventricular arrhythmias, protein losing enteropathy, thromboembolism and reduced exercise tolerance [2–4]. This has prompted modifications leading to the total cavopulmonary connection (TCPC) comprising of the Lateral Tunnel Fontan or later, the Extracardiac Fontan operation [5–7]. Guidelines for their suitability and techniques such as circuit fenestration have evolved along with improvement in operative techniques and postoperative care. Although the literature has addressed the outcomes from early Fontan series, few large series address the long-term outlook in the current era with the advent of these surgical modifications, improved postoperative management and a greater incidence of hypoplastic left heart syndrome (HLHS) patients. To better understand the risk factors for medium term survival and failure of the Fontan circulation in the...
current era, we reviewed a large single-centre European experience over a 16-year period. A better understanding of the late outcome is important in advising families as well as defining long-term management issues.

This study exemplifies the role that the selection criteria play on long-term outcome.

First described by Choussat et al., the ‘Ten Commandments’ have become the basic criteria for patient selection undergoing the Fontan operation. Choussat listed ten criteria that should ideally be satisfied to minimize morbidity and mortality with the Fontan procedure [8]. These 10 commandments have been adapted over the years and are summarised as: age above 4 years, normal ventricular function, adequate pulmonary artery size, no distortion of pulmonary arteries from prior shunt surgery, low pulmonary artery pressure (below 15 mmHg), low pulmonary vascular resistance, normal systemic venous drainage, no atrioventricular valve leak, normal heart rhythm and no right atrial enlargement.

Whether or not all commandments need to be fulfilled for successful late outcome has yet to be demonstrated. This paper reviews whether or not all these hold true in the current era.

2. Materials and methods

Of the 406 patients included in this study, 251 were males (62%) and 155 females. The majority of patients (n = 241, 59%) had a single functional ventricle of left ventricular morphology (mL V). Of the remaining patients, 163 patients (40%) had a single functional ventricle of right ventricular morphology (mRV) and 2 patients (0.49%) had a true single ventricle (i.e. indeterminate morphology). The primary cardiac malformations are detailed in Fig. 1 according to ventricular morphology. Of note, the most common primary cardiac malformation amongst patients with mL V was tricuspid atresia (n = 116, 28.6%), whereas the most common primary cardiac malformation amongst patients with mRV was hypoplastic left heart syndrome (HLHS; n = 95, 23.4%). Forty-five patients had atrial isomerism (11%); 32 with right atrial isomerism and 13 with left atrial isomerism. Sixteen patients were originally diagnosed with abnormal systemic venous drainage, including 13 patients with azygos or hemiazygos continuation of the inferior vena cava (IVC). In these patients, the Fontan procedure was defined at the time at which the hepatic venous blood flow was directed to the pulmonary circulation. Thirteen patients were originally diagnosed with abnormal pulmonary venous drainage, including patients with pulmonary venous obstruction; total or partial anomalous pulmonary venous connection (TAPVC or PAPVC); as well as the patients with right atrial isomerism.

Most patients (n = 389, 95%) had undergone previous surgical palliation. This generally consisted of a systemic-pulmonary arterial shunt (n = 163, 40.1%), a Norwood stage I procedure (n = 108, 26.6%) or a pulmonary artery band (n = 74, 18.2%). Seven patients had repair of TAPVC and 3 patients had creation of an aorto-pulmonary window. A superior CP shunt was created in 284 patients (70.0%) and since 1994, it has been our policy to perform a superior cavopulmonary connection as an interim stage prior to completion of the Fontan procedure.

The Fontan procedure was indicated in patients with progressive cyanosis or increasing dyspnoea on exertion. The median preoperative arterial oxygen saturations in air were 80% (range, 55—95%). Preoperative clinical status had been retrospectively graded using the NYHA classification with 218 (53.7%) patients in NYHA functional class II. However, 115 patients (28.3%) were in a poor functional condition, with 109 patients (26.8%) in NYHA class III and 6 patients (1.5%) in NYHA class IV.

