Is the Extracardiac Conduit the Preferred Fontan Approach for Patients With Univentricular Hearts?

Paul Khairy, MD, PhD; Nancy Poirier, MD

“In theory, theory and practice are the same. In practice, they are not.”
—Albert Einstein

There is, perhaps, no disease entity that better exemplifies the complexities, challenges, and creative innovations characteristic of the evolution in congenital heart disease care than the univentricular heart. The univentricular heart encompasses an array of uncommon and severe inborn cardiac malformations that share a similar physiology, with pulmonary and systemic venous return predominantly directed into a functionally single ventricle, precluding biventricular repair. A prevalence of \( \approx 1 \) per 3000 live births has been estimated. The occasional patient may survive beyond middle age without palliative surgery when certain conditions align, including well-balanced pulmonary and systemic circulations and preserved function of a morphologically left single ventricle. For the vast majority, the prognosis without surgical intervention is grim. In developed countries, most patients undergo a staged surgical approach in view of an ultimate, albeit imperfect, Fontan procedure. Typically completed at between 18 months and 4 years of age, Fontan surgery essentially separates the systemic from pulmonary circulation by directing systemic venous return to the pulmonary artery, usually without an interposed subpulmonary ventricle.

The Extracardiac Conduit Is Not the Preferred Fontan Approach for Patients With Univentricular Hearts

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Response by Kogon on p 2525

Since its original description in 1971, multiple modifications and adaptations to the Fontan procedure have been widely applied to the spectrum of univentricular hearts. Although it is beyond the scope of this article to detail all proposed variants, the 3 most common categories of Fontan surgery are schematically depicted in Figure 1. The classic Fontan consisted of a valved conduit between the right atrium and pulmonary artery. It was subsequently modified to a direct anastomosis of the right atrium to a divided pulmonary artery (Figure 1A). The intracardiac lateral tunnel was the next major innovation. It consists of an end-to-side anastomosis of the superior vena cava to the undivided right pulmonary artery and a composite intraatrial tunnel that uses the right atrial lateral wall and prosthetic material to channel inferior vena caval flow to the pulmonary artery (Figure 1B). The “extracardiac” variant of the total cavopulmonary connection Fontan consists of directing inferior vena caval flow to the pulmonary artery by means of an external conduit (Figure 1C).

Theory

All current forms of Fontan surgery result in a physiological compromise between systemic venous hypertension and con-
comitant pulmonary arterial hypotension, such that complications related to suboptimal hemodynamics are to be expected. Disadvantages of the atrio pulmonary Fontan have been well characterized, and include the potential for atrial brady- and tachyarrhythmias, thromboembolism, protein- losing enteropathy, plastic bronchitis, hepatic dysfunction, and venous insufficiency. The extent to which such complications are predominantly driven by progressive and massive right atrial dilation, as opposed to hemodynamic conditions common to all forms of Fontan surgery, ie, elevated systemic venous pressure with passive nonpulsatile pulmonary arterial flow, has yet to be understood.

Nevertheless, factors that prompted development of the total cavopulmonary connection Fontan included the need to resolve the issue of pulmonary venous obstruction in patients with hypoplastic left heart syndrome and to improve hemodynamics. In a landmark study on fluid dynamics, de Leval et al predicted that an atrio pulmonary Fontan produces an inefficient circulation with a high degree of energy loss. In contrast, the lateral tunnel Fontan provides favorable hydrodynamic characteristics, reduces the quantity of atrium exposed to high pressures, and incorporates growth potential. In comparison with the lateral tunnel, proponents of the extracardiac conduit claim the following: superior fluid dynamics with lower right atrial pressures, relative surgical simplicity with avoidance of aortic cross-clamping, absence of intracardiac prosthetic material with less thrombogenic potential, and less extensive atrial suture lines with consequently fewer arrhythmias. As a result, the extracardiac conduit is now considered the procedure of choice for univentricular hearts in a growing number of centers. It is also frequently performed in the context of Fontan conversion surgery for patients with atrio pulmonary connections and hemodynamic abnormalities and/or recalcitrant arrhythmias.

**Reality**

**Overall Survival**

To place this controversy in context, when one adjusts for the higher perioperative mortality associated with an early surgical era, improved survival with a total cavopulmonary connection in comparison with the very different atrio pulmonary Fontan has yet to be demonstrated. In a cohort study that included 235 perioperative survivors with Fontan surgery followed for up to 20 years, there was no detectible trend suggesting a survival advantage with a total cavopulmonary versus atrio pulmonary Fontan (Figure 2A). It is, therefore, unlikely that the more subtle dissimilarity between different types of total cavopulmonary connections will translate into discernible differences in long-term survival. Not surprisingly, cohort studies comparing intracardiac lateral tunnel with extracardiac Fontans have reported similar operative morbidity and mortality and midterm survival (Figure 2B). Thus, in contrast to anatomic considerations such as ventricular morphology and function, total anomalous pulmonary venous return, and heterotaxy syndromes, the type of Fontan surgery has not convincingly been associated with long-term survival.

