The Adult With a Fontan: A Panacea Without a Cure? – Review of Long-Term Complications –
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The univentricular heart includes a spectrum of complex cardiac defects that are managed by staged palliative surgical procedures, ultimately resulting in a Fontan procedure. Since 1971, when it was first developed, the procedure has undergone several variations. These patients require lifelong management, including a thorough knowledge of their anatomic substrate, hemodynamic status, management of rhythm and ventricular function, together with multi-organ evaluation. As these patients enter middle age, there is increasing awareness of long-term complications and mortality. This review highlights the concept behind the staged surgical palliations, the unique single ventricle physiology and the long-term complications in this complex cohort of patients. (Circ J 2013; 77: 2672–2681)

Key Words: Congenital heart disease; Fontan procedure; Heart defects

Introduction
Many complex cardiac malformations are characterized by the existence of only one functional ventricle, which has to maintain both the systemic and pulmonary circulations. Surgical approaches to palliating single-ventricle (SV) physiology must focus on ameliorating the two major challenges of this parallel circuit of blood flow: (1) cyanosis induced by mixing of systemic deoxygenated and pulmonary oxygenated blood and (2) chronic volume overload assumed by the single functional ventricle, which leads to dilation, hypertrophy, and failure without palliation.

In 1971, Francis Fontan published his successes with a new surgical approach for patients with tricuspid atresia (TA) that completely separated the pulmonary and systemic circulations. The SV was committed solely to the systemic circulation while the pulmonary circulation was driven by venous return directly to the pulmonary arteries, bypassing the right heart. This led to a marked improvement in survival among patients with univentricular physiology.

The Fontan procedure has continued to evolve over the past four decades, leading to improved early and intermediate prognoses. However, it remains a palliative procedure and limited in its ability to fully eliminate the problems associated with SV physiology. As the early Fontan patients move to adulthood, there remains a steady attrition rate attributable to several known complications of the procedure, with the three most common modes of death being heart failure (HF) from ventricular dysfunction, thromboembolism and sudden death. As our knowledge continues to evolve, new therapeutic targets and treatment strategies have been identified that have led to improved overall morbidity and mortality.

Staged Surgical Palliation
The Fontan operation was first used in 1968 for the repair of TA and was described by Fontan and Baudet in 1971. It included the insertion of an aortic or pulmonary homograft valve, at both the inflow and outflow of the right atrium. In 1973, Kreutzer et al described the use of the pulmonary valve of a patient with TA to connect the right atrium (RA) to the pulmonary artery (PA). These initial operations were based on the principle that the RA can act as the “pump” for the pulmonary circulation.

Candidates for the Fontan procedure must be carefully selected to give each procedure an optimal chance of succeeding. The ideal age for the Fontan operation remains a focus of debate despite advances in surgical techniques over the years. Optimal criteria for Fontan completion include normal systolic and diastolic ventricular function, unobstructed pulmonary venous return, near normal pulmonary vascular resistance (PVR), unobstructed PA flow, appropriately sized PAs, and absence of atriorecicular (AV) valve insufficiency or stenosis. The size and caliber of the pulmonary vessels and the functionality of the ventricle remain the most important criteria in the choice of patients for a successful Fontan operation.

Management strategies in the neonatal period are directed toward providing an adequate source of pulmonary blood flow using a surgically created aortopulmonary shunt (Blalock-Taussig shunt), ensuring systemic flow via a Norwood or Damus-Kaye-Stansel procedure and allowing for unrestricted...
Figure 1. Bidirectional Glenn Shunt: The superior vena cava is surgically anastomosed to the right pulmonary artery. RPA, right pulmonary artery; LPA, left pulmonary artery.

