Venous shunts are surgical reconstructions involving an anastomosis between one or both venae cavea to one or both pulmonary arteries (PAs), and were developed to palliate infants born without two ventricular chambers. Staging venous shunts are typically performed during infancy and childhood, and include the older Glenn shunt, which anastomosed the superior vena cava to the PA, and the more recent bidirectional cavopulmonary shunt, which anastomosed the superior vena cava to the PA, leaving both PAs in continuity. Subsequently, a Fontan-type repair is performed to anastomose the inferior vena caval flow to the PAs, resulting in a circulation without a subpulmonary ventricular pumping chamber.

The introduction of venous shunts to the management of patients with univentricular hearts has extended survival for patients with the most complex forms of congenital heart disease to greater than 75% by 25 years following surgery. In general, these procedures are applied to patients with "functionally univentricular physiology". As first performed in 1968, the Fontan surgery channeled systemic venous return to the PAs, with the inclusion of inflow and outflow prosthetic valves. The Fontan palliation was initially applied to patients with tricuspid atresia and anatomic single left ventricles (LVs), whose mortality without surgery was more than 90% in the first year of life. The Fontan principle was extended gradually to more complex forms of functionally univentricular anatomy, including unbalanced biventricular anatomy and later to patients with single right ventricles (RVs) (Fig. 12.1). In centers seeing adults with congenital heart disease, the Fontan palliation represents about 5% of patients. Due to the complexity of their cardiac anatomy, the insidious nature of disease progression, the high incidence of arrhythmias, and the challenges of assessing the Fontan "circulation" as opposed to traditional cardiac assessment of ventricular contractility and valve abnormalities, the patient with Fontan palliation poses unique and growing challenges to optimal care.

**Surgical Techniques for Patients With Univentricular Physiology**

To survive the neonatal period, infants with univentricular physiology require adequate pulmonary flow and protection from excessive pulmonary flow, adequate atrial-level mixing without restriction at the atrial septal level, and relief of aortic outflow obstruction when present. As a first stage of surgical interventions, slightly more than 80% of infants undergo surgery for pulmonary flow modification: augmentation of pulmonary flow with systemic-to-pulmonary shunts in 63% to 80% or restriction of pulmonary flow with PA banding in 12% to 25%. Surgical atrial septectomy to allow adequate atrial mixing without pulmonary venous hypertension was required in up to 14% of patients. Repair of the aortic arch was needed in 7% to 10% of patients subsequent application of Fontan repairs in the 1980s to patients with hypoplastic left heart syndrome required reconstructive surgery of the ascending aorta (Ao) in all of these patients (Damus-Kaye-Stansel or Norwood procedures).

Once pulmonary blood flow and atrial-level mixing are stabilized, the introduction of the classic Glenn shunt (superior vena cava to right PA) or the bidirectional cavopulmonary anastomosis has been used as the second stage of surgery prior to the Fontan repair, often with associated PA augmentation performed (Fig. 12.2). In 1958, Glenn published his series of shunts from the superior vena cava to the right PA, whereby the right PA was divided and anastomosed to the right side of the superior vena cava after ligation and division of the azygos vein. The superior vena cava was then ligated at the cavoatrial junction. This operation quickly gained the eponym the Glenn shunt, and implies that the right and left PAs are not in continuity with each other. The early effects of the unidirectional Glenn shunt showed that it was a relatively simple operation, improved oxygen saturation, and provided excellent palliation for many patients. Unfortunately, late deterioration occurred because of decreased effective pulmonary blood flow, resulting from the development of endovascular pulmonary venous and pulmonary arteriovenous malformations. The increased venous pressure to the lungs caused systemic venous collateral vessels to develop, thereby shunting blood flow away from the PA. Pulmonary arteriovenous malformations were initially attributed to lack of pulsatile flow, but later found to result from the exclusion of hepatic venous flow from the pulmonary circulation.

The development in 1989 of anastomosis of the superior vena cava to the main PA without branch PA division took on the name bidirectional Glenn (or bidirectional cavopulmonary) shunt. The bidirectional Glenn shunt is performed by anastomosing the superior vena cava to the right branch of the PA using fine sutures and then dividing the proximal main PA, leaving the branch PAs in continuity. The introduction of cavopulmonary shunt surgery between neonatal surgery and the Fontan repair of childhood coincided with a marked
improvement in early survival after the later Fontan surgeries, by allowing stepwise diversion of systemic venous return from the upper body directly to the PAs. Subsequently, at the time of Fontan surgery, acute venous volume unloading (which results from the complete separation of pulmonary and systemic flows) is avoided, allowing venous function to adapt to the changed loading conditions. The bidirectional cavo-pulmonary anastomosis improves systemic arterial oxygen saturation without increasing pulmonary vascular resistance and maintains continuity of the PAs but can also lead to development of systemic venous collateral vessels and pulmonary arteriovenous malformations. For these reasons, cavo-pulmonary shunts are usually short-term, palliative procedures performed in children (usually <2 years) who are being prepared for an eventual Fontan procedure. Simultaneously, the age at which Fontan completion surgery is performed has decreased substantially to limit the period of cyanosis and volume overload and is now generally performed before the age of 2 years, compared with ages 5 to 8 years, which was customary three decades ago.