**Hemodynamics and Functional Status**

Computational 3-dimensional hydrodynamic simulations of various types of total cavopulmonary connections suggest that energy loss with a lateral tunnel Fontan is intermediate between a rightward- and leftward-oriented extracardiac conduit. Such insightful simulations do not, however, reproduce human physiological conditions, because they assume, for example, that vessel walls are noncompliant, that flow is steady, and that respiratory effects are nonexistent. In an in vitro model of explanted sheep heart preparations, the rate of fluid-energy dissipation between the intracardiac lateral tunnel and extracardiac conduit was comparable at a flow index of 3 L/min per m², whereas an advantage favoring the extracardiac conduit was observed at the excessive flow rate of 6 L/min per m².

To date, no clinical or preclinical in vivo study has demonstrated superior hemodynamics with the extracardiac versus lateral tunnel Fontan. In a study of pulmonary and caval flow patterns by MRI, patients with atrio pulmonary Fontans had partial backward flow in the inferior vena cava.

In contrast, both lateral tunnel and extracardiac Fontans produced unidirectional flow in the inferior vena cava, with...
equal blood flow distribution between the pulmonary arteries, and low or absent pulsatility. Other studies have similarly found that, whereas extracardiac and lateral tunnel Fontans have inherently different streaming characteristics, one is not systematically superior to the other. Important considerations extend beyond the type of total cavopulmonary connection and include influence from the superior vena cava anastomosis, pulmonary artery diameters, and inferior vena caval offsets. Catheter-based and functional outcome studies, although limited, suggest that similar hemodynamic and functional results are obtained with lateral tunnel and extracardiac Fontans. Studies have consistently shown that postoperative Fontan pressures and transpulmonary gradients are similar with the 2 types of total cavopulmonary connections and that identical functional parameters are obtained on follow-up.

Surgical Considerations

The nonfenestrated extracardiac Fontan is a technically simple and easily taught procedure. However, maintaining a patent fenestration is a technical challenge. Various methods have been attempted, including placement of a 4-mm polytetrafluoroethylene tube graft between the extracardiac conduit and pulmonary venous atrium, or suturing the atrial wall a distance away from the fenestration. Such difficulties have prompted many centers to abandon fenestrations. Although the issue remains controversial, several studies, including a randomized trial, suggest that fenestrations improve outcomes in standard-risk patients by decreasing pleural drainage, hospital length of stay, and need for additional postoperative procedures. In extracardiac Fontan recipients with and without fenestrations, fenestrations significantly decreased the duration of pleural drainage by >3 days, on average. Other alleged surgical advantages of the extracardiac Fontan, which include the possible avoidance of cardiopulmonary bypass and aortic cross-clamping, are likely minor when one considers the already very brief operative time required for Fontan surgery. For example, in a study of 162 patients of whom 113 had lateral tunnels and 49 had extracardiac conduits, time on the extracorporeal circuit was similar between the 2 groups (107 ± 42 minutes for the lateral tunnel versus 117 ± 41 minutes for the extracardiac conduit). Nevertheless, the extracardiac conduit was associated with a significantly longer hospital stay (mean of 25 versus 13 days) and trend toward longer ventilatory support (20.1 versus 8.4 hours). Additional disadvantages of the extracardiac Fontan include the potential for tunnel stenosis requiring stenting or surgical revision, a higher rate of healthcare resource use, and the lack of growth potential of the synthetic tube. The latter limitation has prompted some to suggest that it is less suitable in young children, particularly those <3 years of age.

Thromboembolism

Thromboembolic complications are a well-recognized source of morbidity and mortality in patients with Fontan physiology. Predisposing factors extend beyond the obvious atrial dilation, atrial tachyarrhythmias, and sluggish flow. For example, several clotting factor abnormalities have been reported, including decreased levels of protein C, protein S, and antithrombin III. Increased platelet reactivity has also been recognized.

