Chapter 28
Anatomic Variants of Univentricular Physiology and Fontan Palliation

Ada C. Stefanescu Schmidt

Epidemiology

- There are several congenital diagnoses, most with a wide spectrum of defects, that lead to univentricular physiology (Table 28.1). They can be broadly defined into three categories based on the morphology (right, left, or indeterminate) of the predominant ventricle.
- The defects most likely to lead to single ventricle repair include hypoplastic left heart syndrome (HLHS), tricuspid atresia, double inlet left ventricle, and defects with a straddling atrioventricular valve (such as an unbalanced atrioventricular canal defect). Less often, pulmonary atresia with intact ventricular septum (with a small RV or RV-dependent coronary circulation), double outlet right ventricle, and Ebstein anomaly may require single ventricle repair.

A. C. Stefanescu Schmidt, M.D. M.Sc. (✉)
Massachusetts General Hospital, Boston, MA, USA
e-mail: ada.stefanescu@mgh.harvard.edu

D. DeFaria Yeh, A. Bhatt (eds.), *Adult Congenital Heart Disease in Clinical Practice*, In Clinical Practice,
https://doi.org/10.1007/978-3-319-67420-9_28

Table 28.1 Diagnoses leading to univentricular physiology

Right ventricle dominant	Left ventricle dominant
1. Hypoplastic left heart syndrome (HLHS)	1. Tricuspid atresia (TA)
2. Double outlet right ventricle (DORV)	2. Double inlet left ventricle (DILV)
3. Double inlet right ventricle (DIRV)	3. Pulmonary atresia with intact ventricular septum (PAIVS)
4. Unbalanced AV canal defect (AVCD)	4. Unbalanced AV canal defect (AVCD)

- The most common type of univentricular heart at birth is HLHS, with an estimated incidence of 0.2–0.4 per 1000 live births [1, 2] followed by tricuspid atresia (TA) (0.06–0.08 per 1000 live births).
  - In adults, TA is more common than HLHS, as the latter carries a higher pediatric mortality.
- Incidence is likely to increase, especially in developed countries, as in utero and neonatal interventional options become more available.
- The incidence of some univentricular subtypes (HLHS in particular) is higher in siblings than in the general population and is thus thought to have a strong genetic component.

Hypoplastic Left Heart Syndrome (HLHS)

Anatomy (Fig. 28.1)

- Reduced blood flow during development, either due to lack of inflow (mitral atresia) or outflow (aortic atresia), is the most common cause of HLHS.
- An unbalanced atrioventricular canal defect (AVCD) can also lead to an underdeveloped left ventricle that cannot support the systemic circulation.
- The ascending aorta is often small and underdeveloped; flow is dependent on a patent ductus arteriosus.

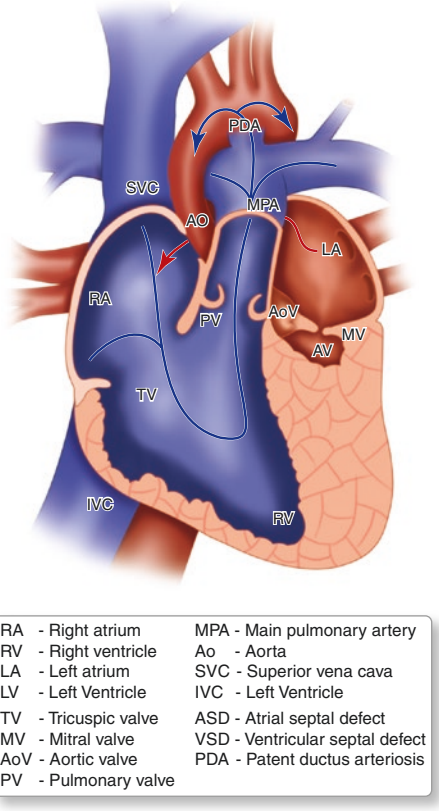

FIGURE 28.1 Hypoplastic left heart syndrome. Oxygenated pulmonary venous return into the left atrium return to the right atrium through an atrial septal defect. Flow into the aorta comes through the patent ductus arteriosus

Physiology

- Patients with HLHS have a systemic right ventricle, responsible for both pulmonary and systemic circulation.
- Progressive right heart failure is common with older age, especially in the setting of atrioventricular valve regurgitation and added volume load.

Spectrum of Disease

- Principal determinants of the severity of HLHS are the presence of a VSD (which generally is associated with a more well-developed left ventricle secondary to flow) and aortic valve defects (if atretic, systemic circulation is dependent on the size of the ductus arteriosus).

Associated Defects

- VSD occurs in a minority of patients.
- Turner syndrome (45, XO).
- Bicuspid aortic valve, subaortic stenosis, and aortic coarctation.