Preoperative cardiovascular function was routinely assessed using echocardiography and elective cardiac catheterisation, as previously described [9]. Preoperative echocardiographic evaluation of ventricular function was available in 369 patients (90.9%). Amongst these patients, the majority (n = 354, 87.2%) had good ventricular function. However, 15 patients (4%) had moderately impaired or poor ventricular function. Preoperative echocardiographic evaluation of valvar dysfunction was available in 375 patients (92.4%), which revealed that most (n = 351, 86.5%) had mild or no atrioventricular valve (AVV) regurgitation. However, 24 patients (5.9%) had clinically important AVV regurgitation (moderate or severe).
Preoperative cardiac catheterisation demonstrated 106 patients (26.1%) had clinically important abnormalities of the central pulmonary arteries, including relatively small pulmonary arteries, isolated stenoses and distorted pulmonary arteries. Cardiac catheterisation also identified six cases (1.5%) in which the superior cavopulmonary shunt was stenosed at the anastomosis, limiting flow in the superior cavopulmonary shunt. Under general anaesthesia, the median pulmonary artery (PA) pressure was 12 mmHg (range, 2–30 mmHg); the median atrial pressure was 8 mmHg (2–18 mmHg); and the median transpulmonary gradient was 5 mmHg (0–24 mmHg). One hundred and sixteen patients (28.6%) had elevated PA pressures (≥15 mmHg) and eight patients (1.5%) had elevated atrial pressures (≥12 mmHg). However, pulmonary vascular resistance was not calculated.

The Fontan procedure was performed at a median age of 4.7 years (range, 9 months–52 years) with 123 patients being <4 years and 23 patients >16 years. Median operative weight was 16.8 kg (3.8–72.5 kg). During the study period, the Fontan procedure was performed using three distinct techniques (Fig. 2), which evolved over time. Between 1988 and 1995, the Fontan procedure was generally performed using an atrio-pulmonary connection, in which the roof of the right atrium was anastomosed to the underside of the pulmonary artery. In most cases, this anastomosis incorporated a patch of autologous or bovine pericardium. The APC was valveless. No homograft conduits were inserted between the inferior vena cava (IVC) and the right atrium (RA) or in the RA–PA anastomosis. In 1995, our unit adopted the total cavopulmonary connection (TCPC) technique. This initially involved a lateral atrial tunnel, in which the atrial septum was resected and a Gore-TEX® or bovine pericardial baffle constructed to direct flow from the inferior vena cava (IVC) to the superior end of the atrophic pulmonic anastomosis. However, since 1998, the Fontan procedure has been performed using an extracardiac conduit TCPC. This involved the interposition of a 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. This technique remains our current practice.

A fenestration was intentionally created in the Fontan circuit in 216 patients (53.2%). 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. No strict criteria were applied to the use of fenestration in our own experience. Fenestration was a surgeon-specific choice, and currently, we routinely fenestrate all patients undergoing an extracardiac conduit TCPC in whom it is anatomically feasible.

All Fontan procedures were performed via a median sternotomy using bicaval (and later SVC, IVC, RA cannulation) cardiopulmonary bypass (CPB). The median cardiopulmonary bypass time for the entire series was 70 min (range, 23–253 min). The aorta was cross-clamped during the construction of all APC Fontan and the lateral atrial tunnel TCPC. Intermittent cold crystalloid cardioplegia was used for myocardial protection. The median aortic cross-clamp time of the entire series was 40 min (range, 0–141 min). Two hundred and thirty-three patients required a period of hypothermic circulatory arrest, with a median duration of 25 min (range, 1–92 min). This was used almost exclusively in the early part of the series and is not part of current practice.

The cardiopulmonary bypass strategy used for the construction of the extracardiac conduit TCPC has evolved during the time of this study. Early in the series, the IVC conduit anastomosis was performed using periods of deep hypothermic circulatory arrest (DHCA). However, since 1999, the extracardiac conduit TCPC was generally performed on the beating heart. The aorta was cross-clamped in those cases in which mainly concomitant intracardiac procedures were performed (n = 126). The median aortic cross-clamp time in these cases was 48.5 min (range, 2–111 min), during which time intermittent cold crystalloid cardioplegia was used for myocardial protection. In 137 patients (33.7%), concomitant surgical procedures were performed, as summarised in Table 1.

2.1. Data analysis

This study involved the retrospective review of all hospital records, operation notes and electrocardiographic, echocardiographic and cardiac catheter data. Particular attention was paid to the postoperative complications of the Fontan circulation, surgical reoperations and cardiac catheter interventions recorded. Current clinical and functional performance was identified based on contemporary clinic notes or direct contact with the current cardiologist responsible for the patient's care. Complete late follow-up was available for 358 patients (92%) with 32 patients (8%) lost to follow-up. with mean follow-up of 6.1 years (±5.7 years).

