Single ventricle physiology: surgical options, indications and outcomes

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Purpose of review
Among the most frequently encountered congenital heart malformations are those with so-called single ventricle physiology, in which there is only one ventricle to pump blood to the pulmonary and systemic vascular beds, respectively. Long-term survival is possible, based on the principle of right heart bypass, whereby the ventricle pumps blood only to the systemic circuit, whereas pulmonary blood flow occurs passively. Such a circulatory system is achieved in a series of staged reconstructive operations, each of which was formerly accompanied by very high rates of major morbidity and mortality. Current approaches to single ventricle physiology as well as areas of controversy will be reviewed.

Recent findings
The development of a number of inventive operations, combined with a greater understanding of the physiologic requirements for success after single ventricle reconstruction has resulted in dramatic improvements in outcomes. The identification and modification of risk factors as well as the recent development of catheter-based intervention offer the real prospect of significant continued improvement.

Summary
Advances in the care of children with single ventricle hearts have resulted in remarkably improved prognosis, with the expectation of continued improvement in not only survival but also quality of life.

Keywords
Fontan operation, Norwood operation, single ventricle, univentricular heart

Introduction

Based on an extensive series of experimental and clinical attempts to 'bypass' the right side of the heart [1•], Fontan and Baudet [2] in 1971 reported an operation to route all of the systemic venous return to the pulmonary circulation without a ventricular power source, and thus the management of children with single ventricle physiology was revolutionized. Subsequently, an increasing experience led to the formulation of a set of guidelines to describe which patient characteristics were associated with optimal outcomes with Fontan-type operations, and these guidelines were termed the Fontan golden rules [3]. Several of these criteria have been shown to be less important or even wrong as the operation has been serially modified. In part, the ability to overcome the strict golden rule criteria represents advances in surgical technique and equipment. A more important influence has been an enhanced understanding of the contribution of various factors to early and late risk after the Fontan operation. Some factors are immutable, such as the particular type of cardiac malformation and unique genetic makeup of the patient. Others factors are very much in the purview of those practitioners caring for the patients, such as which specific operations are done (and when) and what perioperative and long-term medical management is employed.

Management principles

In the management of children with univentricular hearts, certain fundamental principles must be considered, perhaps the most important of which is the concept of *primum non nocere*. The implication is that intervention must be carried out so as to avoid injury to the heart, preserving ventricular systolic and diastolic function, preserving valvular function and preserving electrophysiologic function. Just as important is the concept of optimization of pulmonary vascular circulation, specifically the establishment and maintenance of the lowest possible pulmonary vascular resistance. Potential for injury to other organs, particularly the brain, liver, kidneys and intestines must also be borne in mind as interventions are planned and carried out.

Hemodynamic concepts

Although now often accomplished prenatally, the diagnosis of most children with univentricular cardiac physiology is still usually made in the first few days or weeks of life. In the case of postnatal diagnosis, the presenting symptom may be cyanosis due to inadequate pulmonary blood flow, tachypnea and heart failure due to excessive pulmonary blood flow, or low cardiac output syndrome and shock in the event of ductal dependant systemic blood flow (often in conjunction with excessive pulmonary blood flow). In the initial management of such children, after diagnosis and resuscitation, the dynamic aspect of the neonatal pulmonary vascular bed is a dominant factor. Because the pulmonary vascular resistance is so high initially, the goal of achieving pulmonary blood flow without a ventricular power source is not possible in the neonatal period. Equally important though is the recognition that the initially high pulmonary resistance drops rapidly, falling to its nadir in a few weeks [4]. The consequence of this variably paced maturation of the pulmonary resistance is that children with single ventricles spend their first few months with inefficient parallel systemic and pulmonary circulation, with flow into both vascular beds delivered by single ventricle. There is thus potential for maldistribution of the total cardiac output, with excessive pulmonary flow and inadequate systemic flow. This is addressed by regulating pulmonary blood flow using either a prosthetic conduit of a specific diameter or a pulmonary artery band, depending on the specific anatomy of the cardiac malformation. (Rarely, there will be intrinsic obstruction to pulmonary blood flow, sometimes termed 'balanced circulation', obviating the need for an initial surgical procedure.)

With the reduction in pulmonary vascular resistance completed by approximately 6–12 weeks of age, 'right heart bypass' or conversion to passive pulmonary blood flow becomes theoretically possible. As a practical matter achievement of complete right heart bypass is most commonly accomplished in stages, with an initial connection of the superior vena cava to the pulmonary artery and subsequent addition of the inferior vena cava to the pulmonary circuit [5,6]. Thus, for most children with univentricular hearts, a total of three interventions will be necessary to achieve the Fontan arrangement. In the next sections specific issues relevant to each stage will be discussed.