Although the pathophysiology of thrombogenesis in patients with extracardiac Fontans remains to be elucidated, it was hypothesized that extracardiac conduits would result in a lower incidence of thromboemboli, in part, owing to the avoidance of intracardiac prosthetic material. This hypothesis
was not borne out. Tunnel thrombosis causing death is a recognized complication of the extracardiac Fontan. A study of 65 consecutive patients with an extracardiac Fontan reported a 4.6% incidence of conduit thrombosis. The actuarial incidence of thromboembolic complications has been estimated to be 7.1% at 10 years. In a systematic review that included 1075 patients with an extracardiac Fontan from 20 studies, 5.2% of patients had a thromboembolic event over a mean follow-up that ranged from 2 to 144 months. Preventive strategies have yielded inconsistent to discouraging results, with some studies suggesting similar rates of thromboembolic events in patients with antiplatelet versus anticoagulant agents. The largest studies comparing thromboembolic events found no differences between intracardiac lateral tunnel and extracardiac Fontans, irrespective of the anticoagulant or antiplatelet treatment strategy.

### Arrhythmias

Atrial tachyarrhythmias are a leading source of morbidity in patients with Fontan surgery. The initial episode of sustained tachycardia often heralds a pattern of progression toward more frequent and prolonged recurrences. Importantly, patients with Fontan physiology may not tolerate persistent tachyarrhythmias. Notoriously resistant to antiarrhythmic agents, these arrhythmias may engender a reduction in ventricular systolic function, increase in atrioventricular valve regurgitation, atrial thrombosis, congestive heart failure, syncope, and rarely, sudden death.

In addition to improving hemodynamics, the principal objective of the total cavopulmonary connection Fontan was to minimize atrial arrhythmias. The actuarial incidence of supraventricular tachyarrhythmias in 152 patients with atrio-pulmonary Fontans was reported to be 39% at 15 years of follow-up. In contrast, the corresponding 15-year rate in 105 patients with lateral tunnel Fontans was 13%. Estimates beyond 15 years are few and far between. In conservatively assuming a linear decline in arrhythmia-free survival identical to early follow-up, projected estimates indicate an incidence of 24% and 30% at 30 and 40 years, respectively. These figures are likely underestimates, because the first 10 to 15 postoperative years are typically relatively quiescent from an arrhythmia perspective. Regardless, it may be reasonably forecast that supraventricular arrhythmias will continue to be a leading cause of morbidity as patients with total cavopulmonary connections age.

Historically, the main rationale for abandoning the intracardiac lateral tunnel in favor of the extracardiac conduit was to further reduce the incidence of arrhythmias. This notion was largely based on an important preclinical study involving 17 dogs with simulated lateral tunnels. Macroreentrant circuits could be induced by atrial stimulation in all, although some required isoproterenol. No such experiment has been conducted with extracardiac conduits. Yet, to quote Dr Richard Jonas: “It was this influential study more than any clinical result that convinced many centers to abandon the intracardiac lateral tunnel and to move on to the…extracardiac conduit.”

In reality, there is no clear-cut evidence that extracardiac conduits are associated with fewer arrhythmias. Studies addressing this issue are summarized in the Table. Intrastudy (ie, lateral tunnel versus extracardiac conduit) and between-study comparisons are obscured by imbalances in follow-up duration, heterogeneous populations, variable definitions of qualifying arrhythmias, nonuniform means of assessing outcomes, and differing surgical techniques. Given that the prevalence of arrhythmias increases with time, the systematically longer follow-up duration for lateral tunnels may give the false impression, in some studies, of a higher arrhythmic risk. When actuarial arrhythmia-free survival is considered, as in the large Pediatric Heart Network study, no differences between the

### Table. Prevalence of Arrhythmias Following the ECC and LT Fontan

<table>
<thead>
<tr>
<th>Year</th>
<th>First Author</th>
<th>n</th>
<th>Follow-Up, y</th>
<th>ECC Arrhythmia Prevalence, %</th>
<th>LT Arrhythmia Prevalence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>Cohen MII</td>
<td>30</td>
<td>46</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>2001</td>
<td>Azakie A</td>
<td>60</td>
<td>47</td>
<td>2.5±1.4</td>
<td>2.6±1.9</td>
</tr>
<tr>
<td>2003</td>
<td>Kumar SP</td>
<td>33</td>
<td>37</td>
<td>3.0±2.2</td>
<td>3.6±1.6</td>
</tr>
<tr>
<td>2004</td>
<td>Nürnberg JH</td>
<td>45</td>
<td>29</td>
<td>4.4 (1.6–7.2)</td>
<td>7.9 (5.4–11.1)</td>
</tr>
<tr>
<td>2007</td>
<td>Fiore AC</td>
<td>49</td>
<td>113</td>
<td>3.0±2.3</td>
<td>5.0±3.1</td>
</tr>
<tr>
<td>2007</td>
<td>Attanavanich S</td>
<td>13</td>
<td>14</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>2008</td>
<td>Hakacova N</td>
<td>41</td>
<td>60</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2010</td>
<td>Stephenson EA</td>
<td>63</td>
<td>279</td>
<td>Up to 8 y</td>
<td>Up to 16 y</td>
</tr>
<tr>
<td>2011</td>
<td>Sarkis V</td>
<td>25</td>
<td>26</td>
<td>0.7–7.0</td>
<td>4.8–10.0</td>
</tr>
<tr>
<td>2011</td>
<td>Chungsomsrassong P</td>
<td>64</td>
<td>39</td>
<td>Actuarial 5-y</td>
<td>Actuarial 5-y</td>
</tr>
</tbody>
</table>

