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Single ventricle/total cavopulmonary connection (Fontan circulation)

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Summary

The Fontan operation has allowed the survival of many patients born with severe congenital heart disease. However, this palliation creates a form of man-made circulation characterized by a neo-portal dam that leads to decreased cardiac output and systemic venous congestion. The Fontan circulation itself can trigger a vicious downward spiral, with increasing pulmonary vascular resistance and decreasing ventricular compliance, both leading to circulation failure. The overall treatment options for circulatory failure in a Fontan circuit are disappointing as the critical bottleneck allows little modification. Pulmonary vasodilators have limited effect and there are no effective lusitropic drugs. Avoidance of problems by creating and maintaining good building blocks such as pulmonary vasculature and ventricle is most important.

What is a Fontan circulation?

A Fontan circulation is characterized by the absence of an adequate subpulmonary ventricle. Since the 1990s, a type of circulation has been created by connecting the superior and inferior caval vein to the pulmonary arteries: total caval pulmonary connection (TCPC)[1] (Figure **17.29.1** and Figure **17.29.2**). By doing so, the pulmonary circulation is put, like a portal system, between the venous return of the body and the systemic ventricle (Figure **17.29.3**). This portal system therefore functions like a dam in the cardiovascular circuit, with all of its characteristics: upstream congestion and downstream decreased flow; the energy from the dam is used to get the blood oxygenated. The two features, elevated systemic venous pressure and chronically decreased to low cardiac output, are the root cause of the majority of the physiological impairments of the Fontan circulation. A Fontan circulation is offered to patients who have only one functional ventricle or the inability to split the ventricular mass into two adequate pumps.

Single ventricle/total cavopulmonary connection (Fontan circulation)

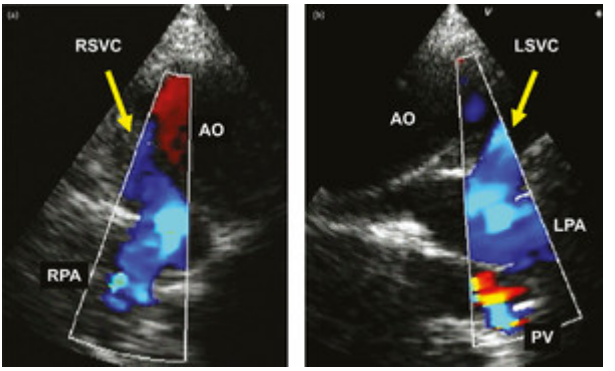

Figure 17.29.1
Right-sided (a) and left-sided (b) Glenn anastomosis (arrows) as seen from suprasternal view. Laminar flow in both cavopulmonary connections confirmed by colour flow mapping. AO, aorta; LPA, left pulmonary artery; LSVC, persistent left superior caval vein; PV pulmonary veins; RPA, right pulmonary artery; RSVC, right superior caval vein.

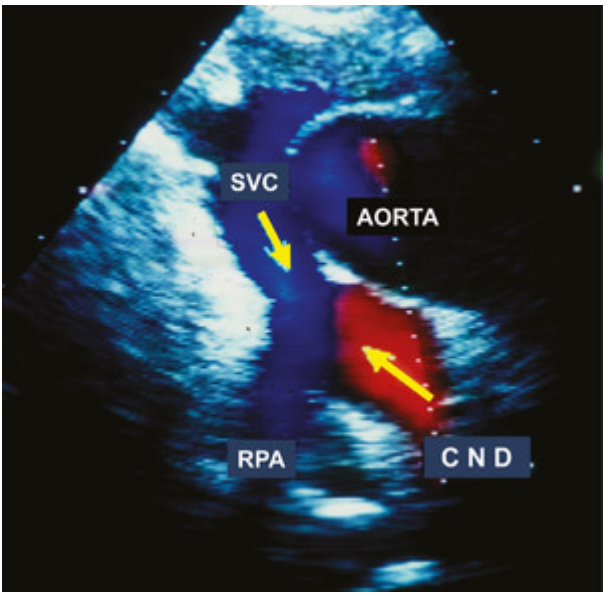

Figure 17.29.2
Total cavopulmonary connection visualized from right infraclavicular view. Arrows indicating flows connected to pulmonary arteries from right superior caval vein (SVC) and from inferior caval vein conduit (CND). RPA, right pulmonary artery.