The third stage of surgical intervention is the Fontan operation and its many modifications, one of which is the Kreutzer procedure (Fig. 12.3). The Fontan repairs are characterized by complete separation of the pulmonary and systemic circulations, and depend on high systemic venous pressure and low PA pressure/resistance to propel nonpulsatile blood flow through the pulmonary circulation without the benefit of a pumping chamber. Fontan and Kreutzer published their findings within 2 years of each other and together proved that systemic venous pressure would be sufficient to propel blood flow through the pulmonary circulation in the absence of a subpulmonary ventricular pump as long as other hemodynamic considerations were optimal. It was Fontan’s thought that the right atrium, which is quite thickened in patients with tricuspid atresia (Fig. 12.4), could be made to function as an RV; hence, the original approach for inflow and outflow bio-prosthetic valves. Kreutzer’s contribution was the direct atrio-pulmonary anastomosis, which eliminated the need for interposed venous valves, and resembles more closely the type of cavo-pulmonary connections that are encountered today. Between 1970 and the early 1990s, the right atrium-to-PA direct connection (both retroaortic and anteroaortic) became standard therapy, as did the Björk modification in which the right atrial appendage is anastomosed to the right ventricular outflow tract or to the main PA (Fig. 12.5). Due to the compliance and growth potential of atrial tissues, progressive right atrial dilation, venous stasis and thrombosis, and atrial re-entrant tachycardia developed in patients with atrio-pulmonary connections, especially those individuals with anteroaortic connections. The gradually enlarging right atrium created a size mismatch to the pulmonary anastomosis, with excessive “power loss” or turbulence of passive venous flow to the PAs, as well as compression of pulmonary venous return from the right lung (see Fig. 12.5). The desire to limit atrial distortion and thus avoid obstruction to atrioventricular valve inflow led to the development of the total cavo-pulmonary lateral tunnel connection, which was demonstrated to have superior blood flow characteristics and allowed unimpeded pulmonary venous return to a right-sided atrioventricular valve. The increased suture load used in the right atrium to construct the lateral tunnel was not initially recognized as a future arrhythmogenic consequence of the procedure. Further surgical modifications were developed to allow application of the Fontan surgery to patients with hypoplastic LVs and to limit the development of atrial arrhythmias, (see Fig. 12.5).

The latest modification of the Fontan operation was the extracardiac total cavo-pulmonary connection, which was introduced by Mancielliet al. in 1989. He and many colleagues showed that an extracardiac tube graft could link the inferior vena cava directly to the PA without the obligatory suture load within the right atrium. Given the relative technical ease of the extracardiac operation, often requiring no cross clamp and sometimes being performed without cardiopulmonary bypass, ideally the surgery would be associated with a decreased incidence of atrial arrhythmias and limit the potential for size mismatch between the enlarging right atrium and PAs. To achieve optimal flow dynamics, the anatomy of the tube graft to the inferior vena cava the PA needs to be offset from the superior bidirectional Glenn anastomosis, avoiding collisioin of blood streams; reconstruction of the left PA is often needed. Attention to each of these technical details is crucial to the long-term flow dynamics. The material that was used for the extracardiac connection has changed over time: aortic homografts were initially used but were prone to calcification and induced pro-eroflA thrombosis. A concern for a population that would potentially require later heart transplantation. As a result, the 16-20 mm polytetrafluoroethylene (Gore-Tex) tube became the graft of choice for initial extracardiac connections, which is not prone to calcification. The extracardiac connection
has the advantage of improved flow dynamics, but does not have growth potential commensurate with body growth, and is noncompliant. As the body surface area of the patient increases and flow increases, the extracardiac connection becomes a potential source of increased pathway resistance and hemodynamic inefficiency, which has been demonstrated by magnetic resonance imaging (MRI) studies. Due to the restrictive size of the graft, the ensuing decrease in ventricular filling and preload may adversely affect ventricular performance. In this scenario, one can expect to see an increased incidence of ascites and protein-losing enteropathy (PLE) at a younger age compared with older extracardiac Fontan patients, presumably with a decreased incidence of atrial reentry tachycardia.

**FONTAN SURGICAL SEQUELAE**

Systemic venous pathway obstruction can result from stenotic atriovenous connections; lateral tunnel or extracardiac graft stenosis, calcification, and size restriction; superior vena cava stenosis; and peripheral PA stenosis. Any obstruction to the passive venous flow to the lungs leads to hepatic congestion, atrial enlargement, and fibrosis with thrombus formation (Fig. 12.6).

**LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION**

Left ventricular outflow tract obstruction occurs most commonly in patients with (1) a double-inlet LV and transposition of the great arteries with a closing bulboventricular foramen producing subaortic stenosis, (2) staged correction of hypoplastic left heart syndrome who develop recurrent coarctation or increased aortic stiffness from the use of prosthetic or homograft material, and (3) anatomic problems from the various forms of Damus–Kaye–Stansel operations causing supraaortic stenosis. Associated lesions that negatively impact the Fontan circulation include aortic aneurysm, residual atrial and ventricular shunts, discontinuous PAs, and the development of venovenous collaterals to the left atrium (LA).

**FONTAN REVISION**

Fontan revision refers to a surgical intracardiac intervention in a Fontan patient, such as subaortic resection, valve repair, or enlargement of PAs, leaving the same form of atriovenous connection in place. In the dilated single ventricle with declining systemic function, atrioventricular valve annular dilatation and regurgitation may be present. By raising left atrial pressure and pulmonary venous pressure, moderate or greater atrioven-tricular valve regurgitation results in further decline of cardiac output; valve repair poses the risk of worsening ventricular function by removing the afterload reduction provided by valve regurgitation. The incidence of significant regurgitation is highest with common atrioventricular valves, followed by tricuspid valves; mitral valve repair in older Fontan patients show inconsistent results and may require prosthetic valve replacement.

**FONTAN CONVERSION SURGERY**

Technically, "Fontan conversion" refers to the replacement of an atrioventricular anastomosis with an extracardiac total cavopulmonary connection, usually in association with arrhythmia surgery. Fontan conversion operative technique consists of three components: takedown of the existing atrioventricular communication and repair of associated hemodynamic lesions, arrhythmia surgery, and epicardial pacemaker implantation. The first stage is challenged by the extensive chest adhesions from multiple prior sternotomies and avoidance of unwanted atrial or aortic entry during sternotomy. The enlarged right atrial anterolateral wall is widely resected, followed by take-down of the existing atrioventricular connection. An extracardiac polytetrafluoroethylene (Gore-Tex) tube graft (usually 24 mm in diameter) replaces the atrioventricular connection, anastomosed inferiorly to the inferior vena cava and superiorly to the underside of the PA. The atrial septum is widely resected to form a single atrium to receive pulmonary venous inflow. Additional right and/or left pulmonary arterioplasty may be necessary, or pulmonary reconnection in cases with a right Glenn shunt and an atrial left PA connection. The coronary sinus may require unroofing in patients with left pulmonary vein compression from massive coronary sinus dilatation.