ECC indicates extracardiac conduit; LT, lateral tunnel; N/A, not available; NS, not significant; SND, sinus node dysfunction; and SVT, supraventricular tachycardia.
extracardiac conduit and lateral tunnel are observed (Figure 3).64 Larger and longer-term prospective studies are required to assess smaller and later differences in outcomes. Current evidence suggests that physiological and anatomic features, such as the presence of heterotaxy syndromes,29 are far more important determinants of arrhythmic risk than type of total cavopulmonary connection.

Reasons as to why the extracardiac Fontan is no less arrhythmogenic despite a lesser degree of atrial surgery remain speculative. Hypoxemia before Fontan surgery may alter gene expression and produce lasting cardiac structural and functional changes that promote arrhythmias.66 In addition, cardiac autonomic nervous activity is impaired to a similar extent in patients with lateral tunnels and extracardiac conduits.67 Indeed, the atro caval junction in the region immediately inferior to the right pulmonary artery, where one of the anastomoses of the extracardiac Fontan conduit is performed, is richly innervated with receptors discharging into unmyelinated C-type vagal afferents.66 Moreover, the relationship between suture lines and arrhythmogenesis is nonlinear and complex. For example, suture lines that connect areas of electrically unexcitable scar may protect against potential reentrant circuits. In addition, the extracardiac Fontan may require a large cuff of atrial tissue for its inferior anastomosis, with resulting damage to the crista terminalis.35 Altered preferential longitudinal conduction along this fibromuscular ridge plays a key role in the initiation and maintenance of focal and reentrant atrial arrhythmias.59,69,70 The particularly high density of adrenergic nerve endings in the crista terminalis has been implicated in arrhythmogenesis.71

Managing Arrhythmias With the Standard Extracardiac Fontan

Even if arrhythmias were less frequent with extracardiac conduits, it may be argued that they should be entirely eliminated, or nearly so, to justify this approach from an arrhythmia perspective. Other forms of Fontan surgery typically allow transvenous atrial pacing for sinus node dysfunction and catheter access for recalcitrant arrhythmias, either directly or via fenestrations, baffle leaks, or low-risk intracardiac transbaffle punctures.56 By bypassing the heart, the extracardiac Fontan, as most commonly performed, introduces an unprecedented and seemingly unnecessary layer of complexity to managing the most common, highly morbid, and predictable complication.

Current options to access arrhythmias in patients with extracardiac Fontans include a transthoracic percutaneous approach, as described in 5 patients with lateral tunnels (Figure 4A).72 In this early experience, 3 patients had pneu-
mothoraxes or hemothoraxes requiring drainage. A single report described a case of transthoracic puncture in a patient with an extracardiac Fontan under computed tomographic guidance (Figure 4B). We performed a hybrid intervention in a hemodynamically unstable child with atrial arrhythmias in the acute postoperative setting after completion of an extracardiac Fontan with surgical accessory pathway ligation. In A, an anteroposterior view is shown at the site of successful ablation, portraying the position of the radiofrequency ablation catheter (black arrow). The sternum is splayed open by means of thoracic retractors. Epicardial bipolar atrial and ventricular pacing leads are seen. B, Recordings from surface ECG leads II, aVL, and aVF; epicardial high right atrium 18 (HRA); distal (MAP d) and proximal (MAP p) electrode pairs of the radiofrequency ablation catheter; and epicardial ventricle (RVA). Orthodromic AV reciprocating tachycardia is seen with the mapping catheter positioned at the site of successful ablation. AV indicates atrioventricular; MAP, roving mapping catheter; RVA, right ventricular apex. Reproduced from Khairy et al.72

Figure 6. Relationship between extracardiac conduit and pulmonary venous atrium. An axial view of a MRI scan is shown in a patient with an extracardiac conduit (ECC). The arrows mark the space between the ECC and neopulmonary venous atrium, composed of the right (RA) and left (LA) atria.