Single ventricle/total cavopulmonary connection (Fontan circulation)

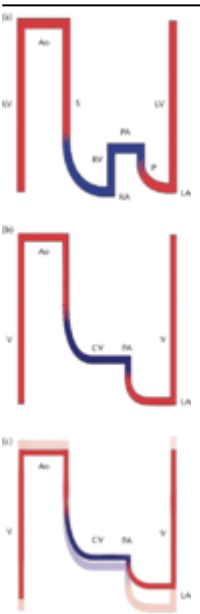

Figure 17.29.3
Scheme of the normal cardiovascular circulation (a), and the Fontan circulation at different stages (b, c). (a) Normal biventricular circulation with two ventricles: the pulmonary circulation (P) is connected in series to the systemic circulation (S). (b) Fontan circuit: the caval veins are directly connected to the pulmonary artery (PA); systemic venous pressures are markedly elevated. (c) Fontan circuit late (superimposed on early Fontan circuit): with time, a negative spiral ensues: pulmonary resistance increases resulting in further increase in CV congestion but even more in reduced flow, which increases ventricular filling pressure. Ao, aorta; CV, caval veins; LA, left atrium; LV, left ventricle; PA, pulmonary artery; RV, right ventricle; V, single ventricle. Line thickness reflects output, and colour reflects oxygen saturation.

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Since its original description by Francis Fontan in 1971,[2] the Fontan circuit has undergone numerous modifications. Early on, surgeons created various connections between the right atrium and the pulmonary artery (anterior atriopulmonary connection, with or without inclusion of a small hypoplastic right ventricle, posterior atriopulmonary connection), with different materials (valved conduits, homografts, patches, direct anastomosis). The very high incidence of obstruction requiring late reoperations reflects the poor design of the early circuits. Such older circuits are no longer created and are considered obsolete; however, many adults still survive with one of them. When assessing a patient with a ‘Fontan circuit’, the clinician needs to know exactly which connection has been made and what material has been used.

Despite the abnormality of the circuit, clinicians are frequently impressed by the ability of most patients with a Fontan circulation to lead a nearly normal life, including mild to moderate sporting activities for many years. More than 90% of all survivors are in New York Heart Association class I or II. Most patients go through education in the same way as the general population and can pursue a wide variety of professional careers.[3]

Haemodynamic characteristics of a Fontan circulation: where is the critical bottleneck?

By damming of the blood flow to the ventricle, the surgeon shifts the critical bottleneck of the circulation out of the heart. The Fontan portal system dams off the blood, causing the venous congestion and the decreased output.[4] The ventricle, while still the engine of the circuit, cannot compensate for this major flow restriction: the suction required to compensate for the damming effect of the Fontan portal system cannot be generated.[5] The components that make up the Fontan neo-portal system then become critically important. These include the Fontan connection itself, the pulmonary arteries, the pulmonary capillary network (including pre-capillary sphincters), the pulmonary veins, and the venoatrial connection. Impairment at any level of this portal system will have profound consequences on the output of the Fontan circuit, much more than a comparable dysfunction in a two-ventricle circulation. These impairments include, but are not limited to, stenosis, hypoplasia, distortion, vasoconstriction, pulmonary vascular disease, loss or exclusion of large vessels or micro-vessels, turbulence and flow collision, flow mismatch, and obstruction by external compression.

The ventricle can make this compromised circulation even worse. With time, the compliance decreases, resulting in increasing filling pressures: the critical bottleneck may therefore shift from the Fontan portal connection to the diastolic function of the ventricle. When a Fontan circuit fails, the cardiologist is typically confronted with a patient with venous congestion, low output, and a large, thick, hypocontractile dyskinetic ventricle; it is intuitive for him or her to ascribe this to a pure or dominant ventricular problem. The Fontan circulation, however, appears to be an exception to that rule.

The Fontan state of decreased flow and congestion has multiorgan effects

The failing Fontan patient may have a plethora of problems including early and late demise, limited exercise ability, ventricular systolic and diastolic dysfunction, arrhythmias, cyanosis, hepatomegaly with secondary fibrosis, cirrhosis and hepatic carcinoma, lymphatic system failure resulting in protein-losing enteropathy and plastic bronchitis, venous thromboses with pulmonary embolism, local thrombus formation in the Fontan conduit, ascites, and peripheral oedema.[6]

The ventricle

The ventricle in a Fontan circulation evolves from being volume overloaded and stretched during fetal life and after initial palliation, to being overgrown and chronically volume deprived, with increasing systemic vascular resistance, during the Fontan state.[7]

In the initial neonatal phase, blood flows to the lungs under high pressure generated by the ventricle. Such overload results in ventricular overgrowth and some spherical dilation. Volume overload is abolished when taking down the high-pressure shunt, but preload to the ventricle is further dammed off when connecting each caval vein to the pulmonary artery. A Fontan connection chronically volume deprives the ventricle, and this effect is amplified by diuretics but attenuated by collateral flow and valve regurgitation. During exercise, normals can increase their stroke volume by 20–50%; in contrast, such an exercise-induced increase can be completely absent in Fontan patients.[8] Chronic deprivation is known to decrease contractility and to increase muscle stiffness, resulting in increasing filling pressures.[9] The Fontan ventricle is chronically volume deprived with reduced to absent exercise-induced stretch; the overgrowth and possibly dilation due to the initial volume overload, the remodelling after unloading resulting in concentric hypertrophy, all accentuate the effects of deprivation. This negative vicious spiral will eventually contribute to Fontan circulation failure.