Table 1

<table>
<thead>
<tr>
<th>Additional surgery at the time of Fontan operation</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery reconstruction/patching</td>
<td>79 (57.7)</td>
</tr>
<tr>
<td>MPA division</td>
<td>18 (13.1)</td>
</tr>
<tr>
<td>AV valve repair</td>
<td>9 (6.6)</td>
</tr>
<tr>
<td>Atrial septectomy</td>
<td>10 (7.3)</td>
</tr>
<tr>
<td>Insert PPM</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td>Correction of TAPVD</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Creation of DKS</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Enlargement of VSD</td>
<td>5 (3.6)</td>
</tr>
<tr>
<td>Resection of subaortic stenosis</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td>Repair of VA valve</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>LIMA to LAD graft</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (1.5)</td>
</tr>
</tbody>
</table>
Data have been examined by analysis of variance with SPSS for Windows (version 12, SPSS Inc., Chicago, IL, USA). Continuous variables are expressed as mean (SD) or median (range) and comparative univariable analyses have been made using the \( t \)-test, Mann–Whitney \( U \)-test or Wilcoxon signed rank test. Binomial or ordinal data are expressed as percentage and comparative univariable analyses have been made using the \( \chi^2 \) test, two-sided Fisher exact test or binomial logistic regression. A probability value, \( p < 0.05 \), was taken to represent a statistically significant difference between groups.

Death, takedown of the Fontan circulation, heart transplantation and deterioration in functional class to NYHA III or IV were used as the primary end-points. In addition, the actuarial freedom from surgical reoperation and cardiac catheter intervention was used as a secondary outcome measure. Early (in-patient or 30-day) and actuarial outcome following the modified Fontan procedure were evaluated with a series of morphologic, preoperative and operative variables using univariable and multivariable analyses. Pulmonary artery pressure was analysed as both a continuous variable and as a categorical variable (\( > \) or \( < 15 \) mmHg) according to Choussat and Fontan's original hypothesis. Univariable analyses of early outcome measures were made using the \( \chi^2 \) 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 analyses have been expressed as odds ratios (OR; 95% CI) for variables with a probability value, \( p < 0.05 \). Actuarial survival was estimated using the Kaplan–Meier product limit method. These results have been expressed as probability estimate (SEM). Univariable analyses of actuarial outcome measures have been made using the log-rank test.

Two separate risk models were developed to predict the early outcome following the modified Fontan procedure. A **preoperative risk model** evaluated the influence of the preoperative variables on early outcome. An **operative risk model** assessed the additional influence of intraoperative events on early outcome. Model 2 used all available preoperative and operative data. Model 1 and Model 2 were used to predict the individual patient risk, based on a logistic transformation of the coefficients (Eq. (1)).

\[
p = (1 + e^{-z})^{-1}
\]

where \( z = B_0 + X_1 B_1 + \ldots + X_n B_n \); \( B_0 \) is the constant, \( X_1-X_n \), are independent predictors and \( B_1-B_n \) represent logistic coefficients for the respective parameters.

The performance of each risk model was evaluated using goodness-of-fit analyses. Calibration was assessed using the Hosmer–Lemeshow \((H–L)\)-test [10] and discrimination was assessed using the receiver operating characteristic (ROC) curve [11].

3. Results

3.1. Early outcome

There were 18 early deaths (4.4%): 15 from low cardiac output states in which 8 were associated with high pulmonary artery pressures postoperatively. Five of these patients had takedown of their Fontan circulation and creation of a central shunt. All eight died from a persisting low cardiac output state or multiple organ failure caused by this low output state.

Seven were with normal pulmonary artery pressures. Three of these patients had poor ventricular function preoperatively. One had intractable supraventricular tachyarrhythmia and died due to multiorgan failure. One had low cardiac output secondary to postoperative bleeding and one patient suffered a left main coronary artery injury whilst removing a pulmonary artery band. One patient died from low cardiac output and ventricular failure as a result of a technical stenosis involving the APC connection, despite later operative correction and Fontan takedown.

The remaining three deaths were related to ischaemic cerebral injuries resulting in brain death. The first was due to prolonged resuscitation following a postoperative cardiac arrest. The second after hypovolaemic arrest following catheter related pulmonary artery rupture during attempted early anastamotic dilation. The third was unexplained, occurring after an apparently uneventful operation and intensive care course.

Early takedown of the Fontan connection was performed in nine patients. Seven patients had their Fontan circulation converted to a central shunt, two converted back to a Bidirectional Glenn shunt. In eight cases, the takedown was for low cardiac output secondary to high pulmonary artery pressures and the last takedown as mentioned above was following technical stenosis of an APC Fontan. There were five early deaths (56%) after takedown, all from low cardiac output state.