First-stage palliation

Except for those rare children with truly balanced circulation, virtually all children with single ventricle physiology will require intervention in the neonatal period to regulate pulmonary blood flow. Many such children will also require reconstruction of ductal-dependant systemic blood flow; most have hypoplastic left heart syndrome or one of its variants. The most common operation for such patients is the Norwood procedure, whereby the aorta is associated directly with the single ventricle, an unobstructed inter-atrial communication is fashioned, and pulmonary blood flow is provided by a prosthetic graft between a systemic artery and the pulmonary artery [modified Blalock Taussig shunt (BT shunt)], or by a graft between the right ventricle (RV) and the pulmonary artery (RV to pulmonary artery shunt) [7,8,9••]. Which shunt is superior remains an unsettled question. Many single center reports describe improved survival with the newer RV to pulmonary artery shunt version of the operation, compared with historical controls, although several other studies do not show a clear benefit [9••]. A multicenter randomized trial comparing the two types of shunt is presently underway, run under the auspices of the Pediatric Heart Network [10•]. The study, known as the Single Ventricle Restoration Trial will examine not only early mortality, but also the important endpoints of transplantation-free survival at 12 months of age, as well as neurodevelopmental outcomes.

An inventive alternative to the Norwood operation, which requires cardiopulmonary bypass (CPB) and in many centers also deep hypothermic circulatory arrest (DHCA), is the 'Hybrid' stage I procedure for hypoplastic left heart syndrome [11]. This procedure, which used neither CPB nor DHCA, involves the placement of a stent in the ductus arteriosus to preserve systemic blood flow and placement of bilateral pulmonary artery bands. An adequate inter-atrial communication is established by a transcatheter atrial septostomy. Experience with the hybrid approach is limited, but encouraging early outcomes have been reported [11–14]. A recent publication described results at intermediate follow-up as good as the best reported with 'conventional' Norwood operation [15••].

Another important group of single ventricle patients are those with aortic arch obstruction in association with unobstructed pulmonary blood flow. Such patients require aortic repair in the neonatal period, with simultaneous pulmonary artery banding (or with pulmonary artery division and systemic to pulmonary shunt placement [16]). In some cases, the aorta may be repaired without CPB via thoracotomy, but in other cases the repair is best accomplished via sternotomy using CPB. In a subset of patients, there is the potential for sub-aortic obstruction to develop if pulmonary artery banding is performed. In these, a Damus–Kaye–Stanzel (DKS) type of operation is necessary at the time of the initial operation with a shunt to provide pulmonary blood flow, which is then equivalent to a Norwood procedure. If obstruction develops later, the DKS procedure may be combined with second stage palliation. Alternatively, for single ventricle lesions with subaortic obstruction, a

palliative arterial switch operation may be preferred to a DKS operation [17].

For single ventricle patients without aortic obstruction, stage I palliation is a much less complex undertaking. In the event that pulmonary blood flow is unrestricted, initial intervention consists of placement of a pulmonary artery band. Although conceptually a simple procedure, banding of the pulmonary artery is a notoriously challenging undertaking, given the dynamic state of the pulmonary vascular resistance as well as issues of growth and the potential for band migration [18]. If the band is too loose, it will not have the desired effect, and the patient will remain in heart failure, with consequent poor growth. Furthermore, the pulmonary bed will remain unprotected from excessive flow, and the heart subjected to volume overload. Alternatively, if the band is excessively tight, the patient will be unacceptably cyanotic and reintervention will be required earlier than intended. Because of the difficulties in achieving perfect band tightness, a variety of adjustable bands have been proposed [19,20]. Regardless of how banding is performed, it remains a procedure associated with a surprisingly high operative mortality, perhaps as high as 10% [18].

The other single ventricle patients without aortic obstruction are those with inadequate pulmonary blood flow, who are most commonly treated by the placement of a modified BT shunt. Like pulmonary artery banding, this procedure does not require CPB, but like banding it is associated with a disappointing mortality rate, probably between 5 and 15% [21]. The majority of risk associated with BT shunt surgery is attributable to acute shunt thrombosis, which may be prevented by the use of early postoperative anticoagulation with intravenous heparin and long-term aspirin or clopidogrel [22,23]. In part because of the pitfalls associated with BT shunts, there has been recent enthusiasm for an alternative approach using intravascular stents in the ductus arteriosus [24].