Right atrial macro-reentry tachycardia is predominantly present and is addressed using a modified right-sided maze procedure (Fig. 12.8). In some patients, the atrial reentry tachycardia is present in the LA, and increasing numbers of adult Fontan patients develop atrial fibrillation in addition to right atrial tachycardia. In the presence of atrial fibrillation or left atrial reentry tachycardia, or in patients with significant left-sided atrioventricular valve regurgitation, the left atrial
Fontan Cardiac Physiology

The systemic venous circulation in the Fontan circulation is comprised of three distinct channels: superior vena cava flow, inferior vena cava flow, and splanchnic flow. Elevated pressures in the superior vena cava impair lymphatic reabsorption, which may contribute to increased pulmonary vascular resistance, development of collateral flow, and unacceptably high systemic venous return to the heart. Arterial and splanchnic flow are generated through the splanchnic system, which is responsible for maintaining systemic perfusion. The Fontan circulation results in an increased pulmonary venous pressure, which may lead to pulmonary hypertension and right ventricular failure. The Fontan circulation also results in a decreased cardiac output, which may lead to systemic hypotension and decreased tissue perfusion. The Fontan circulation is a palliative surgical procedure, and patients require lifelong medical and surgical management to maintain Fontan circuit patency and prevent complications.
end-diastolic pressure, will further decrease transmural flow, resulting in a continuously declining cardiac output. The body tolerates only a small range of increased pressures in the systemic veins (between 12 and 20 mm Hg) and on a small range of ventricular filling pressures; these leaves the impedance of the neonatal system as the major determinant of output.

The single ventricle may undergo variable years of intense cyanoisis and hyperthermia from volume overload prior to Fontan surgery and has developed increased mass and fibrosis, which may be ongoing in the setting of aortic stiffness or obstruction. The ventricle, which is the typical bottleneck in a biventricular circulation, no longer controls cardiac output and cannot decrease the degree of systemic congestion. However, the single ventricle can make the circulation worse: any increase in filling pressure will result in more systemic venous congestion and less cardiac output.

Ventricular systolic function has been shown to remain relatively stable in adulthood in the single-ventricle population, in part due to the development of atrial tachycardia or significant atrioventricular valve pathology.33-35 However, ventricular diastolic dysfunction progresses with age, with gradual increase in filling pressure. Ventricular extension or ventricular outflow tract obstruction results in increased ventricular afterload, ventricular hypertrophy, decreased compliance, and ventricular hypertrophy. Decreased ventricular compliance is associated with increased end-diastolic pressure and diastolic dysfunction, which have a negative back-pressure effect on the Fontan dam, leading to the cascade of progressive Fontan circulatory dysfunction. Obesity contributes significantly to decreased pulmonary compliance as well as increased systemic resistance and ventricular hypertrophy, and is directly detrimental to Fontan hemodynamics. Finally, the gradual increase in pulmonary resistance with normal aging contributes to complicated Fontan circulation with age. To mitigate these competing negative interactions, the future mechanical support of Fontan patients would lower caval pressure and produce increased pulmonary arterial pressure with pulsatile flow. In the meantime, the clinician is challenged to monitor the potential effects of this circulation and improve flow dynamics as feasible, with particular attention to each component of the circuit.

### Clinical Status and Monitoring of the Adult Fontan Patient

The management of adult Fontan patients has, as its goal, the optimization of the circulation to prolong the satisfactory longevity of the unique Fontan physiology. Early anatomy and surgical characteristics, such as ventricular morphology, heterotaxy, prior PA or atrioarch reconstruction, older age at primary Fontan, atrioventricular valve regurgitation or repair, and prolonged postoperative pleural effusions are important predictors of late Fontan adverse outcomes.

To understand the anticipated challenges of the Fontan patient, it is important to understand the many anatomic and surgical variables of the individual patient, as well as the changes in physiology with age (Table 12.1). Among current adults with Fontan circulation, approximately 50% to 75% have a single LV, 30% to 45% have a single RV, and biventricular complex anatomy including heterotaxy syndrome affects up to 15% of patients.5,32,33,41-43 The most common forms of Fontan surgeries encountered in current adults are atrio pulmonary anastomosis in 20% to 60% of patients, lateral tunnel repairs in 25% to 45% of patients, and extracardiac total cavopulmonary connections in 11% to 20% of patients.5,32,33,41,42,43,44,45 The age of the adult patient is an indicator of the more likely form of prior Fontan surgery because the atrio pulmonary anastomosis was performed between 1960 and 1995, the lateral tunnel repair was introduced in 1988, and the extra cardiac conduit became widely used in the mid-1990s. See Table 12.1 for outcomes reported with adult Fontan populations.

### PHYSICAL FINDINGS

See Table 12.3. In general, Fontan patients are slightly shorter than average adult height, with similar prevalence of overweight and obesity.45 Recent data suggest increased morbidity and mortality in Fontan patients with elevated body mass index (BMI),44,45 likely related to decreased pulmonary compliance, ventricular hypertrophy, diastolic dysfunction, and elevated systemic vascular resistance associated with obesity. Many older Fontan patients have progressive cyanosis, which may be more pronounced with exertion. Central cyanosis may be due to atrial level fenestrations, intrapulmonary shunting (arterioarterial pulmonary malformations, ventilation-perfusion mismatch), or venous collaterals often to the LA, which develop as "pop-offs" due to elevated central venous pressure. Hepatomegaly is generally present, frequently with splenomegaly. Abdominal fullness or ascites may also be present. Lower extremity venous insufficiency is present in as many as 60% of Fontan adults, manifests as discoloration, brawny induration, or significant varicocities, and may be related to prior catheterizations and deep venous thrombosis.45 The finding of obesity, resting desaturation, ascites, or advanced lower extremity venous changes are of significant concern and should prompt efforts to improve cardiovascular function.