Tricuspid Atresia

Anatomy and Spectrum of Disease (Fig. 28.2)

- Following the same principle as mitral valve atresia and HLHS, the atretic or imperforate tricuspid valve leads to hypoplasia of the right ventricle; systemic venous return is depending on an ASD to reach the left atrium.
- A VSD is much more common in association with TA, leading to some development of the right ventricle and pulmonary valves, though subpulmonic or pulmonary valve stenosis are common due to insufficient flow.
- ~30% of patients have transposition of the great arteries (with the aorta arising from the hypoplastic right ventricle and the pulmonary artery from the left).

Associated Defects

- Mutations and deletions in the 22q11 chromosome [3].

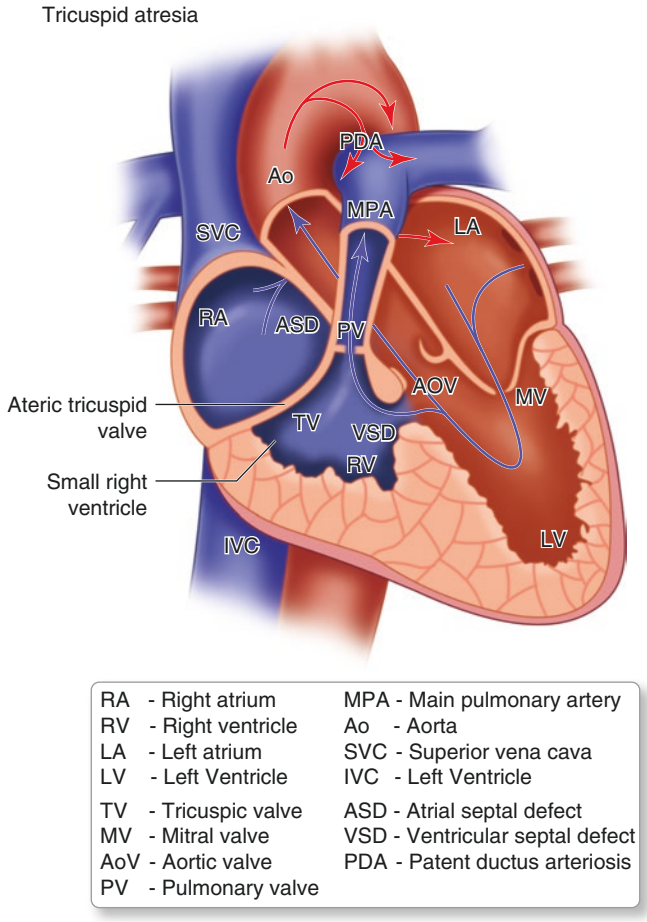

FIGURE 28.2 Tricuspid atresia

Double Outlet Right Ventricle (DORV)

- Spectrum of anatomic defects in which more than 50% of each great vessel (often the entire pulmonary artery and >50% of the aorta) originates from the right ventricle, through a VSD (Fig. 28.3).

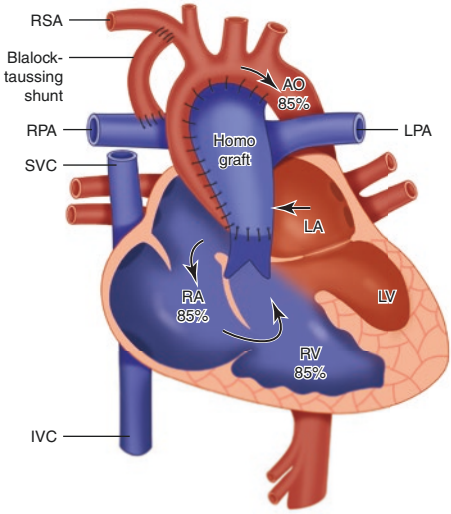

FIGURE 28.3 Double outlet right ventricle, after initial repair including a Blalock-Taussig shunt and Damus-Kaye-Stansel anastomosis of the ascending aorta and pulmonary trunk (indicated for patients with a hypoplastic aorta)

- Pathologic definition of DORV requires the presence of a conus beneath the pulmonic and aortic outflows.
- Location of the VSD (whether subaortic, subpulmonary, doubly committed, or remote from the great vessels) defines the subtype of DORV, as well as the operative repair strategy and in some cases may require a single ventricle physiology approach (see Chap. 22 for more details).

Double Inlet Ventricle (DIRV and DILV)

Anatomy

- More than 50% of each atrium is connected to one ventricular chamber, most commonly the left (DILV) (Fig. 28.4).

