The Fontan Procedure in Greece: Early Surgical Results and Excellent Mid-Term Outcome

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Introduction: The Fontan operation (modified from its original version) affords excellent palliation for many patients with various forms of anatomic or functional single ventricle. The purpose of this study was to evaluate the outcome of our experience with the Fontan procedure in Greece.

Methods: Fifty-eight consecutive patients with single ventricle physiology had a modified Fontan operation between 1997 and 2009. Their records were reviewed retrospectively. Follow up, which included clinical evaluation and echocardiographic functional assessment, was complete.

Results: Median age at operation was 5.7 years (range 3 years to 29.4 years); 46.5% had multistage palliation (stage I and II); 79% had prior bidirectional cavopulmonary shunt (stage II) and 8.6% single stage Fontan. Fifty-four patients had an extracardiac conduit total cavopulmonary connection (EC-TCPC) and 4 an intra-atrial lateral tunnel (LT-TCPC). Fenestration was performed in 26 (44.8%) patients. Operative mortality was 0%. One patient required a short period of extracorporeal membrane oxygenator support. The most frequent complication was prolonged pleural effusion. Median duration of pleural effusion was 17 days (range 6-47 days). Median duration of follow up was 5.44 years (range 0.36 to 11.5 years). There were 2 late deaths (overall mortality 3.4%). One patient died from progressive deterioration of ventricular function within 2 years of operation and the other from fulminant endocarditis. Ten subjects have undergone device closure of a persistent fenestration. All 56 surviving patients are in excellent clinical condition (NYHA class I or II).

Conclusions: We have performed the Fontan procedure over a period of 13 years in Greece with excellent mid- and long-term results. Longer follow up will be necessary to assess the possible incidence of late severe complications, some of which may necessitate heart transplantation.

The surgical management of single-ventricle physiology has been evolving for decades since the original Fontan operation was reported. The current most common modifications are the intra-atrial lateral tunnel total cavopulmonary connection (LT-TCPC) and the extracardiac conduit total cavopulmonary connection (EC-TCPC). The concept of staging the Fontan operation through an intermediate procedure for partially unloading the single ventricle by means of a bidirectional cavopulmonary anastomosis (BCPA) connection has had a positive impact on the results of Fontan completion. The extracardiac inferior vena cava to pulmonary artery connection, as proposed by Marceletti et al in 1990, has theoretical advantages over LT-TCPC, including minimal atrial surgery and cardiac ischemic time, avoidance of pressure-related atrial stretch, low rates of arrhythmia, and optimal laminar flow in the systemic venous pathway, which together could result in better preservation of ventricular function. The staged approach to achieving the Fontan circulation and the EC-TCPC technique have
been at the core of our management strategy for all patients with single-ventricle physiology, except possibly in adults with single ventricle physiology who present with a well balanced circulation, who may be considered for primary Fontan operation. The purpose of this study was to evaluate the overall outcome of all our single-ventricle patients who underwent the Fontan procedure in Greece, focusing on medium to long-term functional outcome.

Methods

**Patient characteristics**

The clinical data obtained from the medical records of 58 patients who all underwent a Fontan operation performed by the same surgeon between 1997 and 2009 (1997-2007 at the Onassis Cardiac Center and 2007-2009 at Mitera Children’s Hospital) were reviewed. All patients underwent a complete follow-up evaluation at Mitera Children’s Hospital. Operative and perioperative variables, and follow-up clinical data, including echocardiographic assessment in all patients, were analyzed.

The final anatomic diagnosis was based on two-dimensional echocardiography, cardioangiography, and operative findings. A preoperative detailed echocardiographic evaluation and cardiac catheterization were performed in all patients to assess the existence of adequate anatomic and physiologic parameters permitting Fontan completion. These included low pulmonary vascular resistance, satisfactory ventricular function, good or correctible cardiac valve function, and unobstructed or reconstructible, adequate sized pulmonary arteries.