### EXERCISE CAPACITY

Exercise in the Fontan patient is characterized by absence of pulsatle flow, and absence of episodes of high flow and high vessel recruitment. Increases in cardiac output for the Fontan patient during exercise rely heavily on increases in heart rate, and are dependent on increased stroke volume. High-intensity exercise in Fontan patients is associated with systemic venous hypertension and renal and cerebral deoxygenation.65 By adulthood, exercise tolerance is reduced to approximately 40% of predicted, with average peak oxygen consumption in the range of 22 to 25 ml/kg per minute, declining by about 1.25%
to 2.6% per year. Nonetheless, in the Euro Heart Survey of adults with congenital heart disease, 91% of adult Fontan patients were considered in New York Heart Association (NYHA) Class I or II. On subjective health questionnaires (SF-36), Fontan patients report high scores, indicating that they do not perceive limitations in their physical and social activities, which did not correlate with their objective exercise testing results. These data may reflect the reality that it is not typical for a Fontan patient to complain of fatigue until advanced stages of circulatory decline; unlike other forms of heart disease, these patients have lived their entire lives having never experienced truly optimal cardiac output and have no "normal" basis for comparison. Daytime napping may be an indicator of changing functional status. Despite exercise studies do not provide information regarding the presence of atrial versus ventricular pacing.

NEUROLOGIC OUTCOMES
Cerebrovascular events or transient ischemic attacks are reported in 12% of adults with univentricular physiology, and are thought to be related to right-to-left shunting, atrial arrhythmias/thrombosis, and hematologic abnormalities. Abnormal posterior circulation anatomy has been identified in Fontan patients, with brainstem ischemia following surgery indicating the need to maintain high perioperative perfusion pressure. Depression was self-reported in 23% of 139 patients undergoing Fontan conversion, similar to 33% mood/anxiety disorders reported in adults with congenital heart disease.

PREGNANCY
Subfertility or infertility is increased in the woman with Fontan circulation, and pregnancy is associated with complications including bleeding and arrhythmias in 10% of pregnancies. Miscarriages occur in 22% to 50% of pregnancies, with prematurity in 71% of live births, low birthweight infants in 12%, and increased risk of congenital heart disease in offspring. Whether the impact of volume overload on the maternal circulation will hasten circulatory failure in the mother remains to be demonstrated. For these reasons, preconception counseling is advised with consideration for surrogacy currently recommended with increasing frequency.

Major Adverse Events
The Fontan state, in which the force driving pulmonary blood flow is solely or largely a residue (in the systemic venous pressure) of the main ventricular chamber's contractile force, imposes a gradually declining functional capacity and precludes late death after an initial period of often excellent palliation. The cause of these trends is speculative. Overall freedom from late adverse events, defined as Fontan failure/transplant, supraventricular tachycardia (SVT), thromboembolism, PLE/plastic bronchitis, NYHA class III/IV, or pacemaker at 25 years following surgery was 29% in a comprehensive long-term follow-up study of 1006 Fontan patients in Australia and New Zealand. The development of atrial tachycardia in adults with atrioseptopulmonary Fontan and requiring diuretic therapy for congestive heart failure was associated with 3-year mortality of 25% in a large multicenter study.

ATRIAL TACHYCARDIA
Atrial tachycardia occurs in over 40% of atrioseptopulmonary Fontan patients by 20 years postoperatively and steadily increases to over 70% by 25 years. The comparable incidence of atrial tachycardia in patients with lateral tunnel or extracardiac conduits is not yet known for this time frame but is approximately 28% at 15 years postoperatively and is likely to increase with longer durations of follow-up. Risk factors for the development of atrial tachycardia include atrial isomerism, lateral tunnel syndrome, atrioseptopulmonary Fontan, sinus bradycardia, advanced age at Fontan surgery, and years since surgery. With longer-term follow-up, years since surgery appears to be the most significant risk factor, rather than type of Fontan repair. The development of atrial tachycardia is associated with increased hospitalizations, right atrial thrombus formation, congestive heart failure, atrioventricular valve regurgitation, thromboembolic events, and mortality. The mechanism of atrial tachycardia is fractionated (atrial flutter or atrial reentrant tachycardia) in about 75% of patients, with focal atrial tachycardia present in 3% to 10%; the incidence of atrial fibrillation is steadily increasing. There is evidence to suggest that atrial fibrillation and focal atrial tachycardia are more likely to be present in lateral tunnel repairs. Similarly, extracardiac

FIGURE 11.11 Freedom from adverse events, including Fontan failure, supraventricular tachycardia, stroke, pulmonary embolism, pacemaker insertion, approximately 30% at 20 years. CI, Confidence interval. (From D’Udekem Y, Yang XR, Wu JS, et al. Redefining expectations of long-term survival after the Fontan procedure: twenty-five years of follow-up from the entire population of Australia and New Zealand. Circulation. 2014;131[11 suppl 1]:552-558.)


Fontan repair may result in an increase in focal atrial tachycardia as opposed to atrial flutter or atrial fibrillation. During pacemaker interrogation or ambulatory monitoring, 24 Ventricular fibbrillation or resuscitated cardiac arrest have been reported in 4% of patients. In contrast to patients with repaired tetralogy of Fallot, it is highly unusual for a Fontan patient to present with sustained ventricular tachycardia, unless prior ventriculotomy has been performed or an ablation channel has been created. If sudden death is increasingly reported in a Fontan population, multiple other reports of this outcome have been recognized, including following successful heart transplantation. 105 The risk of cardiac arrest is 6% or 10% with increasing postoperative duration greater than 16 to 20 years as the most significant predictor of cardiac complications. 105 Liver imaging with ultrasound is recommended at least annually, and the presence of hyperenhancing nodules requires more frequent monitoring. Hyperenhancing nodules may be indistinguishable from carcinoma with imaging techniques and may require biopsy to identify the pathology. Annual monitoring with serum alpha fetoprotein levels has enabled early detection of two cases of carcinoma in our center. The outcome of treatment strategies (including cryosurgery for hepatocellular carcinoma) is improved by early detection of single or small lesions.

**Therapeutic Options**

**MEDICAL THERAPY**

Medical therapy to improve long-term Fontan hemodynamics has traditionally extrapolated efficacy data from patients with two-ventricle circulations, using systemic dilators including angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers, beta-blocking medications, and pulmonary vasodilator medications. 106 In Fontan patients, a failing biventricular circulation is quite different from a cavopulmonary circulation: the critical bottleneck in a biventricular circulation typically lies in the systemic ventricle, whereas in Fontan physiology the bottleneck is situated in the Fontan portal system itself. Risk factors for development of congestive circulatory failure in Fontan patients include a tall patient, prior ventriculotomy, volume overload such as from major aerotransluminal flow, and chronic hyoxia, which may be related to venous collaterals.