The median length of intercostal drainage postoperatively was 8 days (1–83 days) and the median hospital stay was 13 days (5–104 days). Prolonged pleural drainage, defined as drainage longer than 14 days duration, affected 97 patients (23.9%). There was no statistical difference in either duration of intercostal drainage or of hospital stay between the fenestrated and non-fenestrated Fontan patients.

Univariable and multivariable analysis of early and late Fontan take down or death is shown in Table 2. Multivariable analysis by logistic regression identified impaired preoperative ventricular function and elevated preoperative pulmonary artery pressure as risk factors for early death or Fontan takedown. Atrial isomerism, Ventricular morphology and presence of fenestration were not significant factors of takedown or death.

Early postoperative echocardiogram was recorded in 375 patients (92.4%) and showed normal or mildly reduced ventricular function in 340 patients (91%) and poor or moderately reduced in 35 patients (9%). Twenty-nine (7.7%) patients from this group died: 10 early and 19 late. Early AV valve regurgitation was not present or mild in 96% and moderate or severe in 4%. Two further patients successfully underwent Fontan takedown for failure of the Fontan circulation. The early survival with a Fontan circulation was 95.6\% (\( n = 388 \)).

Low cardiac output state occurred in 42 patients (10.3%). Cardiac arrhythmias occurred in 48 patients (11.7%), including supraventricular or nodal tachycardias (39 patients), new heart block (5 patients) and bradycardia (4 patients). Renal impairment requiring dialysis occurred in...
Table 2
Risk factor analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Risk factor analysis for early death, Fontan takedown, or transplantation. Preoperative and predictable operative</th>
<th>Risk factor analysis for early death, Fontan takedown, or transplantation. Preoperative and predictable operative</th>
<th>Risk factor analysis for late death, Fontan takedown, transplantation or NYHA III/IV i.e. ‘Good Fontan’. Preoperative and predictable operative</th>
<th>Risk factor analysis for late death, Fontan takedown, transplantation or NYHA III/IV i.e. ‘Good Fontan’. Preoperative and all operative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariable</td>
<td>Multivariable</td>
<td>Univariable</td>
<td>Multivariable</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>p-value</td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td>Univariable</td>
<td>p-value</td>
<td>p-value</td>
<td>p-value</td>
<td>p-value</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>p-value</td>
<td>p-value</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Staged</td>
<td>0.01 ns</td>
<td>0.01 ns</td>
<td>0.0006 ns</td>
<td>0.0006 ns</td>
</tr>
<tr>
<td>Year of operation</td>
<td>0.03 ns</td>
<td>0.03 ns</td>
<td>0.02 (0.76—0.94)</td>
<td>0.02 (0.89—0.98)</td>
</tr>
<tr>
<td>Preoperative NYHA</td>
<td>0.002 ns</td>
<td>0.002 ns</td>
<td>&lt;0.0001 ns</td>
<td>&lt;0.0001 ns</td>
</tr>
<tr>
<td>Preoperative ventricular</td>
<td>0.03 5.43 (1.17—32.50)</td>
<td>0.046 7.37 (1.32—41.09)</td>
<td>0.001 7.17 (2.30—22.31)</td>
<td>&lt;0.0001 5.54 (1.84—16.64)</td>
</tr>
<tr>
<td>Age at operation</td>
<td>0.02 ns</td>
<td>0.02 ns</td>
<td>ns ns</td>
<td>&lt;0.0001 3.50 (1.15—10.62)</td>
</tr>
<tr>
<td>Weight at operation</td>
<td>0.003 ns</td>
<td>0.003 ns</td>
<td>ns ns</td>
<td>ns ns</td>
</tr>
<tr>
<td>Preop TPG</td>
<td>0.006 ns</td>
<td>0.006 ns</td>
<td>&lt;0.0001 ns</td>
<td>&lt;0.0001 ns</td>
</tr>
<tr>
<td>Preop PAP</td>
<td>&lt;0.001 1.35 (1.17—1.56)</td>
<td>&lt;0.001 1.35 (1.17—1.55)</td>
<td>&lt;0.0001 1.14 (1.04—1.26)</td>
<td>&lt;0.0001 1.13 (1.02—1.24)</td>
</tr>
<tr>
<td>CPB</td>
<td>0.002 1.03 (1.01—1.05)</td>
<td>0.004 ns</td>
<td>ns ns</td>
<td>&lt;0.0001 1.02 (1.01—1.04)</td>
</tr>
<tr>
<td>AoXC</td>
<td>0.004 ns</td>
<td>ns ns</td>
<td>ns ns</td>
<td>&lt;0.0001 ns</td>
</tr>
<tr>
<td>DHCA</td>
<td>0.05 ns</td>
<td>ns ns</td>
<td>ns ns</td>
<td>&lt;0.0001 1.03 (1.01—1.05)</td>
</tr>
</tbody>
</table>
| Preop atrial pressures, preop SaO2, interval CC—III, PA stenosis, gender, anatomical group, isomerism, surgeon, ventricular morphology, previous procedure, previous Norwood, PA problem—size, stenosis, distortion, fenestration PA surgery, AVV surgery, Fontan technique, Preoperative AVVR and PA size were all analysed but were not significant. ns: non-significant values.
27 patients (6.6%) with 3 requiring haemodialysis and 24, peritoneal dialysis.