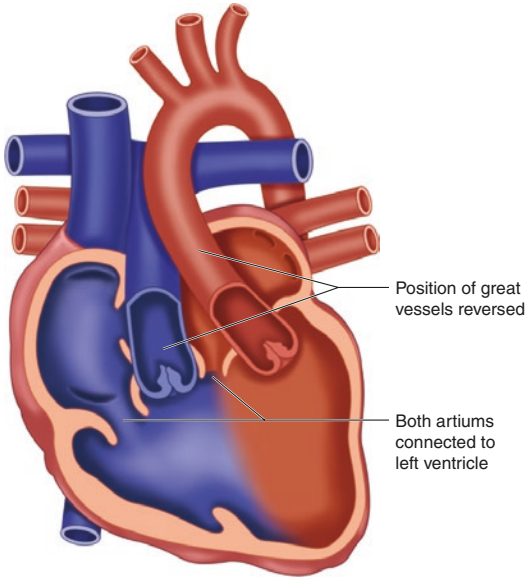

FIGURE 28.4 Double inlet left ventricle

- Usually both atrioventricular valves are near one another and have a morphology more similar to the mitral valve.
- Inlet septum is absent, giving rise to a large inlet VSD.

Physiology

- Cyanosis is common due to mixing of deoxygenated systemic venous return and pulmonary venous return in the ventricles through the large VSD.

Spectrum of Disease

- Size of the non-dominant chamber is dependent on the size of the VSD (a larger VSD allows greater flow in development to the non-dominant chamber resulting in a larger

chamber size and contribution to function). One of the atrioventricular valves may be atretic (if there is an ASD which allows mixing of venous return). If there is straddling of an AV valve that may also affect surgical repair strategy.

Associated Defects

- ASD is common.
- Levo-transposition of the great arteries (L-TGA) is common.

Pulmonary Atresia with Intact Ventricular Septum (PA-IVS)

Anatomy

- Imperforation of the pulmonary valve leads to lack of flow through the RV, leading to a small or hypoplastic RV.

Physiology

- Pulmonary circulation dependent on a patent ductus arteriosus (aortic to pulmonary shunt).
- Often multiple collaterals from the aorta to the pulmonary artery may be present and can be identified on exam as multiple continuous murmurs over the precordium and back.

Spectrum of Disease

- The function of the tricuspid valve (spectrum from tricuspid atresia to significant tricuspid regurgitation) has important implications for the possibility of a two-ventricle surgical repair.

Associated Defects

- When occurring in conjunction with PA-IVS, tricuspid atresia leads to a hypoplastic RV.
- RV to coronary artery connections can be seen and require coronary angiography for confirmation. If present, assessment of the coronary flow is important, as patients with RV-dependent coronaries (where flow depends on high RV pressures providing flow to the coronaries) will not tolerate interventions that decompress the RV and decrease RV pressure below systemic diastolic pressures (such as pulmonary valvuloplasty or insertion of RV-PA conduit) without addressing the coronary anatomy.

General Principles of Univentricular Repair

Operative Repair Options

- The choice of palliative surgery for univentricular heart depends on the underlying anatomy, size, and development of the non-dominant ventricle.
- Re-creating two ventricular chambers, by closing a VSD and redirecting venous return to the pulmonary artery, and pulmonary venous return toward the aorta, leads to the best long-term results, though is often challenging to realize and with serious short-term hemodynamic consequences.
- The more common procedure, termed "single ventricle repair," creates a baffle for deoxygenated systemic venous return to go to the pulmonary artery passively. Oxygenated blood from the pulmonary veins enters the univentricular chamber and is pumped to the systemic circulation (pulmonary outflow must be oversewn).
- If the non-dominant ventricle is developed well enough to provide some, but not all flow to the pulmonary circulation, a "1.5 ventricle repair" can be attempted. In this circulation, some of the systemic venous flow returns to the subpulmonary ventricle, while the rest is directed through

a baffle to the pulmonary artery (typically via a Glenn shunt).

- Staging of these palliative procedures is generally undertaken in order to accommodate the changing hemodynamics (in particular, the initially elevated pulmonary pressure) in the neonatal period.

Staged Procedures

1. Pulmonary artery (PA) band
   (a) Patients with univentricular physiology and without pulmonary stenosis are at risk for overcirculation of the pulmonary arteries. High flow results in increased pressures through the lungs in the first few months of life causing injury and progressive pulmonary endothelial dysfunction. The development of pulmonary hypertension precludes later Fontan palliation.
   (b) To prevent pulmonary overcirculation, a PA band made of synthetic material placed around the main PA (without the need for intracardiac surgery or cardiopulmonary bypass) creates a fixed stenosis that limits flow through the lungs and prevents the development of pulmonary hypertension.
   (c) The PA band is often removed during subsequent surgery; however, the area of the band may be scarred and present later in life as recurrent supra-pulmonary valve stenosis.
2. Blalock-Taussig shunt (BT shunt, also termed Blalock-Thomas-Taussig)
   (a) Patients who have insufficient pulmonary arterial flow (such as those with a dominant left ventricle and a small VSD or intact ventricular septum or with significant subpulmonic, pulmonary valve, or supra-pulmonic stenosis), a Blalock-Thomas-Taussig shunt can be performed to augment the flow to the lungs and allow normal development (see Fig. 28.5).