Operative mortality was defined as death occurring within 30 days of the operation or within the same hospitalization. Overall mortality was defined as death occurring from the time of surgery to the time of most recent follow up. Duration of pleural drainage was defined as the period from the date of surgery until final removal of pleural catheters. Pleural effusions were considered prolonged if they persisted for a period greater than 14 days after surgery.

**Surgical technique**

All Fontan procedures were performed through a median sternotomy with cardiopulmonary bypass and mild hypothermia at 34-35°C, unless either the lateral tunnel technique was used or other concomitant procedures were required, in which cases greater degrees of hypothermia (26-28°C) and aortic cross-clamping were employed. In 54 patients (EC-TCPC), an expanded polytetrafluoroethylene extracardiac tube conduit (Gore-Tex® Vascular Graft, W. L. Gore & Associates, Inc., Flagstaff AZ, USA) was used (Figure 1), whereas the remaining 4 patients received a lateral tunnel intracardiac TCPC (LT-TCPC) utilizing a Gore-Tex® baffle to partition the atrium. The mean diameter of the extracardiac conduits used was 19.5 ± 1.2 mm. Graft size was 18 mm in 17 patients, 20 mm in 33 patients, and 22 mm in 4 patients.

A fenestration was performed electively prior to weaning from cardiopulmonary bypass in 26 (44.8%) patients (all 4 of the LT-TCPC and 22 patients with EC-TCPC; Figure 2). The criteria for constructing a fenestration included: 1) Pre- or postoperative pul-

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**Figure 1. A.** Operative photograph demonstrating completed extracardiac conduit. B. Schematic diagram of extracardiac Fontan operation. Patient has situs inversus. AscAo – ascending aorta; ECC – extracardiac conduit; IVC – inferior vena cava; LPA – left pulmonary artery; LSVC – left superior vena cava.
monary arterial pressure greater than 18 mmHg, or a transpulmonary gradient greater than 10 mmHg, or both; 2) diagnosis of hypoplastic left heart syndrome; and 3) when preoperative variables, such as small pulmonary arteries or the need for concomitant procedures, were judged to potentially increase the risk. In 2 EC-TCPC patients, fenestration was added after initial weaning from cardiopulmonary bypass, since pulmonary arterial pressure was judged to be unacceptably high ($\geq 18$ mmHg).

Postoperative management included early extubation, careful fluid management, and anticoagulation. Chest tubes were removed when daily drainage was less than 2 mL/kg. The follow up included physical examination, echocardiographic evaluation, and functional assessment.

**Statistical analysis**

Statistical analyses were performed using SPSS version 17.0 software (SPSS Inc., Chicago IL, USA). All results were expressed as mean ± standard deviation and range, unless otherwise specified. The impact of perioperative variables on duration of pleural drainage was investigated using one-way analysis of variance (ANOVA).

**Results**

Of the 58 patients who underwent the Fontan operation, 33 (56.9%) were male and 25 (43.1%) were female. The median age at operation was 5.7 years (range 3 years to 29.4 years; Figure 3).

Primary diagnoses are listed in Table 1. Diagnostic categories were grouped according to ventricular morphology, relationship of the great arteries or the presence of heterotaxy (Table 2).

The systemic atroventricular valve was a tricuspid valve in 36 patients (62%), a mitral valve in 17 patients (29.3%), and a common atrioventricular valve in 5 (8.6%).