Figure 2. Atriopulmonary Fontan: The atrial septal defect is closed, and the right auricle is surgically anastomosed to the right pulmonary artery. RPA, right pulmonary artery; LPA, left pulmonary artery.
atrial mixing via an atrial septectomy. The first cavopulmonary connection is created in the first year of life via the bidirectional Glenn shunt (Figure 1). The Fontan circulation is completed by connection of the inferior vena cava (IVC) to the PA once growth of the pulmonary vasculature is appropriate, usually between 1 and 5 years of age. This staged surgical process serves to slowly acclimate the pulmonary vessels to the increased blood flow and the SV to decreased volume load in a stepwise fashion. The end result achieves a complete separation of pulmonary and systemic blood flow, and allows the SV to function solely as the systemic ventricle.4,7

Historically, the IVC connection was made by anastomosing the “ventriculized” RA to the PA in an attempt to maintain some pump function in the pulmonary circuit.4,12 This “old style”atriopulmonary (AP) Fontan (Figure 2) has since been replaced by the total cavopulmonary connections, which have the advantage of preserving energy and eliminating less effective blood flow. The lateral tunnel (LT) (Figure 3) and the extracardiac (EC) conduits (Figure 4) have shown improved survival and hemodynamic superiority over the AP technique.5,7 The LT operation was introduced in the 1980s and creates a path from the IVC to the PA using a prosthetic baffle sutured to a portion of the lateral wall of the RA.7 It has the advantage of being able to grow with the patient, but still assumes a significant risk of inducing atrial arrhythmias because of the suture lines in the atrial wall and pressure induced on the RA from venous return to the PA. The EC conduit was introduced in the early 1990s and uses a tube of synthetic graft material to connect the IVC to the PA, bypassing the RA entirely and minimizing risk of inducing atrial arrhythmias.8 However, this variant cannot grow with the patient and cannot be performed until the patient is large enough to receive an appropriately sized graft. Additional disadvantages of the EC Fontan include the potential for tunnel stenosis requiring stenting or surgical revision.9 Frequently, in high-risk patients, a small fenestration is created between the conduit and the pulmonary atrium to allow a residual right-to-left shunt, thereby limiting caval pressure and congestion, but increasing the preload of the systemic ventricle and cardiac output (CO) at the expense of mild cyanosis. Fenestrations may be electively closed via percutaneous catheter techniques. Low-risk Fontan patients can be managed surgically without a fenestration, thereby eliminating the need to close the fenestration if it persists over many years.

Fontan Physiology: An Interplay of Pulmonary Vascular Resistance, Ventricular Contractility and Cardiac Output

Unlike normal cardiac physiology, which functions ideally with balanced contributions of preload, afterload and contractility, the loss of ventricular contractility to the pulmonary circulation in the Fontan physiology results in CO that is almost entirely dependent on preload, which itself is dependent on PVR.5,10 Current estimates indicate that preload and CO at rest are reduced to approximately 70% of expected for body surface area following a Fontan operation.14 The most important variable in determining preload (and thus CO) is PVR, a concept that is supported by multiple studies on Fontan hemodynamics. The lack of pulsatility in the pulmonary circulation is thought to induce endothelial dysfunction, which leads to increased PVR. Such increments in PVR lead to decreased CO and exercise intolerance, increased risk of Fontan failure and decreased survival.10-12 In addition, nonpulsatile preload in the Fontan circulation is affected by the role of gravity on regional pulmonary blood flow. West et al divided the upright lung into 3 zones. The superior zone has no flow because the alveolar pressure is higher than the arterial pressure. The inferior zone has the maximum flow because the arterial and venous pressures are higher than the alveolar pressure. In between, the arterial pressure is higher than the alveolar pressure but lower than the venous pressure, causing the so-called waterfall phenomenon.12 This zone is likely to be smaller in Fontan patients whose “pulmonary vascular capacitance” is thereby reduced. The Fontan circulation often leads to a contractility-afterload mismatch, consisting of an increase in ventricular afterload and a lack of compensatory increase in contractility. In a biventricular circulation, CO and stroke work are maintained, despite increased ventricular afterload (eg, aortic stenosis and systemic hypertension) by increased ventricular contractility. This compensatory mechanism does not exist in the Fontan circulation and leads to decreased CO and stroke work.13,14 It should be emphasized that the driving force of the circulating blood volume between the systemic and pulmonary veins is the pressure gradient between central venous pressure and the left atrium (LA), assisted mechanically by the thoracic muscles and respiratory function.5

Ventricular function and contractility in the SV patient are often depressed, thought to be because of abnormal pre-Fontan development when the ventricle is subjected to large volumes and often high pressures following PA banding, leading to ventricular hypertrophy and dilation.15 The rapid reduction of preload that occurs after cavopulmonary connection results in an under-loaded ventricle, leading to a mismatch in diastolic volume and ventricular mass. Although hypertrophy may decrease over time following the Fontan operation, abnormal ventricular relaxation and decreased ventricular compliance persist, leading to a slow decline in diastolic function and CO with relatively well-preserved systolic function.10,15,16