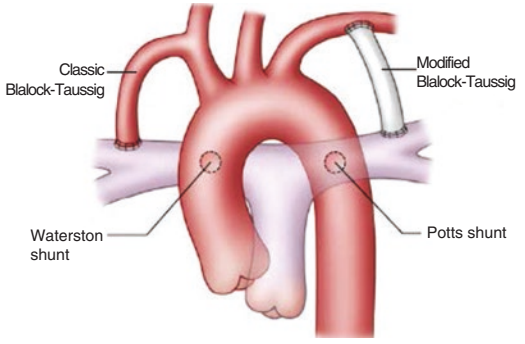

FIGURE 28.5 Palliative shunts (Figure from: DeFaria Yeh D, et al. Adult Congenital Heart Disease. In: H. K. Gaggin and J. L. Januzzi, eds. *Massachusetts General Hospital Cardiology Board Review*: Springer; 2014(1): 345–377)

(b) This procedure, developed by the surgeons Dr. Alfred Blalock and Dr. Vivien Thomas (a surgical technician at the time) and the cardiologist Dr. Helen Taussig, was first performed in 1944 in an infant with tetralogy of Fallot.

(c) The classic BTT shunt is an anastomosis of the subclavian artery (usually contralateral to the aortic arch), to the branch of the pulmonary artery. The arm therefore receives blood flow through collaterals, usually without symptoms, though with a markedly decreased brachial artery pulse which often makes a blood pressure measurement by sphygmomanometry unobtainable in that arm.

(d) A modified BTT shunt is created by the use of a synthetic graft between the subclavian and the pulmonary artery, retaining some flow to the arm.

(e) While the BTT shunt is often reversed with later stages of the procedure, the area of the pulmonary artery at the anastomosis site is often scarred and may develop stenosis leading to asymmetric pulmonary arterial flow (diagnosed by a lung perfusion scan, unexplained elevation in RVSP with branch PA gradient assessed by echocardiography, CT, or MRI). In the classic BTT

shunt patient, the decreased blood flow to the arm remains despite reversal of the BTT shunt (the subclavian artery is not reconnected).

(f) Central shunts, including the Waterston and Potts shunts (ascending or descending Ao to PA, respectively), may also have been employed in patients who are now older.

(g) Unintended consequences of any systemic to pulmonary arterial shunt include volume loading of the systemic ventricle, distortion of branch PAs, heterogeneous microscopic pulmonary vascular changes, and cyanosis.

3. Glenn shunt

(a) After the first few months of life, when pulmonary vascular resistance and pulmonary artery pressures have decreased to levels similar to the venous systemic pressures, the superior vena cava can be anastomosed directly to the pulmonary artery to allow gravity to provide passive flow of deoxygenated blood from the head and neck to the pulmonary arteries (typically done when infants are able to hold their head up).

(b) This can be the first palliative procedure in children with enough pulmonary blood flow in the neonatal procedure (or a large patent ductus arteriosus) or follow a BTT shunt in those infants who did not. It may also be the second step of a Norwood procedure.

4. Fontan procedure

(a) The Fontan procedure, named after Dr. Francois Marie Fontan who first performed it in 1971 [4], is a complete connection between systemic venous return and the pulmonary arteries (Fig. 28.6). The subtypes are:

- RA-to-PA: connection of the right atrial appendage to the pulmonary artery.
- The Bjork procedure was a Fontan modification which utilized a valved conduit between the RA and RV.
- Intracardiac: atrial tissue used to create a baffle from atrium to right pulmonary artery (lateral tunnel).

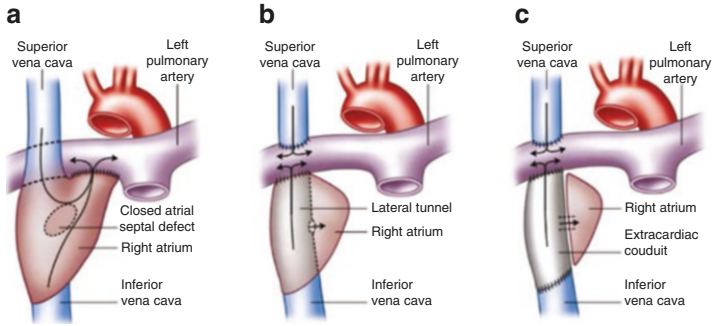

FIGURE 28.6 Fontan procedure (**a**) right atrial to pulmonary artery connection; (**b**) lateral tunnel Fontan, intracardiac; (**c**) extracardiac Fontan. (Figure from: DeFaria Yeh D, et al. Adult Congenital Heart Disease. In: H. K. Gaggin and J. L. Januzzi, eds. *Massachusetts General Hospital Cardiology Board Review*: Springer; 2014(1): 345–377)

- Extracardiac: synthetic material used to create a baffle from the IVC outside of the atrial chamber to the pulmonary artery.