Complete data for each of the variables identified by the multivariable analyses were available for 308 patients (76%) with an early mortality of 3.9% (n = 12). For the remaining 98 patients, either preoperative ventricular function (n = 39) or pulmonary artery pressure (n = 85) data were missing. The early mortality risk models were constructed using complete data only. The mean predicted mortality derived using Model 1 and Model 2 was 4.2% and 4.1%, respectively. Both models predicted a marked variation in the risk-adjusted probability of early mortality, ranging 0.04—81% (median 1.7%) in Model 1 and 0.1—79% (median 1.4%) in Model 2.

Goodness-of-fit analyses demonstrated that both models were well calibrated. The SMR was 0.94 and 0.98 and the H—L-test statistic was 4.29 (p = 0.83) and 10.31 (p = 0.24), respectively. The calibration remained reasonably consistent across all deciles. Both models had good discrimination characteristics with an area under the ROC curve (95% CI) of 0.85 (0.77—0.92) for Model 1 and 0.89 (0.82—0.96) for Model 2.

3.2. Late outcome

There were 21 late deaths. Twelve patients died of ventricular failure, one of which died on the operating table after receiving a cardiac transplant. Three patients died from respiratory infections. One patient, thought to be arrhythmic had a sudden death at home, and one patient died following aVF arrest. One patient died from each of the following: gastrointestinal haemorrhage, traumatic head injury, following a motor vehicle accident, and for one patient the cause of death was unknown.

There was one late Fontan takedown. This patient had DORV, sub-pulmonary stenosis, VSD and straddling tricuspid valve, and had previously had an APC Fontan. An attempted biventricular repair with Rastelli procedure and VSD closure was performed; however, the patient was unable to be weaned from cardiopulmonary bypass and died on the operating table.

Three patients with an APC Fontan had successful conversion to TCPC connections due to morbidity associated with right atrial dilation.

Including early deaths, the Kaplan—Meier actuarial survival was 90 (+2.2)% at 5 years, 86 (+2.1)% at 10 years and 82 (+3)% at 15 years (Fig. 3).

Three patients required cardiac transplantation all for ventricular failure.

Univariable and multivariable analysis of late Fontan takedown, transplant or death is shown in Table 2. Multivariable analysis identified preoperative impairment of ventricular function and high preoperative pulmonary artery pressure (>15 mmHg) as the only risk factors on multivariable analysis.

At latest follow-up, 316 patients were in NYHA class I or II, with 15 patients in class III and 2 in class IV. Thirty-two patients had documented evidence of supraventricular tachyarrhythmias. Of the 324 surviving patients, 229 (70%) were on angiotensin converting enzyme inhibitors (ACE inhibitors). Ninety-three patients (29%) were on diuretic therapy. Five patients developed clinical evidence of protein losing enteropathy. Two died while the other three are still being treated.

Latest echocardiographic data were available for 298 patients and revealed that 281 patients had (94%) normal or...
and grow older there is a need to understand what the future holds for these patients and document the morbidity and survival of the condition. There have been three large series providing long-term outcome data on the Fontan operation [2—4], but these early studies have under-represented conditions such as hypoplastic left heart syndrome (HLHS) and heterotaxy patients and do not reflect the influence of important changes in surgical practice and peri-operative management that has occurred recently. This series provides a recent large European experience representing the operative techniques and morphological case mix seen in current practice.