Long-Term Complications in the Adult With Fontan Physiology

Functional Status and Exercise Capacity In the early stages following a Fontan operation, most patients report a satisfying quality of life and functional status.17,18 Maximal exercise capacity at baseline has been shown to be lower than expected compared with healthy individuals and progressively declines as Fontan patients age.19,20 Although the reasons for this decline are not well understood, predictors for poor functional status include time since Fontan surgery, right ventricular (RV) morphology, pre-Fontan end-diastolic pressure, and pre-Fontan oxygen saturations.21 Blaufox et al22 showed that in pediatric patients (6–18 years) after the Fontan procedure, a lower resting heart rate and a higher peak heart rate are each independently associated with better physical function as measured by anaerobic threshold and Child Health scores. However, these correlations are weak, suggesting that other factors may have a greater effect on the functional outcome of pediatric patients after the Fontan operation.22

PVR In the absence of the hydraulic force of the RV, Fontan circulation results in a paradox of systemic venous hypertension and PA hypotension. The absence of pulsatile blood flow and low mean pressure in the PA underfills the pulmonary vascular bed and increases the PVR. The PAs may often be abnormal (ie, small, discontinuous, or stenosed) and it is important to identify restricted blood flow to and from the lungs.23 It is well known that pulmonary over circulation leads to increased PVR and over time will lead to PA hypertension.
Figure 3. Lateral tunnel Fontan. RPA, right pulmonary artery; LPA, left pulmonary artery.

Figure 4. Extracardiac Fontan. RPA, right pulmonary artery; LPA, left pulmonary artery.
(PAH). The pre-Fontan surgical stages attempt to limit pulmonary blood flow either by PA banding or PA division with shunt placement. Maintaining a low PVR after the Fontan operation is crucial to its success, as this allows for maximal blood return to the pulmonary vascular bed in the nonpulsatile pulmonary circulation. As a result, the Fontan CO is driven by heart rate, stroke volume and contractility.

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Figure 5. Image from a transesophageal echocardiogram showing a large thrombus (arrow) in a 32-year-old patient with an atrio pulmonary Fontan.

Causes of increased PVR and subsequently decreased CO include mechanical obstruction of the Fontan circuit (ie, thrombus, pulmonary stenosis) and PA vasoconstriction. Mechanical obstruction is often amenable to repair via cardiac catheterization with stenting or angioplasty. Treatment of diffuse PA vasoconstriction is more complex, largely targeting the impaired production of vasoactive mediators such as nitric oxide and prostacyclin by the pulmonary vascular endothelium and overproduction of endothelin-1. Historically, patients have been minimally responsive to pulmonary vasodilators, although improved exercise capacity has been demonstrated with the use of sildenafil and inhaled iloprost. Further research to evaluate the benefits of PAH medications in the failing Fontan patient, either as a maintenance medication or as a bridge to transplant, is warranted.

Arrhythmias Atrial arrhythmias are one of the most common complications associated with the Fontan repair, affecting more than 50% of patients, often as early as 5 years following the surgery. This complication has been attributed to atrial dilation and hypertrophy, atriotomy and suture lines, and disruption of normal atrial blood flow during surgery. Incidence has decreased over the past 30 years as the surgical technique has moved away from the AP Fontan toward the LT and the EC conduit, both of which exclude the atrial cavity from the circulation. Overall, the EC conduit seems to have the lowest incidence of postoperative atrial arrhythmias, making it the surgery of choice in many centers. Rarely, atrial arrhythmias can recur, with access to the arrhythmia substrate via a transbaffle puncture may be considerably complicated by an EC conduit. The LT technique is a risk factor for the development of arrhythmias because of the suture lines placed inside the atrium.

Bradyarrhythmias have also been observed in patients undergoing the EC technique. By far, the most common arrhythmia is intraatrial re-entrant tachycardia (IART), which is thought to be caused by postoperative atrial scarring. Atrial fibrillation is a less common complication and more often associated with the LA. Often atrial arrhythmias are difficult to control using conservative treatment and can lead to progressive ventricular dysfunction.