Two recent reviews of drug therapy in Fontan patients have emphasized the lack of efficacy of angiotensin-converting enzyme (ACE) inhibition therapy in single ventricle patients. 107,108 The data base supporting ACE inhibition as an important role of the renin-angiotensin system in the Fontan circulation. The use of ACE inhibitor is ideally reserved for symptomatic patients. Additional medical therapies that have shown promise include beta-blockade, 109,110 and anticoagulant therapy. 111,112 Although, as Fontan patients are chronically volume depleted in patients with severe hypoxemia, arterial vasoconstriction, afterload reduction may result in hypotension without increase of cardiac output, and may increase right-to-left shunting. In patients with cirrhosis and ascites, beta-blocker usage has been found to be useful in Fontan patients, and varices, ascites, splenomegaly, and thrombocytopenia (VAST) scores. 113 Liver biopsy has not been useful in Fontan patients for predicting disease severity or mortality as opposed to cardiac output. 114,115 Mectilation of liver stiffness using transient elastography appears to be the most promising current technique. 116,117 Liver stiffness is elevated in Fontan patients versus controls. 116,117,118 Marked ventricular nodule size is markedly increased liver stiffness scores. 116,117 Annual monitoring of gamma glutamyl transferase, bilirubin, albumin, international normalized ratio (INR), vitamin D levels, and alpha fetoprotein levels is advisable. Avoidance of hepatotoxicity, including medications and alcohol, is recommended.

Hepatocellular carcinoma is becoming recognized with increasing frequency since the report by Arai et al. of four cases of hepatocellular carcinoma detected in Fontan patients. 119 In subsequent, multiple other reports of this outcome have been recognized, including following successful heart transplantation. In the case of cirrhosis, the most significant predictor of hepatic complications. Liver imaging with ultrasound is recommended at least annually, and the presence of hyperenhancing nodules requires more frequent monitoring. Hyperenhancing nodules may be indistinguishable from carcinoma with imaging techniques and may require biopsy to identify the pathology. Annual monitoring with serum alpha fetoprotein levels has enabled early detection of two cases of carcinoma in our center. The outcome of treatment strategies (including cryosurgery for hepatocellular carcinoma) is improved by early detection of single or small lesions.

**CATHETER-BASED INTERVENTIONS**

Surgical modifications of the Fontan repair have focused on improving the flow dynamics by adoption of the cavopulmonary connection compared with the atrialpulmonary anastomosis. However, it is becoming apparent that the total cavopulmonary connection, with uniform nondiseased diameter and the potential for colliding flows from the lower body and superior vena cava, in addition to the frequently encountered PA narrowing, provide important areas of resistance that become magnified with exertion. The resistance provided by the total cavopulmonary connection is a secondary to pulmonary vascular resistance, as might be supposed, and the physiologic effect is magnified under conditions of exercise or volume loading. 119,120 Modeling studies have demonstrated the relationship between pathway size and pressure drop, and in one report, it was suggested that a minimum pathway diameter of 20 mm or more is optimal for avoiding exercise-induced increase in pathway resistance. 121,122 Cardiac MRIs illustrate the important power loss introduced by variances in caval offset and geometric angle, as well as the minimum diameters of the Fontan pathway and PAs (Fig. 12.13).123 Although it is uncommon to document resting pressure gradients across lateral tunnel or extracardiac conduit cavopulmonary connections, both may present unintentional resistance units in the setting of increased inferior caval flow.
which may contribute to the inherent hemodynamic inefficiency of a Fontan circulation, and experience cardiac output.

Cardiac catheterization should carefully assess sites of Fontan narrowing and may identify 1- to 2-mm Hg gradients, which in this passive flow state are hemodynamically significant. Acute fluid challenge may unmask increased gradients as well as diastolic dysfunction, particularly in patients with mildly elevated end-diastolic pressures. Accordingly, catheter intervention with angioplasty or stenting may effectively reduce the physiologic load imposed by pathway narrowing or small sites, and should be performed if the mean pressure gradient is very low or even absent in the setting of angio- graphic narrowing.127,128 Similarly, treatment of branch PA narrowing or stenosis, if not caused by intramyocardial pathway resistance and minimize exercise-related power loss and hydrodynamic inefficiency.123 Occlusion of major collateral or venovenous collaterals may reduce volume overload or increase oxygen saturation, thus improving cardiac output, but occlusion of venovenous collaterals may result in elevation of central venous pressures while decreasing preload. Creation of an atrial-level defect is sometimes used for patients of PLE, accepting cyanosis, to achieve increased cardiac output.

ARRHYTHMIA THERAPY

The hemodynamic consequences of elevated atrial rates greater than 90 bpm occur rapidly, resulting in elevated atrial pressure and decreased ventricular contractility within 24 hours, emphasizing the limited functional reserve of Fontan patients. Thus, the threshold rate of atrial fibrillation (AF) is more apparent in Fontan patients with symptoms and high, and a sense of urgency for achieving a normal heart rate should prevail, in contrast to less urgent or pericardial tamponade.123 Acute therapy for SVT in Fontan patients includes intravenous adenosine, diltiazem, or esmolol for termination or rate control, with synchronized cardioversion/defibrillation if necessary without delayed125. Chronic antiarrhythmic is indicated in patients with atrial tachycardia123. For patients with atrial tachycardia,123,125 Assessment for hemodynamic abnormalities is warranted, and the presence of intracardiac thrombus is recommended. Catheter ablation for atrial tachycardia in Fontan patients has significantly lower acute success rates and much higher recurrence rates than ablation in other forms of congenital heart disease.126 Ablation is challenged by the hyper- trophied atrial tissue and multiple reentrant circuits, with the risk of hemobright and complete atrioventricular nodal lesions. More importantly, focusing on arrhythmia ablation without addressing underlying hemodynamic abnormalities may allow progression to multigorgan system dysfunction, missing a window of opportunity for surgery or transplantation. Due to the high morbidity associated with atrial tachycardia, efforts to improve hemodynamics with catheter or surgical intervention is indicated, as well as the use of atrial pacing as technically feasible to minimize recurrences.126 Because the absence of a regular atrial rhythm may increase the likelihood of developing or worsening right ventricular dysfunction, each patient in nature, vigorous efforts to maintain sinus rhythm as opposed to rate-control strategies are recommended in Fontan patients. When pacing is required, tachyarrhythmia and ventricular fibrillation in patients undergoing atrial arrhythmia surgery. Freedom from rate-responsive pacing with pacemaker reprogramming during exercise testing is an important modality to optimize cardiac output, because the Fontan patient relies heavily on increments of the systemic circulation and increase cardiac output. Recent observation has been the frequent occurrence of marked exac- teration of asystole following abdominal pacemaker generator change immediately postoperatively, and asystole has required weekly to months for improvements.