Regardless of form of first stage palliation of children with univentricular hearts, it must be emphasized that these children are left with a very inefficient circulation. This is associated with poor growth velocity [25•,26], and in some anatomic subsets, especially hypoplastic left heart syndrome and pulmonary atresia/intact ventricular septum, a significant incidence of sudden death after hospital discharge [21,26]. In an attempt to reduce the incidence of what is euphemistically termed 'interstage attrition', some centers have initiated home surveillance programs, consisting of daily monitoring of weight and oxygen saturation by parents or visiting nurses [26]. Although the results from such efforts are encouraging, interstage death has not been completely eliminated, emphasizing the fragility of single ventricle patients with parallel circulation.

Second stage palliation

With the establishment of the principle that a bidirectional superior cavopulmonary anastomosis provided good palliation to children at high risk for one-stage Fontan operation [5] and that the volume unloading effect of converting from parallel to series circulation provided salutary effects on coronary blood flow and ventricular energetics [6], it has become standard to proceed from initial palliation to the Fontan circulation by means of an intermediate operation. In general, the operation takes one of two forms: an end-to-side anastomosis of the cephalic end of the transected superior vena cava to the superior aspect of the right pulmonary artery, often termed the bidirectional Glenn shunt (BDG); or an augmented side-to-side anastomosis between the back of the opened superior vena caval-right atrial junction and the anterior surface of the right pulmonary artery, with an intra-atrial patch placed to close the communication between the atrium and the pulmonary artery, termed the hemi-Fontan (HF) operation. The BDG operation is performed in anticipation of subsequent performance of an extracardiac Fontan operation, whereby a tube graft is interposed between the transected inferior vena cava and the underside of the right pulmonary artery. The HF operation is performed in anticipation of a lateral tunnel Fontan operation, whereby an intra-atrial baffle is placed in the right atrium to divert the inferior vena caval flow toward the superior aspect of the atrium and the pulmonary artery, and the patch placed at the time of HF operation is removed.

From a functional perspective, the BDG and the HF are equivalent in that both consist of a superior cavopulmonary anastomosis, with no convincing evidence that the HF/lateral tunnel sequence produces different results than the BDG/extracardiac Fontan sequence. The HF is a slightly more extensive operation, but may allow for a larger connection between the superior vena cava and the pulmonary artery. The BDG is a simpler procedure, and is applicable in patients with bilateral superior vena cava.

Several aspects of second stage palliation remain controversial, including the question of whether to eliminate any antegrade source of additional pulmonary blood flow [27]. Advocates of antegrade flow point out the higher oxygen saturations that result, as well as the theoretical effect of pulsatile flow on enhancing pulmonary artery growth [27,28]. Proponents of eliminating antegrade blood flow report a reduction in the extent and duration of postoperative pleural effusions as well as the difficulty in establishing how much antegrade blood flow is too much [29].

Another area of controversy is the optimal timing of second stage operation. Proponents of early operation

point to the shortening of the risky interstage period [30,31]. Other theoretic benefits include early achievement of the salutary effects of volume unloading on the ventricle, the establishment of more normal growth patterns [25•], as well as studies showing equivalent survival outcomes as in patients having later second stage operation. Opponents of early second stage operation point to significant early postoperative cyanosis in younger patients, as well as increased resource utilization and longer hospitalization in younger children [30]. In general, the age at second stage operation has decreased slightly over the past several years [31].

An additional unsettled question in second stage operation is whether or not diagnostic cardiac catheterization is necessary before surgery. A recent retrospective study suggested that the hemodynamic measurements at cardiac catheterization in patients identified by echocardiography as being good candidates for surgery did not yield unexpected information [32]. A randomized trial of cardiac magnetic resonance angiography (CMRA) and cardiac catheterization in patients being evaluated for second stage surgery found that CMRA was as useful, and was also less invasive and less expensive [33].

Third stage palliation

For children with single ventricle physiology, the ultimate physiologic goal is attained with the performance of the Fontan operation. This operation results in near normal arterial oxygen saturation as a result of the diversion of all of the systemic venous return to the pulmonary vascular bed before its return to the heart, with the exception of coronary sinus effluent that may not be routed to the lungs (depending on the type of Fontan construction). Since the introduction of this operation, the understanding of the necessary conditions for its success has increased tremendously, with a corresponding reduction in early morbidity and mortality [34–36]. It is reasonable to expect that a similar improvement will be reflected in later outcomes as well [35,37–39]. Despite significant advances in the understanding of Fontan physiology, several issues about the technical performance of the Fontan procedure and subsequent management remain unsettled. Among these are which type of operation is optimal (extra-cardiac or lateral tunnel), whether to leave a fenestration (a small communication between the Fontan pathway and the pulmonary venous atrium) and if so whether to close it, whether to use anticoagulation postoperatively and if so how long, and even whether the operation is best performed using CPB, DHCA, or neither. In this section, these issues are explored in more detail with the acknowledgement that there are several other issues of great interest, such as the fundamental question of what age is optimum for the Fontan operation, which for reasons of space are not discussed here.