Since its first description in 1971 [1], the Fontan procedure has undergone significant evolution in operative techniques and peri-operative management and has been associated with improvements in early mortality from 20 to 40% in the late 1970s to below 6.6% in the current literature [12]. In earlier studies mid- and long-term survival revealed the potentially finite life span of the Fontan circulation, with the overall 1-, 5- and 10-year survival being 77%, 70% and 60%, respectively, in the Mayo clinic study. Follow-up also often suggested poor functional capacity. At 5 years only 26% of patients were free of significant cardiac symptoms [3]. In an attempt to improve long-term survival and reduce late complications such as atrial arrhythmias and thrombus formation, most centres have adopted the lateral tunnel Fontan and extracardiac Fontan procedure. Excellent short- and intermediate-term results have been reported for both techniques [5—7].

In keeping with most reported studies in the more contemporary era, we have demonstrated improving late outcome with a 5-year survival of 90% and a 10-year survival of 85%. Despite concerns from earlier studies, we have demonstrated prolonged survival with the Fontan circulation, with 15-year survival of 82% in this series. When looking at functional state of these patients, the majority of these patients at a median follow-up of 6 years are in functional class I and II NYHA status (94%) with 55% attending some form of schooling from primary all the way to university. Twenty-nine (27%) of the adult patients are working in normal jobs and two women have had successful pregnancies.

Improvements in surgical technique are likely to have played a significant role, and medical therapies such as angiotensin converting enzyme inhibitors (ACE inhibitors) and the long-term benefits of anticoagulation may also have been important in the improved long-term outcome for these patients. However, no randomised trials exist to evaluate the role of many of these developments. Our institutional policy is to maintain all patients on warfarin indefinitely following Fontan and ACE inhibitors are used in patients with evidence of impaired ventricular function or AV valve regurgitation.

As with other studies, time is a factor for Fontan failure with an inherent attrition rate and complications such as atrial arrhythmias and reduction in functional status. Despite encouraging outcomes at 15 years in this study, the hazard ratio of Fontan failure demonstrated a progressive risk with time. Historically, it has been reported that patients with APCs tend to have poorer late outcomes, but they also tend to be the earlier Fontan patients and it can be difficult to determine whether poor outcome is related to the technique or to the actuarial survival of the Fontan circuit. On the basis of the censored data in this series, it remains to be seen if a

3.3. Reintervention

Postoperatively, 232 catheter studies were performed in 180 patients. One hundred and eleven catheter interventions were performed (Table 3). The majority of these interventions were for device closure of fenestrations (38%) and ballooning (18%) and stenting (12%) of the pulmonary arteries or Fontan pathways.

Surgical reintervention occurred in 57 patients (Table 4). Three patients with an APC Fontan had conversion to TCPC connections due to morbidity complications associated with right atrial dilation.

The freedom from surgical or catheter intervention at 1, 5, 10 and 15 years was 90 ± 2%, 82 ± 4%, 75.7 ± 4% and 74.4 ± 8%, respectively (Fig. 4).

Multivariable analysis revealed that preoperative high pulmonary artery pressure, small pulmonary arteries, right atrial isomerism and poor preoperative ventricular function were risk factors for post-Fontan surgical or catheter reintervention. Fontan fenestration and low postoperative saturations were also independent risk factors for reintervention but only for specific reintervention of fenestration closure.

4. Discussion

As the population of Fontan patients continues to expand and grow older there is a need to understand what the future
different pattern of late survival and functional outcome will emerge in patients with lateral tunnel and extracardiac conduit Fontan.

There is much debate regarding the pros and cons of Fontan circuit fenestration. Some studies have found that fenestration significantly reduces the duration of postoperative effusions, length of time in hospital and in some centres reduced early mortality [13,14]. The disadvantages of fenestration included the ongoing risk of paradoxical embolus, persistent cyanosis and lastly the increased incidence of late catheter intervention for devise closure of the fenestration. Some centres have advocated selective fenestration for high-risk patients with good results in the early postoperative period [15]. However, a number of recent studies have shown no significant difference in early or late mortality, duration of pleural drainage or length of hospital stay between fenestrated and non-fenestrated patients [16]. In our study, fenestration was a surgeon-specific choice. In recent years, we have routinely fenestrated all patients. However, we found no difference between these two groups, in early or late mortality, duration of pleural drainage or length of hospital stay. There is a significantly higher incidence of catheter reintervention of which the majority of these were for devise closure of the fenestration. These results and those of others may question the validity of routine fenestration, and the benefits of fenestration in high-risk Fontan candidates remain uncertain.