Short-term treatment options are often limited to direct current (DC) cardioversion, as preload-sensitive Fontan patients respond very poorly to the rapid ventricular rate, particularly in the setting of high PVR and poor contractility. However, antiarrhythmic medications can also be effective in the hemodynamically stable patient. Long-term treatment options include radiofrequency ablation (RFA) and medication. RFA may be only temporarily effective, with new re-entrant pathways emerging from scar tissue and suture lines. Patients with AP Fontans who develop IART may experience the greatest benefit from Fontan conversion, atrial reduction surgery with RA Maze procedure. AV nodal ablation and pacemaker placement is considered a last resort for therapy-resistant IART.

Sinus node dysfunction is frequently seen because all Fontan operations involve surgery around the sinus node, and may directly damage the node or affect its innervation or blood supply. Damage to the sinus node will ultimately require epicardial pacemaker placement in symptomatic patients. Transvenous leads may be an option in the AP or LT Fontan patients, but are not feasible with the EC conduit because of the absence of a RA communication. Patients with heterotaxy syndromes and anomalies of the AV valve can also develop such arrhythmias. Ventricular arrhythmias leading to sudden death have rarely been reported in patients with SV physiology and may occur in the setting of progressive ventricular dysfunction. When atrial tachyarrhythmias are detected, underlying hemodynamic causes, such as obstruction of the RA to PA anastomosis, should be sought and anticoagulation pursued.

Thromboembolism Thromboembolism is a commonly encountered complication of the Fontan circulation, occurring in up to 20% of patients both early and late in the surgery.
increased risk is secondary to a variety of factors, including low flow states and venous stasis because of the loss of pulsatile flow to the pulmonary circulation and atrial arrhythmias. The Fontan circulation also produces a hypercoagulable state because of deficiencies of protein C, protein S, and antithrombin III. Increased platelet reactivity has also been recognized in patients with SV physiology. Venous thrombi complicate the pulmonary circulation by obstructing the Fontan circuit, which may lead to hemodynamic instability and increased PVR in the case of emboli reaching the pulmonary vasculature (Figure 5). They may also embolize through graft fenestrations and into the systemic arterial system. Thrombi originating from the systemic circulation (SV, ligated PA stump, atria) may embolize to the central nervous system causing stroke, to the coronary arteries leading to myocardial ischemia, or to the systemic circulation leading to various embolic phenomena. In addition, as many as 13–19% of patients experience “silent” emboli, the clinical significance of which is not yet known.

Consensus has not been reached on optimal medical management to reduce the risk of thromboembolism. Multiple studies have evaluated the use of anticoagulation and antiplatelet agents as prophylaxis against thromboembolic events without clear improvement in morbidity and mortality and without superiority of heparin or warfarin over aspirin. Current guidelines recommend either aspirin or therapeutic unfractionated heparin followed by vitamin K antagonists over no therapy. Treatment of confirmed thromboembolic events is recommended in accordance with established adult guidelines for the specific neurological event.

Liver Disease Prevalence of liver disease, even in well-compensated and asymptomatic Fontan patients, has not been well demonstrated, but seems to be more common than previously thought. The spectrum ranges from abnormal liver function tests and coagulation factors to fibrosis and even liver failure. Although the process of chronic liver injury is not completely understood, the mechanism is thought to be related to chronic hepatic congestion induced by the Fontan circulation, as well as pre-Fontan hypoxemic injury and during the multiple surgeries the patient undergoes early in life. Although most patients are asymptomatic, presenting complaints related to liver disease may include vague right upper quadrant pain, nausea, vomiting, or abdominal swelling related to ascites. Because of its association with hepatic congestion, hemodynamic assessment is required in any patient with ongoing liver dysfunction.

Evaluation of liver tissue has shown histopathologic abnormalities across the board in Fontan patients, even preceding the actual Fontan operation. The most common finding is some degree of liver fibrosis, but cirrhosis as well as portal hypertension, hypervascular nodules, and rarely hepatocellular carcinoma. Given the increasing morbidity associated with liver disease, identifying it early with appropriate ongoing surveillance is becoming an increasingly applied goal of many congenital cardiologists. Although liver biopsy is the gold standard for evaluating fibrosis, its invasiveness and risk of significant complications make it a less desirable screening and surveillance tool. Imaging has been shown to accurately identify structural liver disease, but not necessarily the degree or severity, and laboratory evaluation of serum biomarkers has been shown to correlate with the degree of fibrosis in various types of liver disease. However, no studies to date have accurately correlated imaging and laboratory findings with histopathology from liver biopsy specimens. This will be an important area of future research in developing screening guidelines for liver disease in adult patients with Fontan palliation.