Oral antiarrhythmic medications such as dofetilde or sotalol may be diastolic dysfunction, particularly in Fontan patients with symptoms and high, and a sense of urgency for achieving a normal heart rate should prevail, in contrast to less urgent or pericardial tamponade.123 Acute therapy for SVT in Fontan patients includes intravenous adenosine, diltiazem, or esmolol for termination or rate control, with synchronized cardioversion/defibrillation if necessary without delayed125. Chronic antiarrhythmic is indicated in patients with atrial tachycardia123. For patients with atrial tachycardia,123,125 Assessment for hemodynamic abnormalities is warranted, and the presence of intracardiac thrombus is recommended. Catheter ablation for atrial tachycardia in Fontan patients has significantly lower acute success rates and much higher recurrence rates than ablation in other forms of congenital heart disease.126 Ablation is challenged by the hyper- trophied atrial tissue and multiple reentrant circuits, with the risk of hemobright and complete atrioventricular nodal lesions. More importantly, focusing on arrhythmia ablation without addressing underlying hemodynamic abnormalities may allow progression to multigorgan system dysfunction, missing a window of opportunity for surgery or transplantation. Due to the high morbidity associated with atrial tachycardia, efforts to improve hemodynamics with catheter or surgical intervention is indicated, as well as the use of atrial pacing as technically feasible to minimize recurrences.126 Because the absence of a regular atrial rhythm may increase the likelihood of developing or worsening right ventricular dysfunction, each patient in nature, vigorous efforts to maintain sinus rhythm as opposed to rate-control strategies are recommended in Fontan patients. When pacing is required, tachyarrhythmia and ventricular fibrillation in patients undergoing atrial arrhythmia surgery. Freedom from rate-responsive pacing with pacemaker reprogramming during exercise testing is an important modality to optimize cardiac output, because the Fontan patient relies heavily on increments of the systemic circulation and increase cardiac output. Recent observation has been the frequent occurrence of marked exac- teration of asystole following abdominal pacemaker generator change immediately postoperatively, and asystole has required weekly to months for improvements.

Oral antiarrhythmic medications such as dofetilde or sotalol may be diastolic dysfunction, particularly in Fontan patients with symptoms and high, and a sense of urgency for achieving a normal heart rate should prevail, in contrast to less urgent or pericardial tamponade.123 Acute therapy for SVT in Fontan patients includes intravenous adenosine, diltiazem, or esmolol for termination or rate control, with synchronized cardioversion/defibrillation if necessary without delayed125. Chronic antiarrhythmic is indicated in patients with atrial tachycardia123. For patients with atrial tachycardia,123,125 Assessment for hemodynamic abnormalities is warranted, and the presence of intracardiac thrombus is recommended. Catheter ablation for atrial tachycardia in Fontan patients has significantly lower acute success rates and much higher recurrence rates than ablation in other forms of congenital heart disease.126 Ablation is challenged by the hyper- trophied atrial tissue and multiple reentrant circuits, with the risk of hemobright and complete atrioventricular nodal lesions. More importantly, focusing on arrhythmia ablation without addressing underlying hemodynamic abnormalities may allow progression to multigorgan system dysfunction, missing a window of opportunity for surgery or transplantation. Due to the high morbidity associated with atrial tachycardia, efforts to improve hemodynamics with catheter or surgical intervention is indicated, as well as the use of atrial pacing as technically feasible to minimize recurrences.126 Because the absence of a regular atrial rhythm may increase the likelihood of developing or worsening right ventricular dysfunction, each patient in nature, vigorous efforts to maintain sinus rhythm as opposed to rate-control strategies are recommended in Fontan patients. When pacing is required, tachyarrhythmia and ventricular fibrillation in patients undergoing atrial arrhythmia surgery. Freedom from rate-responsive pacing with pacemaker reprogramming during exercise testing is an important modality to optimize cardiac output, because the Fontan patient relies heavily on increments of the systemic circulation and increase cardiac output. Recent observation has been the frequent occurrence of marked exac- teration of asystole following abdominal pacemaker generator change immediately postoperatively, and asystole has required weekly to months for improvements.

Oral antiarrhythmic medications such as dofetilde or sotalol may be diastolic dysfunction, particularly in Fontan patients with symptoms and high, and a sense of urgency for achieving a normal heart rate should prevail, in contrast to less urgent or pericardial tamponade.123 Acute therapy for SVT in Fontan patients includes intravenous adenosine, diltiazem, or esmolol for termination or rate control, with synchronized cardioversion/defibrillation if necessary without delayed125. Chronic antiarrhythmic is indicated in patients with atrial tachycardia123. For patients with atrial tachycardia,123,125 Assessment for hemodynamic abnormalities is warranted, and the presence of intracardiac thrombus is recommended. Catheter ablation for atrial tachycardia in Fontan patients has significantly lower acute success rates and much higher recurrence rates than ablation in other forms of congenital heart disease.126 Ablation is challenged by the hyper- trophied atrial tissue and multiple reentrant circuits, with the risk of hemobright and complete atrioventricular nodal lesions. More importantly, focusing on arrhythmia ablation without addressing underlying hemodynamic abnormalities may allow progression to multigorgan system dysfunction, missing a window of opportunity for surgery or transplantation. Due to the high morbidity associated with atrial tachycardia, efforts to improve hemodynamics with catheter or surgical intervention is indicated, as well as the use of atrial pacing as technically feasible to minimize recurrences.126 Because the absence of a regular atrial rhythm may increase the likelihood of developing or worsening right ventricular dysfunction, each patient in nature, vigorous efforts to maintain sinus rhythm as opposed to rate-control strategies are recommended in Fontan patients. When pacing is required, tachyarrhythmia and ventricular fibrillation in patients undergoing atrial arrhythmia surgery. Freedom from rate-responsive pacing with pacemaker reprogramming during exercise testing is an important modality to optimize cardiac output, because the Fontan patient relies heavily on increments of the systemic circulation and increase cardiac output. Recent observation has been the frequent occurrence of marked exac- teration of asystole following abdominal pacemaker generator change immediately postoperatively, and asystole has required weekly to months for improvements.