(b) The baffle may initially be fenestrated (creation of a small hole within the baffle), in order to allow for pressure release (through creating a right-to-left shunt). This fenestration is then often closed in the postoperative period.

5. Norwood procedure (Fig. 28.7)

(a) The Norwood procedure refers to a sequence of three surgeries, specifically in infants with HLHS:

- Stage 1:
  - Atrial septectomy.
  - Main pulmonary artery is disconnected from the right and left pulmonary artery branches and is connected to the ascending aortic arch. The aorta is reconstructed and arises off the native pulmonic root.
  - Shunt from the aorta (often BTT shunt) is connected to the right and left pulmonary arteries to restore pulmonary blood flow.

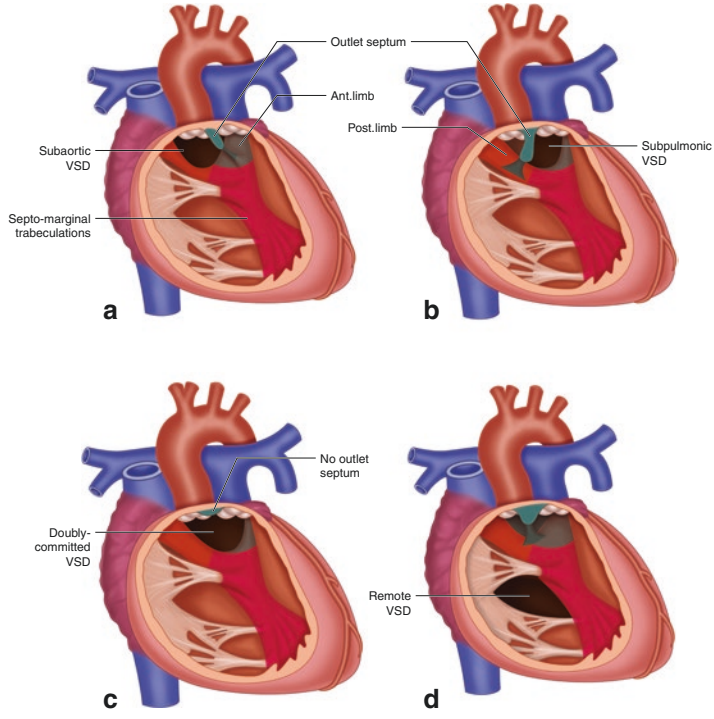

FIGURE 28.7 Norwood procedure

A Sano shunt or modification involves placement of a conduit between the RV and the PA branches (instead of a BTT shunt).

– Venous systemic return arrives to the right atrium → right (systemic) ventricle → pulmonic trunk → aorta → systemic circulation, a subset of which is shunted to the pulmonary arteries via BTT shunt → lungs → pulmonary veins → left atrium → right atrium (through septectomy) → back in systemic right ventricle.

- Stage 2:
  - About 6 months later, superior vena cava connected to the pulmonary arteries (usually through a Glenn procedure).

- Stage 3:
  - Two to three years later, a Fontan procedure is performed to direct all systemic venous return to the lungs as described above.

Diagnosis

Clinical Presentation in Adults

- Adults lost to follow-up after a childhood Fontan surgery generally present with hypoxia and cyanosis (due to right-to-left shunts, either through a Fontan fenestration or through systemic to pulmonary venovenous collaterals), atrial more often than ventricular arrhythmias, significant venous insufficiency, and cardiac cirrhosis.

Physical Exam

- Patients with a Fontan will have a single second heart sound (A2).
- An elevated JVP is concerning for elevated Fontan pathway pressures and should be investigated. Recall that the jugular venous pulsation will be challenging to assess as it is not classically pulsatile.
- Similarly, hypoxia is abnormal and should be worked up for possible baffle leaks or systemic to pulmonary venovenous collaterals.
- Chronic venous insufficiency in the lower extremities is common, with medial malleolar ulcers often being overlooked.
- Signs of hepatic dysfunction (jaundice, ascites, caput medusa, asterixis).

Electrocardiogram

- Variable depending on the primary anatomic defect.
- Atrial arrhythmias are common.

Chest X-Ray

- Assess atrial and ventricular size, the presence of pulmonary edema, or decreased pulmonic flow if branch PA stenosis is present, aortic dilation, especially in the conotruncal defects.

Echocardiography (see Table 28.2)

- Obtain an accurate surgical history in order to focus imaging on the baffles and vascular connections which were created.
- Assess the Fontan pathway for baffle leaks, obstruction, and intracardiac thrombus.
- Assess for systemic ventricular function as well as systemic AV valve regurgitation.