Among the 58 patients, 34 patients (58.6%) had received at least one operation before the bidirectional cavopulmonary shunt (BCPS) or the Fontan operation. The initial (stage 1) palliations were Blalock-Taussig shunt in 14 (24%), Waterston shunt in 3 (5.2%), pul-

![Figure 2. Use of fenestration. EC-TCPC – extracardiac conduit total cavopulmonary connection; LT-TCPC intra-atrial lateral tunnel.](image1)

![Figure 3. Age distribution (years) at modified Fontan operation. Two-year age intervals are depicted.](image2)

| Table 1. Anatomic diagnoses of 58 patients undergoing a modified Fontan operation. |
|-----------------------------------------------|------------------|
| Primary diagnosis                             | No. of patients  |
| Tricuspid atresia                             | 17               |
| DORV with RV hypoplasia                       | 11               |
| Congenitally corrected TGA                    | 10               |
| DILV                                          | 8                |
| CAVSD, unbalanced                             | 5                |
| Mitral atresia                                | 2                |
| Criss-cross heart                              | 2                |
| Pulmonary atresia with IVS                    | 2                |
| HLHS                                          | 1                |

CAVSD – complete atrioventricular septal defect; DILV – double-inlet left ventricle; DORV – double-outlet right ventricle; HLHS – hypoplastic left heart syndrome; IVS – intact ventricular septum; TGA – Transposition of the great arteries.

| Table 2. Diagnostic categories                  |
|-----------------------------------------------|------------------|
| Diagnosis                                     | No. (%)          |
| Single left ventricle with normally related    |                  |
| great arteries                                | 23 (39.7%)       |
| Single left ventricle with transposition of    |                  |
| the great arteries                            | 12 (20.7%)       |
| Single right ventricle                        | 13 (22.4%)       |
| Heterotaxy syndrome                           | 10 (17.2%)       |
monary banding in 16 (27.5%), and Norwood stage I in 1 (1.7%).

Forty six patients (79%) underwent a BCPS (stage II procedure; of these, 19 patients had primary BCPS without initial stage I procedure), and 5 (8.6%) had a one-stage Fontan operation (Figure 4).

**Surgical procedure**

The Fontan connection was created using an extracardiac conduit in all except 4 cases. Concomitant surgical procedures included aortic valve replacement in one patient, atrial septectomy in one patient, main pulmonary artery reconstruction/enlargement in 3 patients, and transventricular excision of anomalous obstructive subaortic muscle bundles (enlargement of the bulboventricular foramen) in one patient.

Mean duration of cardiopulmonary bypass was 165.8 ± 69 minutes (range 78-388 minutes). Cardioplegic arrest was used in 8 patients, with a mean duration of cross-clamp time 150.7 ± 84.4 minutes (range 69-309 minutes).

**Postoperative course**

There was no in-hospital mortality. One patient with a diagnosis of hypoplastic left ventricle who had EC-TCPC and aortic valve replacement as a concomitant procedure required a 24-hour period of postoperative extracorporeal membrane oxygenator support and subsequently had an uneventful recovery. The mean duration of hospital stay was 21.8 ± 8.1 days (range 8 to 52 days).

Although 3 patients had preexisting stroke with residual deficit (partial right hemiparesis), no patient developed postoperative neurologic dysfunction.

Normal sinus rhythm was documented before discharge in 52 of 58 hospital survivors (89.7%). Discharge electrocardiograms demonstrated new dysrhythmias in 6 patients. Five (EC-TCPC) patients had sinus node dysfunction, which remained asymptomatic and did not require specific treatment. One patient developed late complete heart block and received a permanent pacemaker.

**Effusions**

The mean duration of pleural effusion was 18.4 ± 7.7 days (range 6-47 days). Prolonged effusions (greater than 14 days) were observed in 43 patients (74%); they were managed with drainage and fat-free diet when there was evidence of chylothorax, and chemical (doxycycline) pleurodesis if drainage persisted beyond 3 weeks. The influence of the presence of fenestration, duration of cardiopulmonary bypass, and postoperative transpulmonary gradient on duration of pleural drainage was investigated using one-way ANOVA. No factor associated with increased pleural drainage was identified (Table 3).

The mean arterial oxygen saturation at discharge was 94.9 ± 2.64 (range 87-98%).