An area of significant interest to surgeons in particular has been the question of whether the extracardiac conduit version of the Fontan procedure, introduced by Marcelletti [40], is superior to the lateral tunnel version of the operation [41,42]. Advocates of the extracardiac conduit suggest several advantages: avoidance of multiple suture lines in the atrium that might serve as substrate for later re-entrant tachycardia [43], creation of a smooth-walled (and presumably less turbulent) pathway [40], and even the possibility of doing the operation without bypass [44]. Disadvantages of the extracardiac conduit include the lack of growth potential in the pathway and the requirement for prosthetic or bioprosthetic material. Proponents of the lateral tunnel emphasize its growth potential and the ease of construction after a prior HF operation [45]. To date, there has not been a randomized comparison of the two approaches. Data from the most recent Society of Thoracic Surgeons (STS) database harvest suggest that approximately two thirds of Fontan operations in recent years have been performed as external conduit-type operations.

As widely discussed as the type of Fontan operation is the question of whether to create a small connection between the Fontan pathway and the pulmonary venous atrium, a so-called fenestration. This modification to the Fontan procedure was proposed by Bridges [46] to provide temporary decompression of the Fontan circuit after surgery. Proposed advantages of the fenestration include a reduction in surgical mortality rate and a decrease in the magnitude and duration of pleural effusions after surgery. Comparison with historical controls has suggested that the touted benefits have in fact been realized, although there are numerous reports of excellent post-Fontan outcomes without fenestration or with selective usage in high-risk patients. There is very little prospective, randomized data available, although a moderate sized series [47] did show an advantage of fenestration in 'usual risk' patients. The most recent information from the STS database reveals that fenestration is performed in approximately 75% of Fontan operations. When and whether to close the fenestration remain unanswered questions. Closing the fenestration results in higher oxygen saturation and eliminates the possibility of paradoxical embolism, but at a cost of reduced resting cardiac output [48]. A recent report suggested that late fenestration closure did not result in any change in exercise capacity, but did result in improvement in the ventilatory abnormalities observed during exercise in Fontan patients with open fenestrations [49].

A troublesome late complication seen in Fontan patients is thromboembolism in either the Fontan pathway or in the systemic side of the circulation. In the presence of an open fenestration, thrombus may cross from one pathway to the other. The incidence of thromboembolism is difficult to determine, time-related, and probably multifactorial, making prophylaxis and therapy more difficult.

The frequency of thromboembolism is probably higher than often suspected, as evidenced by a study in adult Fontan patients which showed that approximately 20% had unsuspected pulmonary thromboembolism [50]. It is likely that longer one lives with Fontan circulation, the more likely thromboembolism is to occur, as is true in patients without cardiac disease; in Fontan patients such events are much less well tolerated, however. A major difficulty in confronting the problem is that multiple factors may contribute to the formation of thrombus including areas of sluggish flow in the Fontan circuit, atrial arrythmias, as well as intrinsic or acquired abnormalities in hemostatic pathways. At present there is no consensus about whether or how to attempt thromboprophylaxis in Fontan patients, nor about how long to continue with such an approach [51•].

Regardless of the type of Fontan circulation, it must be acknowledged that it is a far from ideal hemodynamic circumstance. Exercise capacity is abnormal and likely to worsen over time. As cohorts of patients with Fontan circulation are followed, there is a steady attrition with survival curves never flattening or paralleling the general population. For patients whose Fontan circulation is failing as evidenced by either heart failure symptoms or protein-losing enteropathy, the only effective solution is cardiac transplantation. Outcomes after cardiac transplantation after Fontan failure are generally quite good, albeit perhaps slightly less satisfactory than in patients transplanted for other indications [52,53]. At present, however, there is no other reasonable alternative for such patients.

Conclusion

For patients born with univentricular hearts, a series of surgical interventions allow the establishment of a separated, in-series circulation. Success depends on a series of thoughtfully designed and appropriately timed interventions. Each of these interventions can be achieved with ever decreasing risks of morbidity and mortality, and with the anticipation of excellent long-term outcomes. A number of issues remain unsettled in designing the optimum strategies for such patients, but it is certainly true that the outlook is better than ever before.

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