Cardiac Catheterization

- Catheterization may be performed to assess hemodynamics to aid in management and assess for Fontan pathway

Table 28.2 Echocardiographic Essentials for Assessment [5]

1.	Inferior vena cava (IVC) and SVC size and flow pattern
2.	Right atrial size
3.	Right atrial to PA anastomosis patency and flow patterns, if present
4.	Interatrial or extracardiac venous conduit flow patterns
5.	Branch PA size and flow pattern
6.	Thrombus within the systemic venous pathway
7.	Baffle fenestration flow and Doppler gradient
8.	Pulmonary venous inflow and left atrial size
9.	Atrioventricular valve function
10.	Systemic ventricular size and function
11.	Outflow tract obstruction
12.	Aortic valve stenosis or incompetence, size of the ascending aorta, and possible coarctation

leaks or stenoses, which can then be intervened on with device closure, balloon, or stenting.
- Cardiac catheterization can identify systemic to pulmonary venovenous collaterals as a recurrent source of hypoxia in these individuals. Coiling of the vessels or use of occluder devices to exclude the aberrant vessel can improve oxygen saturation and exercise tolerance and perceived quality of life.
- Procedures should only be performed by experienced congenital interventionalists at a tertiary center.
- At rest, the typical Fontan has systemic venous pressure which equals the PA pressure and ranges from 12 to 20 mmHg (different for each individual). The indexed pulmonary vascular resistance should be in the 1–3 Woods unit range. Although cardiac index in a Fontan may be low (1.5–3.5 L/min/m^2), it can augment up to two- to threefold with exercise.

Advanced Imaging Techniques

- CT and MRI are useful to assess for Fontan pathway fenestration/leaks or obstructions, ventricular size and function, late gadolinium enhancement, and the presence of and access to systemic to pulmonary venovenous collaterals.

Management in the Adult Survivor

The modified Choussat criteria for a favorable Fontan candidate, while useful to decide upon intervention in childhood, also serves as an excellent guide for potential complications in adulthood. The four tenets are:

[1] unobstructed ventricular inflow and outflow (including stenosis and regurgitation)
[2] good systolic and diastolic ventricular function
[3] good-sized proximal pulmonary arteries without obstruction and PVR <2.5 WU
[4] unobstructed pulmonary venous return.

See Table 28.3 for summary of guidelines.

Table 28.3 ACC/AHA guidelines 2008 for follow-up and treatment of patients after a Fontan procedure [6]

Class I

1. Lifelong follow-up is recommended for patients after a Fontan type of operation; this should include a yearly evaluation by a cardiologist with expertise in the care of ACHD patients (*Level of Evidence: C*)
2. Catheterization of adults with a Fontan type of repair of single ventricle physiology should be performed in regional centers with expertise in ACHD (*Level of Evidence: C*)

Class I

3. Management of patients with prior Fontan repair should be coordinated with a regional ACHD center. Local cardiologists, internists, and family care physicians should develop ongoing relationships with such a center with continuous availability of specialists (*Level of Evidence: C*)
4. At least yearly follow-up is recommended for patients after Fontan repair (*Level of Evidence: C*)
5. Arrhythmia management is frequently an issue, and consultation with an electrophysiologist is recommended as a vital part of care (Level of Evidence: C)
6. New-onset atrial tachyarrhythmia should prompt a comprehensive noninvasive imaging evaluation to identify associated atrial/baffle thrombus, anatomic abnormalities of the Fontan pathway, or ventricular dysfunction (Level of Evidence: C)
7. Warfarin should be given for patients who have a documented atrial shunt, atrial thrombus, atrial arrhythmias, or a thromboembolic event (Level of Evidence: C)
8. Reoperation after Fontan is indicated for the following:
   (a) Unintended residual ASD that results in right-to-left shunt with symptoms and/or cyanosis not amenable to transcatheter closure (*Level of Evidence: C*)
   (b) Hemodynamically significant residual systemic artery-to-pulmonary artery shunt, residual surgical shunt, or residual ventricle-to-pulmonary artery connection not amenable to transcatheter closure (*Level of Evidence: C*)
   (c) Moderate to severe systemic AV valve regurgitation (*Level of Evidence: C*)
   (d) Significant (greater than 30-mmHg peak-to-peak) subaortic obstruction (*Level of Evidence: C*)
   (e) Fontan pathway obstruction (*Level of Evidence: C*)
   (f) Development of venous collateral channels or pulmonary arteriovenous malformation not amenable to transcatheter management (*Level of Evidence: C*)

(g) Pulmonary venous obstruction (*Level of Evidence: C*)
(h) Rhythm abnormalities, such as complete AV block or sick sinus syndrome, that require epicardial pacemaker insertion (*Level of Evidence: C*)
(i) Creation or closure of a fenestration not amenable to transcatheter intervention (*Level of Evidence: C*)

Class IIa

1. Reoperation for Fontan conversion (i.e., revision of an atriopulmonary connection to an intracardiac lateral tunnel, intra-atrial conduit, or extracardiac conduit) can be useful for recurrent atrial fibrillation or flutter without hemodynamically significant anatomic abnormalities. A concomitant maze procedure should also be performed (*Level of Evidence: C*)