**Follow up**

Mean follow-up time was 62.7 ± 4.6 months (range 4

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**Table 3. Impact of fenestration, postoperative transpulmonary gradient, and duration of cardiopulmonary bypass on pleural effusions.**

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
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<th>p</th>
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<td></td>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
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<td>Fenestration (yes/no)</td>
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<td>CPB (time)</td>
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<td>0.017</td>
<td>0.049</td>
<td>0.318</td>
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<tr>
<td>TPG (postoperative)</td>
<td>-0.015</td>
<td>0.471</td>
<td>-0.005</td>
<td>-0.032</td>
</tr>
</tbody>
</table>

CPB – cardiopulmonary bypass; TPG – transposition of the great arteries.
months to 11.5 years) and was complete. Late deaths occurred in two patients. One patient aged 19 years, with a diagnosis of hypoplastic right ventricle and history of intravenous substance abuse, died due to septicemia/endocarditis one year later. The second, aged 3 years, with a diagnosis of mitral atresia, died due to severe progressive ventricular dysfunction 2 years postoperatively and 4 months after undergoing systemic atioventricular valve replacement at another institution.

At last follow up, 9 patients were in New York Heart Association class II, 1 patient was in class III, and the remaining 46 survivors were in class I.

Re-intervention

Ten patients underwent percutaneous transcatheter closure of a fenestration. No patient required re-intervention for extracardiac conduit revision. One patient had a pacemaker implanted.

Medications

According to our protocol recommendation, the majority of patients (82%) were receiving low-dose warfarin with a target international normalized ratio (INR) between 1.5 and 2.0. A minority (18%) of patients were converted to aspirin (5 mg/kg daily), usually because of difficulties with control of warfarin. An angiotensin-converting enzyme inhibitor was prescribed for 79% of our patients. Other medications included β-blockers (6%), diuretics (11%), and digoxin (4%).

Discussion

Since the introduction of the technique for successful palliation of patients with tricuspid atresia by Fontan and Baudet in 1971, modifications of the Fontan procedure and staging with BCPS have extended the indications for this operation, which is now used for the treatment of most forms of single ventricle.4,6

Some of the major changes have included the lateral tunnel,4 the use of fenestration,7 and the extracardiac conduit modification.2 The evolution of the Fontan procedure has been associated with improvements in initial operative survival (<30 days) from 60% to 80% in the late 1970s to as high as 95% in more recent series.8,9 Indeed, for patients with tricuspid atresia operated between 1988 and 1997, the reported operative mortality was only 2%.10

Despite the evolutionary changes in surgical techniques that have improved early survival after this operation, late deterioration in functional status has been observed with a longer duration of follow up.10-15

In earlier studies, mid- and long-term survival varied in reports from a number of investigators. Some of these studies were from different eras, but from the same institution, so there was some overlap of patients. Survival at 10 years ranges from 60 to 90% and at 15 years from only 50 to 80%.

Consistent with the findings of others, we have demonstrated an improved overall outcome. There was no early mortality (0%) in our study population, despite the presence of heterotaxy syndrome (17.2%, n=10), known to be a high risk factor for the Fontan operation. Medium-term (up to 12-year) survival was 96.6%. At a mean follow up of 5.22 years and up to 11.5 years, the majority of these patients were in New York Heart Association functional class I or II (82% and 16%, respectively).

Because of the palliative nature of the Fontan procedure, as well as the presence of prosthetic material, it is our policy that patients should be treated with cardiovascular protective and anticoagulant medications. Angiotensin-converting enzyme inhibitors are used in patients with evidence of impaired ventricular function or atrioventricular valve regurgitation. Post-Fontan patients are believed to manifest increased systemic vascular resistance and others have reported that afterload reduction therapy may have contributed to the improved long-term outcome of such patients.16-18