Protein-Losing Enteropathy Protein-losing enteropathy (PLE) is one of the least understood complications associated with the Fontan operation, yet it is also one of the most significant in terms of its effect on mortality. It is defined as the loss of serum proteins into the gut as a result of a compromised intestinal barrier, which occurs in 3.7% of patients with Fontan-type surgery and is clinically characterized by fatigue, peripheral edema, pleural and pericardial effusions, ascites, and chronic diarrhea. The etiology of PLE is unproven, but thought to be related to low CO in combination with an increase in systemic venous pressure (specifically mesenteric) that leads to dilated lymphatics and loss of protein in the gut. The diagnosis has historically been associated with increased mortality, with survival at 5 years after PLE diagnosis being 50%, although this may have improved in the past 15 years with the advent of multiple treatment options for this complex problem.

Treatment of PLE can often be frustrating, with few treatment options proven to have significant benefit in reducing symptoms or improving mortality. Hemodynamic assessment via cardiac catheterization is recommended to evaluate for structural complications with the Fontan that may be amenable to directed intervention or for ventricular failure that may be optimized with medications. Atrial pacing to increase CO may be of some benefit in patients with sinus node dysfunction. If hemodynamic compromise is not found, the diuretic combination of furosemide and spironolactone is often the first-line treatment for mild PLE. Short-term symptomatic relief in patients with severe hypoalbuminemia may be attained with 25% albumin followed by furosemide for diuresis, although these effects cannot be maintained long term. Other medical options include use of subcutaneous heparin or systemic corticosteroids; these therapies have caused remission in specific cases, but an overall benefit has not been demonstrated in large cohorts, and significant side effects associated with each medication may limit their use. There have been anecdotal therapeutic successes with approaches involving dietary modifications with high-protein and high–medium-chain triglycerides, afterload reduction agents, inotropic agents, octreotide and prednisone.

Surgical options for treating PLE include Fontan conversion in patients with an AP connection, fenestration creation, and cardiac transplantation. Cardiac transplantation is the only intervention that is a consistently proven “cure” of PLE, with very low rates of recurrence demonstrated post-transplant.

Systemic Ventricular Dysfunction Physiologic changes affecting the systemic ventricle, as described before, frequently lead to HF, prompting management strategies to focus on correcting and preventing ventricular dysfunction. Prior studies have suggested that the systemic left ventricle (LV) tends to have better preserved function than the RV, with the hypothesis that the RV is not physiologically designed to pump against higher systemic pressures; however, this observation has not necessarily affected survival or ventricular function in the long-term.

Effective medical therapy for ventricular dysfunction is well established for adult patients with HF in the absence of congenital heart disease (CHD), and is often applied to patients with SV physiology after extrapolation from adult HF data. Medications used in chronic HF, such as angiotensin-converting enzyme (ACE) inhibitors and β-blockers, have theoretical benefits for patients with SV dysfunction, but there is only limited evidence in the literature to support this theory. Beta-blocking agents inhibit neurohumoral activation in chronic HF and when used in conjunction with ACE inhibition.
can result in improved ventricular ejection fraction (EF), reduced symptoms and lower mortality.24 The use of carvedilol has been demonstrated to improve EF as well as NYHA class in patients with a Fontan, though further studies are required to determine if the long-term use of beta-blockers will be of benefit to the patient with failing Fontan physiology.35,65 Several studies have demonstrated elevated levels of antidiuretic hormone, aldosterone, renin, and angiotensin in patients with Fontan circulation, leading to salt and water retention.32 Diuretic therapy with loop diuretics and aldosterone antagonists has been described as commonly used to treat fluid overload related to ventricular dysfunction.65

There is a role for the use of intravenous inotropic postoperatively in pediatric patients with single ventricles, particularly phosphodiesterase inhibitors, which provide inotropy, lusitropy, and vasodilatory properties that would appear beneficial to the failing Fontan patient.65 Chronic intravenous therapy with milrinone has been described, despite the absence of long-term supportive data in patients with failing Fontan physiology with ventricular dysfunction.70 Similarly, nesiritide, a recombinant B-type natriuretic peptide, is currently used with success in acute decompensated HF in adults;71 however, there is very limited experience in pediatric patients with acute HF, with no data on its use in chronic HF in adults with SV dysfunction.