Class IIb

1. Heart transplantation may be beneficial for severe SV dysfunction or PLE (*Level of Evidence: C*)

Class IIa

1. It is reasonable to treat SV dysfunction with ACE inhibitors and diuretics (Level of Evidence: C)

Class I

1. Arrhythmia management is frequently an issue in patients after the Fontan procedure, and consultation with an electrophysiologist with expertise in CHD is recommended as a vital part of care (*Level of Evidence: C*)
2. New-onset atrial tachyarrhythmias should prompt a comprehensive noninvasive imaging evaluation to identify associated atrial/baffle thrombus, anatomic abnormalities of the Fontan pathway, or ventricular dysfunction (*Level of Evidence: C*)
3. Electrophysiological studies in adults with Fontan physiology should be performed at centers with expertise in the management of such patients (*Level of Evidence: C*)
4. Clinicians must be mindful of the high risk for symptomatic IART in adult patients who have undergone the Fontan operation. This arrhythmia can cause serious hemodynamic compromise and contribute to atrial thrombus formation. Treatment is often difficult, and consultation with an electrophysiologist who is experienced with CHD is recommended whenever recurrent IART is detected (*Level of Evidence: C*)

Class III

1. The estrogen-containing oral contraceptive pill is not recommended for ACHD patients at risk of thromboembolism, such as those with cyanosis related to an intracardiac shunt, severe PAH, or Fontan repair (*Level of Evidence: C*)

Arrhythmia

- Patients with an intracardiac Fontan are at highest risk for a bradyarrhythmia (heart block or sinus node dysfunction) or atrial tachyarrhythmia.
  - In particular, intra-atrial reentrant tachycardia (distinct from atrial flutter in that the reentrant circuit is around suture lines, and the atrial rate is generally slower than typical flutter) is seen over half of patients in their lifetime after a Fontan procedure [6].
- Avoidance of nodal agents with negative ionotropic effects is important (e.g., diltiazem) to prevent systemic ventricular dysfunction.
- A high burden of atrial arrhythmias in patients with an RA-PA or an intracardiac Fontan may be an indication for a revision and extracardiac Fontan creation.
- Ablations should be performed by electrophysiologists with ACHD experience.
- If a pacemaker is needed, epicardial placement is ideal; placement of leads in the atrium and through the coronary sinus to the systemic left ventricle is occasionally utilized but carries a high risk of perforation, right-left shunting, and embolization.

Heart Failure

- Fontan conduit failure, manifesting as "right" heart failure (venous hypertension, ascites), is prevalent in adults after a Fontan repair, in particular if increased pulmonary vascular resistance or LV systolic or diastolic dysfunction develops.
- Addressing any pulmonary or systemic arterial stenosis such as branch PS at old shunt sites or aortic coarctation is important.
- Treatment includes diuretics and, in select cases, pulmonary vasodilators.

- Screening for cirrhosis and hepatocellular carcinoma is recommended. Our center has every Fontan patient follow with a hepatologist annually.
- Systemic ventricular failure may occur, especially with a systemic right ventricle; close control of blood pressure and afterload reduction is essential.
- Given atrial tachyarrhythmias are common, prolonged duration of tachycardia may contribute to systemic ventricular dysfunction. Prompt restoration of normal sinus rhythm, rather than a rate control strategy, is usually recommended.
- Single ventricle patients typically live with low or low normal cardiac output.
- Serial cardiopulmonary exercise testing can be useful in better understanding potential causes to address in the aging or failing Fontan.
- In the "failing Fontan," several factors should be investigated and addressed if found: pathway obstruction, pulmonary vein compression, intracardiac regurgitation or obstruction, giant right atrium, any thrombosis or thromboembolism, atrial (more often than ventricular) arrhythmias, ventricular dysfunction or decreased cardiac output, protein-losing enteropathy, hepatic disease, and abnormalities of the pulmonary vascular bed.

Protein-Losing Enteropathy

- Protein-losing enteropathy (PLE) is a debilitating consequence of a Fontan procedure, thought to be due to chronically elevated systemic venous and portal pressures.
- It is diagnosed in 4–14% of patients after a Fontan procedure, usually in the first two decades after initial surgery [7, 8].
- Median survival is 5 years after diagnosis.
- Low albumin, recurrent ascites, and diarrhea should prompt investigation with a stool alpha-1 antitrypsin.

- PLE is further stimulated by elevated venous pressures in conjunction with increased inflammation (circulating tumor necrosis factor and other inflammatory markers).