Catheter reintervention post-Fontan was common in this series. Even when excluding reintervention to close fenestration there were 18% of patients requiring catheter intervention. The majority of work was to balloon or stent discrete stenosis or hypoplasia of the pulmonary arteries. This emphasises the need for continued follow-up of the patient, particularly during the years of somatic growth when distortion or failed development of the central PAs can occur [17].

On multivariate analysis the additional factors of right atrial isomerism and preoperative small pulmonary arteries were significant for reintervention. In the light of this large dataset, it is timely to revisit Choussat et al., the 'Ten Commandments' and apply them to the outcome of this study. The most noteworthy finding is that only two criteria have emerged as carrying significant impact on both early and late outcome: preoperative ventricular function and preoperative pulmonary artery pressure. One striking finding is that ventricular morphology (left vs right) does not appear to be a significant factor for either early or late outcome.

The morphological right ventricle has certain features, such as the position of its papillary muscles and the crescent shape of its cavity that potentially impairs its ability to adapt to pressure and volume overload [18]. There are also valid concerns regarding the ability of morphological right ventricle to sustain the systemic circulation and function long-term as the systemic ventricle as is evident in the poor long-term outcome in patients with classical repair of congenitally corrected transposition [19] and patients who have had atrial switches for simple transposition [20]. The results in this series provide some encouraging evidence that the outlook for the morphologic right ventricle may not be as poor as previously thought.

The principal message is that the preoperative ventricular function is more relevant to outcome (both early and late) and that ventricular dysfunction is seen equally in ventricles of both left and right morphology. With time, we may find that ventricular morphology becomes significant. Some of these findings may be the beneficial results of early pursuit of cavopulmonary connection and the use of ACE inhibitors to reduce volume and pressure load on the circulation.

High preoperative PA pressure was the only other significant factor for poor outcome. This was recognised by Choussat and Fontan, and the stage approach to TCPC and early protection of the pulmonary vessel bed have been adopted as a fundamental principle of managing the functionally single ventricle circulation. Pulmonary artery pressures as a continuous variable was significant on univariate analysis but only remained significant on multivariate analysis when considered as a categorical variable of > or < 15 mmHg. This supports Choussat and Fontan's original hypothesis, although it is not clear why this particular value is so central. Nevertheless, the poor progress associated with high pulmonary pressures should not be underestimated and any tendency to push the limits for Fontan suitability and to take on higher risk cases should be tempered by this consistent finding of the impact of high pulmonary artery pressures. The role of pulmonary vasodilator therapy in remodelling pulmonary vascular resistance is an area for targeted research to establish whether high-risk patients can become suitable for conversion to Fontan circulation.

Our current protocol in patients who fall into these high-risk groups is firstly to review all the data in detail. Full consideration is given as to whether there are any surgically (or interventionaly) correctable lesions such as AV valve regurgitation amenable to repair or isolated stenoses or hypoplasia within the central pulmonary arteries. Ventricular function, if impaired, may be optimised by altering medical management (vasodilators, diuretic therapy and trial of oral enoximone if appropriate). Evidence of raised pulmonary vascular resistance is treated with a course of pulmonary vasodilator therapy (Sildenafil or Bosentan). The patients are then reassessed for suitability for Fontan completion.

The data from this series suggest that many of the original commandments may not be strict requirements for a successful outcome. Some studies have reported that TCPC can be performed on many patients younger than 4 years with successful outcomes [21–23]. Sinus rhythm can be maintained pharmacologically or with ativoventricular pacing. Venous drainage can be surgically corrected and large atria may undergo reduction atrioplasty, discrete stenoses in otherwise normal central PAs can now be managed by stenting or surgical enlargement and would not be considered a contra-indication to TCPC if pressures were otherwise normal.

Pulmonary vascular resistance data were not analysed fully because it is an extremely complicated variable to measure in routine practice and is actually derived by measuring the flow and made more difficult to calculate in context of forward flow, shunts and collaterals.

This study has focused on the early and late mortality after the Fontan procedure. As we come to recognise the morbidity associated with late arrhythmias and Protein
Losing Enteropathy, it may be valuable to apply similar analyses to the morbidity variables in future studies.

5. Conclusion

In this series, the Fontan procedure was associated with low early mortality, excellent long-term survival and good long-term functional outcome. The only two significant risk factors for both early and late Fontan procedure were preoperative ventricular function and preoperative pulmonary artery pressures >15 mmHg. They can, therefore, be viewed as relative contraindications for Fontan completion. However, with the construction of the model, one can calculate the risk and make an informed decision.