There are multiple studies that have repeatedly shown that cardiac resynchronization therapy (CRT) improves measures of cardiac function and clinical status in adult patients with moderate-to-severe HF and a prolonged QRS interval.72,73 CRT reduce the degree of ventricular dyssynchrony (as evidenced by a shortened duration of the QRS interval), and increase in the left ventricular EF, a decrease in the LV end-diastolic dimension and in the magnitude of mitral regurgitation in patients with biventricular anatomy.72,74 CRT with multisite pacing was found to improve the myocardial performance in Fontan patients in acute postoperative settings; however, its role is unclear in chronic Fontan patients with progressive myocardial dysfunction.75

With improved medical therapies, late deaths have diminished dramatically from 25% early in the experience to 5% over the past decade.7 However, optimal medical management of the failing Fontan has generally been anecdotal and continues to vary widely among academic centers.21

**Hypoxemia/Shunts** Fontan patients are mildly hypoxic with oxygen saturations in the low 90s, even after full repair and closure of atrial level shunts.76 This slight desaturation is secondary to coronary sinus drainage into the LA, pulmonary arteriovenous malformations, and venovenous collaterals that drain to the pulmonary veins or directly to the LA.77 More significant desaturation may be attributable to surgically created fenestration or baffle leaks. These shunts may be identified via catheterization techniques or echocardiography and managed with transcatheter device therapy as indicated. Other causes include pulmonary pathology that includes a restrictive respiratory function pattern, hepatic venous connection to the coronary sinus or LA, right-to-left interatrial shunting via small thebesian veins, and diaphragmatic paresis.33

**Plastic Bronchitis** A very rare but serious complication of the Fontan circulation is plastic bronchitis, the formation of mucoid bronchial casts caused by leakage of lymphatic fluid into the airway mucosa. Casts vary in size from small plugs that can be expectorated to large branching structures that fill the tracheobronchial tree. Depending on the extent of cast formation, patients may present with symptoms ranging from a productive cough and mild dyspnea to respiratory distress, failure and often death.78 It seems plausible that plastic bronchitis in patients with Fontan physiology is similar to PLE, having a multifactorial pathogenesis with genetic factors, inflammation, and elevated systemic venous pressures all contributing to the pathogenesis and eventual outcome.

The incidence of plastic bronchitis remains low and an effective treatment strategy has not been established. A number of therapies have been tried with mixed success, including vasodilation with sildenafil or bosentan, destruction of casts with aerosolized fibrinolytics, cast expectoration with mucolytics, and immunosuppression with inhaled or systemic steroids.79 Similar to PLE, attempts to optimize Fontan hemodynamics with directed interventions, surgical Fontan revision, or cardiac transplantation may also be used to treat plastic bronchitis.

**Pregnancy** As survival of Fontan patients improves, many women are reaching child-bearing age and becoming pregnant. During pregnancy, the cardiovascular system undergoes multiple physiologic changes, including doubling of intravascular volume and CO, and a decrease in SVR. These changes peak around the third trimester, primarily between 24 and 30 weeks’ gestation. If a patient’s hemodynamics remain optimized, pregnancy and delivery are usually tolerated well. Nonetheless, the risks to both mother and fetus in this patient population are best assessed on an individual basis.

The most commonly encountered complication of Fontan patients during pregnancy is atrial arrhythmias. Other notable morbidities include a decline in functional status, increased thromboembolic risk and an increased risk of HF. An increased rate of miscarriage has been observed as well.80,81 Such patients should be managed via a multidisciplinary approach that includes high-risk obstetric and anesthetic care, specialized adult congenital cardiology assessment with close follow-up, and genetic counseling.82

**Fontan Failure** The term “Fontan failure” is used to describe the constellation of complications described leading to late morbidity and mortality following the Fontan operation. Although this clinical picture was previously seen much earlier in cases of the AP Fontan, the introduction of the total cavopulmonary connection via the LT and EC conduit techniques has markedly improved outcomes.24,82 Fontan failure is characterized by a low CO state, markedly decreased exercise tolerance, and persistent and difficult to treat comorbidities such as recurrent tachyarrhythmias, edema, and PLE. It is historically resistant to medical therapy, although the use of medications may help bridge patients to a more definitive surgical solution.77