One report described successful transvenous transbaffle access through the extracardiac conduit. Difficulties crossing the Gore-tex tube resulted in deformation of a radiofrequency-powered transseptal needle. Efforts to position the dilator across the baffle failed. Finally, balloon angioplasty was performed to create a channel between the extracardiac conduit and pulmonary venous atrium. It was cautiously concluded that further studies are required to determine the safety of this procedure. Safety hinges, in large part, on the premise that, over time, the inflammatory process results in fibrotic adhesion of the conduit to the pulmonary venous atrium, so as to eliminate the space between these 2 structures. Although this may be true in some, it cannot be predicted with certainty. Gore-tex material was deliberately engineered to minimize or prevent protein absorption and cell adhesion. A resulting space between the extracardiac conduit and pulmonary venous atrium may be appreciated by imaging studies (Figure 6). Our surgical experience in adults indicates that low-resistance tissue planes, along which blood may tract, typically surround extracardiac conduits years after Fontan surgery.

The most elegant approach to targeting atrial arrhythmias in the setting of extracardiac conduits may be by remote magnetic-guided ablation. Although, to our knowledge, magnetic-guided ablation has yet to be reported for this indication, a retrograde aortic approach has been described for patients with intraatrial conduits. However, this technology is costly, available in a restricted number of centers, and subject to the limited contact force that can be generated. In reality, many older patients with extracardiac Fontans continue to experience intractable arrhythmias and are frequently hospitalized for electric cardioversions, despite various combinations of antiarrhythmic agents. Suboptimal arrhythmia
control is having an unmistakable and major impact on their quality of lives and functional status.

**Creative Solutions**

Examples of potential solutions to improve access to arrhythmias include favoring the intracardiac lateral tunnel, fenestrating the extracardiac conduit (although difficulty maintaining the fenestration is a recognized disadvantage), and tacking the extracardiac conduit to the atrium, while marking the point of contact with a radiopaque ring. As illustrated in Figure 7, other proposed creative solutions include the so-called trapdoor modification and a hybrid intra/extracardiac Fontan.\(^5^9\)

**Conclusions**

There are numerous examples of major inroads in congenital heart disease care achieved through an iterative paradigm of technical innovations later informed and improved by systematically cataloguing limitations and sequelae in early patient cohorts. The Fontan story epitomizes this model of progress. As the first cohorts of patients with extracardiac conduits age, it is both timely and imperative to critically assess the current state of knowledge. In so doing, it becomes apparent that the purported advantages of the commonly performed nonfenestrated extracardiac Fontan, in comparison with other forms of total cavopulmonary connections, are largely theoretical and not supported by the weight of clinical evidence. Moreover, associated issues and potential compli-
cations are major and real concerns. For example, although the principal rationale for the extracardiac conduit was to minimize arrhythmias, there is no clear evidence that this has been achieved. The procedure not only fails to eliminate arrhythmias, it prevents their appropriate management when they do arise. This situation is clearly undesirable and merits the care and attention of our congenital heart community.

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None.

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Response to Khairy and Poirier

Brian E. Kogon, MD

Although I maintain my enthusiasm and support for the extracardiac Fontan, Dr Khairy does indeed make some valid points. Although there may be differences between the extracardiac and lateral tunnel Fontans with respect to flow characteristics, arrhythmias, thromboembolism, and access for electrophysiological intervention, he points out that the survival advantage is unclear. With this in mind, our emphasis and focus likely needs to shift away from Fontan design. We need to identify innovative ways to reduce the subsequent morbidity and improve the quality of life in patients with Fontan anatomy and physiology. One means is through arrhythmia management. I agree with his proposal for creative solutions: the “intracardiac/extracardiac Fontan” (Figure 7A through 7C) and the “closed fenestrated” Fontan (Figure 7D through 7F). These are simple modifications of the extracardiac Fontan that may greatly facilitate access for subsequent electrophysiological intervention. Another means is through mechanical support. Consider the future, when routine right-sided univentricular mechanical support may become a valid therapeutic option to improve symptoms and quality of life. The superior and inferior cavopulmonary connections would likely be taken down and the cavae rejoined to form a single assist device inflow vessel. This feat may be greatly facilitated by an extracardiac Fontan in which cardioplegic arrest and reentry into the heart could be avoided. Despite an unclear survival advantage, I continue to support the extracardiac Fontan for the other reasons stated. Subtle modifications to the extracardiac Fontan may be beneficial. As these patients age, additional benefits of the extracardiac Fontan may become more evident.
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