Thromboembolic Risk

- The low pressures and slow flow through the Fontan circulation increase the risk of thrombus formation.
- The presence of a baffle leak (either created as a fenestration or developing over time due to baffle dehiscence) can lead to right-to-left embolization and stroke.
- The risk is particularly high in patients with a right atrial appendage to pulmonary artery Fontan.
- Aspirin may be utilized for thromboembolic prophylaxis; anticoagulation with warfarin is indicated for high-risk patients (RA-to-PA Fontan, pulmonary arterial stump, atrial tachyarrhythmias, prior thromboembolic events, underlying coagulopathy, PLE, depressed systemic ventricular function).
- There is not yet data available on the use of direct oral anticoagulants.

Non-cardiac Surgery

- As pulmonary circulation is dependent on passive venous return, patients are preload-dependent after a Fontan procedure and particularly sensitive to dehydration, venodilators, and positive-pressure ventilation. Early extubation after procedures is important to encourage when possible.
- If intubation is required, blood pressure must be closely monitored.
- Non-cardiac surgery, unless an emergency, should be performed at a center with ACHD expertise (Class 1, LOE C) [6]. At our center, we also request cardiac anesthesia consultation.

Indications for Transplant

- For patients with defined anatomic issues with the Fontan pathway, or symptoms linked to a high burden of atrial arrhythmias, conversion to an extracardiac Fontan (termed "Fontan revision") is often the first step in surgical management.
- Operative repair options are limited for patients with rising pulmonary artery pressures and a failing Fontan pathway or those with declining systemic ventricular function.
- Fontan patients represent ~40% of transplant recipients with a history of CHD based on a recent analysis of US administrative data [9].
- Short-term posttransplantation outcomes in Fontan patients are worse than in other ACHD patients [9, 10], though improving in recent studies. In those who survive the postoperative period, medium- and long-term outcomes are similar to other CHD patients and better than transplants recipients without CHD [11].
- Low peak oxygen consumption and heart rate reserve are helpful in determining transplant eligibility; the morbidity and mortality associated with transplant must however be weighed against that of the current palliated anatomy or possible surgical procedures, especially as the techniques for the latter continue to improve [11].
- Mechanical circulatory support is under investigation in congenital heart disease, but univentricular hearts still present a unique challenge, and underlying coagulopathy and early and progressive liver disease often pose significant bleeding risks in addition to anatomic and physiologic challenges.

Pregnancy

- Pregnancy in women who have undergone Fontan palliation carries a high risk of complications, particularly if there is systemic ventricular dysfunction, uncontrolled

arrhythmias, pulmonary hypertension, severe cyanosis, or chronic heart failure.

- Atrial arrhythmias should be managed in a timely way with medical therapy (beta blockade, digoxin), and cardioversion is safe in pregnancy if medical therapy fails.
- Cardiopulmonary exercise testing can be useful in predicting potential complications and in shared decision-making regarding risk/benefit with the patient.
- All individuals with complex congenital heart disease should have updated anatomic assessment, genetic counseling, and multidisciplinary assessment with the high-risk obstetric team, ACHD team, and obstetric anesthesia prior to pregnancy.
- Ensuring adequate preload during vaginal delivery is important.
  - Leg elevation or left lateral decubitus positioned may augment preload.

References

1. Bernier PL, Stefanescu A, Samoukovic G, Tchervenkov CI. The challenge of congenital heart disease worldwide: epidemiologic and demographic facts. Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu. 2010;13:26–34.
2. Hoffman JIE, Kaplan S, Liberthson RR. Prevalence of congenital heart disease. Am Heart J. 2004;147:425–39.
3. Khairy P, Poirier N, Mercier LA. Univentricular heart. Circulation. 2007;115:800–12.
4. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax. 1971;26:240–8.
5. DeFaria Yeh D, King ME. Congenital heart disease in the adult: what should the adult cardiologist know? Curr Cardiol Rep. 2015;17:25.
6. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 guidelines for the management of adults with congenital heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice guidelines (writing committee to develop guidelines on the manage-

ment of adults with congenital heart disease). Circulation. 2008;118:e714–833.
7. Feldt RH, Driscoll DJ, Offord KP, et al. Protein-losing enteropathy after the Fontan operation. J Thorac Cardiovasc Surg. 1996;112:672–80.
8. Mertens L, Hagler DJ, Sauer U, Somerville J, Gewillig M. Protein-losing enteropathy after the Fontan operation: an international multicenter study. PLE study group. J Thorac Cardiovasc Surg. 1998;115:1063–73.
9. Karamlou T, Diggs BS, Welke K, et al. Impact of single-ventricle physiology on death after heart transplantation in adults with congenital heart disease. Ann Thorac Surg. 2012;94:1281–7; discussion 1287–8.
10. Karamlou T, Hirsch J, Welke K, et al. A United Network for Organ Sharing analysis of heart transplantation in adults with congenital heart disease: outcomes and factors associated with mortality and retransplantation. J Thorac Cardiovasc Surg. 2010;140:161–8.
11. Ross HJ, Law Y, Book WM, et al. Transplantation and mechanical circulatory support in congenital heart disease: a scientific statement from the American Heart Association. Circulation. 2016;133:802–20.