Fenestration made no difference to hospital stay, pleural drainage or long-term survival but did influence reintervention rates. Surgical technique had no influence on outcome. Fontan failure was unaffected by ventricular morphology or age at Fontan, but right atrial isomerism and low postoperative saturations were risks for reintervention.

The two preoperative variables can reliably predict the early outcome following the Fontan procedure in the current era. The outcome predicted using the preoperative model varied markedly between individual patients. For example, the expected early mortality for patients with good ventricular function and pulmonary artery pressures of 7 mmHg is 0.4%. In contrast, the expected early mortality for a patient with impaired ventricular function and pulmonary artery pressures of 15 mmHg is 24%. This is clinically important information, which could help counsel parents about the likely risk of death. Nevertheless, the patient’s preoperative risk is modified by intraoperative events [24]. The inclusion of the duration of cardiopulmonary bypass in the operative risk model improved the ability of the risk model to discriminate between patients who died and survived, though this is not part of the original 10 commandments.

The evidence would suggest that only two of the original 10 commandments carry significant weight for both early and late outcome over the Fontan procedure and that they are preoperative ventricular function and preoperative pulmonary artery pressures <15 mmHg.

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References

Appendix A. Conference discussion

Dr Y. d’Udekem (Victoria, Australia): I think the first point is that you are demonstrating better results than in the past, mainly probably because you had an improvement in the indications for surgery and also obviously because you had excellent surgeons. The point that interested me as a congenital heart surgeon is the one you briefly mentioned at the end of your conclusion. For Fontan circulation my question is, will they all finally fail or is there a group of Fontan patients who will eventually have long-lasting results? So from what you have seen in your series of patients now, what is your feeling? Do you think that there is a significant proportion of patients that will have long-lasting results for 20, 30 years or more?

Mr McGuirk: Thank you very much for your question, which highlights one of the unresolved areas of ongoing interest with regards to the management of these patients. I think the answer is unknown. The instantaneous hazard curve that corresponds to the observed survival curve for the patients in this study rises progressively with time. However, at no stage have we reached a point where zero percent survival is observed or where we might even estimate when there may be zero percent survival in this group. Nevertheless, based on the long-term follow-up observed in this study of almost 15 years, we can start to suggest that there may well be a substantial group who survive for more than 20 years. What proportion that will be I think remains to be seen.

Dr D. Metras (Marseille, France): I want to congratulate you for a very nice presentation and experience that brings us important information, in particular, that the morphology of the ventricle does not affect long-term survival, which is I think something rather new. I have a question to you concerning the performance of the fenestration. You showed that the fenestration or the nonfenestration does not affect early or late outcome. Has this modified your policy of performing or not performing the fenestration and do you have specific indications not to do it or to do it?

Mr McGuirk: Our practice has not, to date, been influenced by the results of this study. Our current practice involves, where surgically possible, the use of a 20 mm Gore-Tex interposition tube graft as an extracardiac Fontan procedure. This is fenestrated with a 4–6 mm fenestration. In patients in whom this is not possible, the circuit is left unfenestrated. Our preferred practice is to fenestrate all patients irrespective of their preoperative condition.

Dr Metras: But why do you do that, if that doesn’t change?

Mr McGuirk: That is the practice that we’ve evolved over time and that is what we feel comfortable with.

Dr F. Fontan (Bordeaux, France): I have just a little question and I would like to give a reply to the previous question. The reply to the previous question is in a study that we performed with Dr Blackstone and Dr Kirklin, a cooperative study between the University of Bordeaux and the University of Alabama in Birmingham in 1988, it was possible to demonstrate that in the long term it remains a hazard for death. This is a palliative operation. I have a question. Why did you start your study just in 1988?

Mr McGuirk: The study was started in 1988 after the appointment of Mr Brawn, the corresponding author for this paper. Following his appointment, the Fontan procedure was introduced at Birmingham Children’s Hospital. Up until that time, children had been palliated with a superior cavopulmonary shunt and when they subsequently developed cyanosis or reduced exercise capacity, this was supplemented with additional shunts or the formation of an upper limb arteriovenous fistula to augment the pulmonary blood flow. They had had, however, not used the Fontan procedure at that time.

Dr Fontan: So that means that your study represents the overall experience of your center?

Mr McGuirk: Absolutely.