**FontanRevision** Many adult Fontan patients who have survived into their third or fourth decades invariably undergo the AP connection. Many of these have benefited from Fontan revision, a surgical intervention that includes conversion of pulmonary venous return to total cavopulmonary anastomosis via a LT or an EC conduit, debunking of the dilated RA and removal of atrial thrombi, epicardial pacemaker placement, surgical cryoablation, atrial scar removal, and often a modified right atrial Maze procedure.2,23 Left-sided atrial Maze procedures are not routinely performed, primarily because of the long ischemic time.22,34 Perceived advantages of Fontan revision include a lower incidence of atrial arrhythmias and thrombosis related to atrial distension and improved hemodynamics.33 There has been improved exercise tolerance, improved NYHA class, decreased incidence of late arrhythmias and sinus node dysfunction and avoidance of thromboembolic risk associated with intracardiac prosthetic material.35,85,87

**Mechanical Assist Devices and Cardiac Transplantation** In
Despite surgical advances that have led to markedly improved morbidity and mortality among Fontan recipients, there remains an almost inevitable late decline of the Fontan circulation. When medical therapy and other surgical interventions fail, cardiac transplantation has become an increasingly utilized and successful solution for the failing Fontan. Cardiac transplantation provides an option for treating these patients; however, the indications for, timing of, and outcomes after transplantation remain undefined.

Survival following orthotopic heart transplant in patients with the Fontan diagnosis is significantly lower than that of patients without CHD, as well as non-Fontan patients with CHD, although recent survival has improved as reported from a single institution. The highest risk for mortality appears to be in patients who are transplantation because of early Fontan failure, with much better outcomes observed in patients with late Fontan failure.

Increased survival in the recent era of cardiac transplantation in patients with CHD has been attributed to improved patient selection, as well as advances in critical care management. Fontan failure in the absence of ventricular dysfunction, mechanical ventilation at time of transplant, and listing for transplant soon after the Fontan operation appear to predict worse outcomes and higher mortality post-transplant.

Though transplantation remains the standard of care to improve survival and quality of life when conventional medical and surgical therapies have failed, it remains limited by the scarcity and unpredictability of donor organ availability. As such, the use of ventricular assist devices (VADs) as a bridge to transplant is gaining popularity. Recent advances in pulmonary vasodilators and implantable devices (eg, axial flow blood pumps) may have a major effect on future transplantation indications in patients with failing univentricular physiology. Based on data from the Pediatric Heart Transplant Study (PHTS) and Cardiac Transplant Research Database, the most common cardiac lesion from 6 months of age to adulthood necessitating a cardiac transplant is SV anatomy. However, it has been a disappointing endeavor, with only 50% survival when compared to overall pediatric and adult VAD survival of 70–86%. The approach of VADs as destination therapy is expanding in adults with CHD who have end-stage HF, though it remains reserved for patients with significant comorbidities or other obstacles precluding transplantation.

**Conclusions**

The Fontan operation is the repair of choice for patients with a variety of congenital heart lesions with a functional SV. Suitable patient selection and selection of the appropriate surgical modification are crucial for ensuring the best long-term outcome. It remains a palliative, complicated operation with a high incidence of long-term complications. Despite proper selection criteria, PLE, arrhythmias, thromboembolic concerns, liver dysfunction and ventricular failure lead to therapeutic and management challenges. Despite careful long-term follow-up, there remains continual but late attrition of patients from long-term complications. Management of these patients includes a detailed assessment to treat any correctable lesions, management of arrhythmias, treatment for PLE and plastic bronchitis, manipulation of systemic and pulmonary vascular resistances and Fontan conversion of the less favorable AP connection to an EC or LT cavopulmonary connection together with arrhythmia surgery. There is a growing role of VADs in adults with end-stage HF with complex CHD, although its primary purpose is reserved for cases of significant comorbidities that preclude a cardiac transplant. The adult patients with complex failing Fontan physiology are only growing in numbers, with cardiac transplantation being the only successful long term definitive palliation in such patients.

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