Oral antiarrhythmic medications such as dofetilde or sotalol may be diastolic dysfunction, particularly in Fontan patients with symptoms and high, and a sense of urgency for achieving a normal heart rate should prevail, in contrast to less urgent or pericardial tamponade.123 Acute therapy for SVT in Fontan patients includes intravenous adenosine, diltiazem, or esmolol for termination or rate control, with synchronized cardioversion/defibrillation if necessary without delayed125. Chronic antiarrhythmic is indicated in patients with atrial tachycardia123. For patients with atrial tachycardia,123,125 Assessment for hemodynamic abnormalities is warranted, and the presence of intracardiac thrombus is recommended. Catheter ablation for atrial tachycardia in Fontan patients has significantly lower acute success rates and much higher recurrence rates than ablation in other forms of congenital heart disease.126 Ablation is challenged by the hyper- trophied atrial tissue and multiple reentrant circuits, with the risk of hemobright and complete atrioventricular nodal lesions. More importantly, focusing on arrhythmia ablation without addressing underlying hemodynamic abnormalities may allow progression to multigorgan system dysfunction, missing a window of opportunity for surgery or transplantation. Due to the high morbidity associated with atrial tachycardia, efforts to improve hemodynamics with catheter or surgical intervention is indicated, as well as the use of atrial pacing as technically feasible to minimize recurrences.126 Because the absence of a regular atrial rhythm may increase the likelihood of developing or worsening right ventricular dysfunction, each patient in nature, vigorous efforts to maintain sinus rhythm as opposed to rate-control strategies are recommended in Fontan patients. When pacing is required, tachyarrhythmia and ventricular fibrillation in patients undergoing atrial arrhythmia surgery. Freedom from rate-responsive pacing with pacemaker reprogramming during exercise testing is an important modality to optimize cardiac output, because the Fontan patient relies heavily on increments of the systemic circulation and increase cardiac output. Recent observation has been the frequent occurrence of marked exac- teration of asystole following abdominal pacemaker generator change immediately postoperatively, and asystole has required weekly to months for improvements.
complex anatomy including dextrocardia and abnormal venous return, and extensive bleeding from collateral flow are daunting, and contribute to longer bypass and ischemic times. Early mortality following transplantation in the adult Fontan patient ranges from 18% to 33% currently, and is related to acute graft failure, intractable bleeding, multigorgan system failure, and infection. Variables identified as risk factors for early mortality have included older recipient age, the need for preoperative mechanical ventilation, elevated pulmonary vascular resistance greater than 4 Woods U, three or more prior sternotomies, elevated panel reactive antibody greater than 10%, hepatic or renal dysfunction as quantified by the MELD-XI score, PLE, and delayed nutritional status.

The impact of PLE on transplant survival was assessed in 243 younger Fontan patients enrolled in the Pediatric Heart Transplant Study from 1999 to 2012. Of the 70 Fontan patients with PLE undergoing heart transplant during the study period, 22 (31%) died, compared with 40 (23%) of the 173 non-PLE Fontan patients. The recent multicenter European study of 61 Fontan patients undergoing transplantation included PLE in 23% of patients. Although PLE resolved post-transplant in 78% of PLE, it was an independent predictor of increased 5-year mortality. Because the majority of adult Fontan patients have some evidence of liver fibrosis on imaging, the risk of liver failure during heart transplantation is a source of major concern. As stated previously, neither liver biopsy nor biomarkers correlate with outcome following heart transplantation.142,144-146 Greenway et al. summarized their criteria for proceeding with heart-only transplantation in Fontan patients: normal synthetic liver function, normal hepatic venous anatomy, liver volume greater than 880 ml, only mild portal hypertension, and no evidence of hepatocellular carcinoma.147 Combined with right heart failure, PLE and transplantations have been successfully performed, and patients with hepato-cellular carcinoma are offered this option.148

For Fontan patients, 1-year survival following transplantation is 71%, compared with 83% for other forms of heart disease, with 5-year survival of 66%.135 Late survival following successful heart transplantation in Fontan patients is similar to that of other patients. However, overall, adult congenital heart disease patients have improved late survival compared with other adult transplant patients.123

Long-Term Survival

Recent studies of long-term outcomes have been published by several groups.148,149,151 Among atrio pulmonary Fontan patients, 25-year survival was reported at 76% by D’Oleker,133 while 30-year survival of older Fontan patients was reported as 43% by Pundi et al.153 Freedom from Fontan failure, defined as death, transplant, surgical takeaway or conversion, NYHA Class III/IV, or PLE, at 25 years post-Fontan was 56% in the large series from Australia and New Zealand (see Fig. 12.11). In a cohort of survival series of 123 young adult Fontan patients, transplant-free survival rates at 10 years following surgery were 60%; risk factors for death or transplant were portal hypertension, presence of a pacemaker, and resting oxygen desaturation.154 Patients with tricuspid atresia have improved survival, with patients with heterotaxy syndrome or hypoplastic left heart syndrome showing the lowest event-free survival.155,156 There are some data to suggest that mortality among patients with extra-cardiac conduits is increased in the second decade of life compared with atrio-pulmonary or lateral tunnel Fontan repairs, although this has not been reported in other series.157-159 of note, mild to moderate degrees of ventricular systolic function have not proven to be a measure of long-term outcomes to date.160,161,162