The optimal anticoagulation regimen after TCPC is unknown.19,20 However, previous reports have shown an incidence of 20% to 23% of thrombus formation in the extracardiac conduit if anticoagulants were not given.21,22 Our policy for anticoagulant prophylaxis after the Fontan procedure is lifelong treatment with warfarin. In some patients it was difficult to control the INR and they were maintained on low dose warfarin and low dose aspirin, or aspirin alone. With this policy, we have not had thromboembolic phenomena or documented conduit thrombosis or obstruction in our patients. We believe this favorable result to be at least partly related to the improved hemodynamics of the extracardiac modification, as thromboembolism risk may be more closely associated with suboptimal hemodynamics or an underlying coagulopathy, rather than with the conduit itself.19

Atrial arrhythmias, protein-losing enteropathy (PLE) and cyanosis because of systemic venous collateralization are known important early, mid-, and long-term problems after the Fontan operation.17,23-26
In our series, however, we have no cases of late cyanosis from systemic to pulmonary venous collaterals, and no PLE. In earlier studies, the incidence of early and late postoperative arrhythmias (1 to 10 years) was found to be 6% to 30%. However, in our series, the incidence of arrhythmias was low and, in particular, the incidence of atrial arrhythmia was rare. This is in keeping with the reported assessment that the extra-cardiac Fontan modification reduces the incidence of significant postoperative arrhythmias.

Because of concerns for the extracardiac conduit’s absence of growth potential, we have generally aimed to perform Fontan completion at about 5 years of age, in order to be able to insert a conduit big enough for adult body size. However, the patient’s growth may still theoretically result in distortion of the right pulmonary artery, compression of the right pulmonary veins, or flow disturbances. Although we and other investigators have not observed such problems so far, longer follow-up is needed.

Since the introduction of the use of fenestration as part of the Fontan operation 20 years ago, there has been intense discussion of the appropriate use of this modification. It has been suggested that fenestration may significantly reduce the duration and volume of chest tube drainage, the duration of hospital stay, and may possibly improve early survival. The purported mechanism involves lower central venous pressure, and improved single ventricle preload at the expense of some cyanosis. Disadvantages include the ongoing risk for a paradoxical embolus, persistent cyanosis, and an increased incidence of late catheter intervention for device closure of the fenestration.

Therefore, the overall benefit of routine fenestration in Fontan patients remains uncertain and many studies imply that a patent fenestration is not universally beneficial after the Fontan procedure. In our study, selected patients with higher pulmonary arterial pressure, transpulmonary gradient, and pulmonary vascular resistance, or other unfavorable preoperative factors (ventricular dysfunction or atrioventricular valve regurgitation) received a fenestration. In addition, a fenestration was used rarely if immediate hemodynamics after weaning from cardiopulmonary bypass were deemed suboptimal. Despite the presence of a patent fenestration in almost half of our patients, no one has experienced a paradoxical thromboembolic phenomenon, perhaps, in part, due to the protection afforded by our anticoagulation policy. Catheter re-intervention after the Fontan procedure was infrequent in “fenestrated” patients because spontaneous closure of the fenestration occurred in most (62%) without the subsequent need for re-fenestration, and significant residual right-to-left shunt was infrequent.

The absence of a fenestration, higher postoperative transpulmonary gradient and a longer duration of cardiopulmonary bypass have been associated with prolonged pleural fluid drainage. However, in our experience, none of these variables were significantly associated with prolonged pleural effusions.

Conclusions

We have routinely performed the modified Fontan operation in properly prepared (by means of a carefully planned multistage strategy) single ventricle patients in Greece since 1997, mostly employing the extracardiac conduit technique. Early and mid to late follow-up results, including overall survival and functional status, have been gratifying in this challenging group of patients. Appropriate patient selection—including, when indicated, multistage preparation for the Fontan circulation—careful attention to achieving optimal hemodynamics at the time of operation, and close follow-up and management are crucial for ensuring optimal long-term outcome. Naturally, true long-term follow-up measured in decades will be necessary to determine the potential incidence of possible late severe complications, which may lead to the necessity of drastic re-intervention such as heart transplantation.

References

Fontan Operation in Greece