Causes of late mortality are usually multifactorial, and are related to heart failure in 35% to 52%, perioperative issues 37% to 68% (reperfusion or transplantation), sudden or arrhythmic events 9% to 19%, thromboembolic issues 8%, liver failure 3% to 10%, and cancer 3%.163,164,165 Thromboembolic events were reported in 25% of single-ventricle patients in one study,166 whereas most series report an incidence of 3% to 10%.167 likely related to the high incidence of atrial tachycardia and the presence of atrial-level shunts. Endocarditis is rare, reported in less than 2% of patients,168 whereas sepsis as a cause of death is reported in 3% to 18%.169,170 In the series of 123 adult Fontan patients followed in Atlanta, independent predictors of death related to heart failure were PLE, morphology RV, and higher right atrial pressure.171 Although median survival for single-ventricle patients was reported as 49 years in the CONCOR registry in the Netherlands,170 most studies report mortality among Fontan patients at an earlier age than other forms of congenital heart disease, with a median age at death to 27 to 41 years (Fig. 12.16).174-177

REFERENCES

14. Pfeifer JS, Chavira-Cruz M, Hager DL. Modifications of the Fontan operation applicable to patients with left atrioventricular valve atresia or single atrioventricular valve. Circulation. 1987;76(2 part II):313S-316S.
23. Video of the 2017 World Congress on Pulmonary Circulation and Heart Failure, LWCH. 2017;5(9):36.
Late Complications Following the Fontan Operation

Paul Hairy | Gruschen R. Veldman

The univentricular heart encompasses a spectrum of rare and complex congenital cardiac malformations whereby both ventricles predominately egress into one functionally single ventricular chamber, precluding biventricular repair.1 Population studies indicate an overall prevalence of approximately 2 per 10,000 live births. Subtypes include hypertrophic or left ventricles, absence or atretic atrioventricular (AV) valves, common AV valves with only one well-developed ventricle, and heterotaxy syndromes (or isomerism), that is, disorders of lateralization whereby the arrangement of abdominal and thoracic viscera differ from normal and mirror-image of normal.

The general objectives of initial surgical palliation are to provide unobstructed systemic outflow, unobstructed systemic and pulmonary venous return, and controlled pulmonary blood flow. Most patients will be managed by a staged surgical approach in view of a Fontan procedure. A minority will not undergo Fontan palliation because of reasonably balanced systemic and pulmonary volume after the initial result of unbalanced ventricular or hemodynamics. In patients with severe pulmonary obstruction or atresia, initial palliation may consist of aortopulmonary shunts (Fig. 13.1A to D) or a bidirectional cavopulmonary anastomosis (see Fig. 13.1E). In contrast, in patients with unrestrictive pulmonic blood flow, pulmonary artery banding or division may afford improved protection.

Fontan procedures are typically completed between 18 months and 4 years of age, at an ideal weight of approximately 14 kg, and of directing systemic venous return to the pulmonary artery, characteristically without an interposed right ventricle (see Fig. 13.1F to H). Several modifications and adaptations have been proposed since its original description in 1971.2 The classic Fontan procedure involved a valved conduit between the right atrium and pulmonary artery. Older adults will have had a modified Fontan procedure, consisting of a direct atriovenous connection of the right atrium to a divided pulmonary artery (see Fig. 13.1F). This technique has been supplanted by so-called total cavopulmonary connection Fontan procedure, operated by De Leval, consists of an end-to-side anastomosis of the superior vena cava to the undivided right pulmonary artery, a composite intrarterial conduit using the right atrial posterior wall, and a prosthetic patch to channel the inferior vena cava to the transected superior vena cava (see Fig. 13.1G). A subsequent modification includes directing inferior vena cava flow to the pulmonary artery by means of an external conduit (see Fig. 13.1H). Individual Fontan pathways may be "trastated" by creating an atrial septal defect (ASD) as an escape valve for elevated Fontan pressures postoperatively.3 Such fenestrations may subsequently be closed, hemodynamic conditions permitting.

Patients with univentricular hearts and systemic outflow obstruction, the most severe form being hypoplastic left heart syndrome, constitute the most prevalent subtype. These patients typically undergo a variation of Norwood stages that culminate in a Fontan-type circulation.4

- Objectives of the Norwood stage I procedure, performed within the first 2 weeks of life, are to provide unobstructed pulmonary venous return, permanent systemic outflow from the right ventricle, and temporary pulmonary blood supply to allow the pulmonary vasculature to develop and mature (see Fig. 13.1 and 3).

- The Norwood stage II procedure, performed prior to 6 months of age, consists of a bidirectional Glenn shunt or hemi-Fontan and closure of the Blalock-Taussig shunt.

- At 18 months to 3 years, the stage III procedure completes the total cavopulmonary Fontan by connecting the inferior vena cava directly to the pulmonary arteries (see Fig. 13.1 and 4).

To understand long-term sequelae, the Fontan circulation may be viewed as a hemodynamic compromise. In normal biventricular hearts, cava pressures are typically less than 10 mm Hg, and mean pulmonary pressures exceed 12 to 15 mm Hg. Fontan physiology imposes systemic venous hypertension with consequent concomitant pulmonary arterial hypotension.5 Long-term complications, the focus of the current chapter, are numerous, highly prevalent, and increasingly well characterized as the first Fontan recipients enter their fifth decade of follow-up. Lifelong surveillance in centers with expertise in adult congenital heart disease is recommended for all.

Clinical Evaluation

Routine follow-up typically involves one to two clinical visits per year. In addition to a thorough clinical history and physical examination, minimum testing includes resting oximetry, 12-lead electrocardiogram (ECG), chest x-ray, echocardiography with Doppler interrogation, complete blood count, biochemical analyses for liver function, serum protein, and albumin, and intracardiac rhythm monitoring. Testing for viral hepatitis should be considered, particularly in those exposed to blood products prior to universal screening for hepatitis B. Additional Fontan monitoring may include transesophageal echocardiography, cardiac catheterization, liver imaging, exercise spiroergometry, stool monitoring for enteric protein loss, cardiac magnetic resonance (CMR) imaging, isotopic ventriculography, and electrophysiological study.