The lungs

The lungs in a Fontan circulation also have their story. The initial shunting procedure(s) may cause symmetric or asymmetric over- or underflow. As a result, hypoplasia or mild pulmonary vascular disease of the pulmonary vascular bed is common. Stenosis resulting from abnormal connections, (bilateral) ductal constriction, or surgical scarring can further compromise the normal pulmonary architecture. The Fontan circulation itself creates in the pulmonary vasculature a situation in which there is chronically decreased flow, minimal to mild desaturation, increased collateral flow, suboptimal mixing of inferior and superior caval flow, absence of pulsatility, endothelial dysfunction, and absence of episodes of high flow and high pressure as are normally seen during exercise. This will induce a negative vicious spiral which eventually contributes to Fontan circulation failure.

The lymphatic system

A Fontan circulation operates close to the functional limits of the lymphatic system. With time, lymphoid fluid may leak into the interstitium, the gut, or the bronchi, and result in protein-losing enteropathy or plastic bronchitis. Protein-losing enteropathy is a rare complication, occurring in 1–5% of Fontan patients. High-protein chyle with lymphocytes leaks into the gut, resulting in hypoalbuminemia, oedema, abdominal bloating, diarrhoea, lymphocytopenia, and

progressive cardiac cachexia.[10] Plastic bronchitis results in bronchial casts with life-threatening asphyxiating cough. The Fontan circulation causes significant flow redistribution, with flow reduction in the gut. Moreover, the splanchnic vasculature then drains to the heart through a double portal system (first hepatic then pulmonary). Increased venous congestion, poor perfusion and dilated lymphatic vessels, sometimes in combination with inflammation (after an intercurrent infection), diminished expression of glycosaminoglycan (required to stabilize the lymphoid and gut epithelium), and a genetic predisposition are thought to be responsible for the development of protein-losing enteropathy.

The liver

The liver is in a particularly precarious state following the Fontan operation. It is wedged between the capillary bed of the organs of the abdominal viscera and the capillary bed of the lungs (double portal system). This results in substantially diminished perfusion of the liver with decreased portal flow, in addition to the decreased arterial flow and the burden imposed by the chronic elevation of pressure in the inferior caval vein, and subsequently the central veins of the liver.

These abnormal haemodynamics can result in significant fibrosis and cirrhosis. The timing of the onset and the development of these pathological changes in the liver is variable. In most patients, the liver tolerates the Fontan state for several decades but, in some patients, this has led to the need for heart–liver transplant while, in other cases, changes to the liver parenchyma have resulted in hepatocellular carcinoma.[11]

How to make a Fontan circulation as good as possible?

When creating a Fontan circuit, the limiting factor or critical bottleneck of the circuit shifts from the heart to the Fontan portal system. It is therefore essential that the impedance of the Fontan portal system is as low as possible. The critical hallmarks or building blocks are therefore the pulmonary vasculature, the surgical connection, and ventricular diastolic function.

The pulmonary vasculature is critical. If the resistance is too high, a Fontan circuit is completely non-viable. Ideally the pulmonary vasculature should have low impedance, including low resistance at rest, and high capacitance with vascular recruitment during exercise. Adequate growth and development are therefore essential; however, catch-up growth, which is frequently required in these malformations, is only available in the initial palliative state with a high-pressure–high-flow shunt. Once pulmonary flow is provided by a cavopulmonary connection (Glenn shunt or Fontan), no significant catch-up growth can be expected. The initial neonatal palliation is therefore the most important phase in the

development of the future building blocks of the final Fontan circuit. Pulmonary hypoplasia, stenosis, distortion, vascular disease, and loss or exclusion of large- or micro-vessels must be avoided.

The surgical connections have significantly improved since the 1990s with the emphasis on effective flow without turbulence or flow collision, and distribution of hepatic venous blood to both lungs to avoid late arteriovenous malformations.[12,13] With current cavopulmonary connections, little gain in efficiency is to be expected from further surgical modifications.

The ventricle in a Fontan circuit is still the pump, but it has lost the control over the circulation; both systemic venous congestion and output are now controlled by the Fontan portal system. The ventricle can influence the flow through the critical bottleneck by its diastolic function: low filling pressures will (slightly) enhance flow though the lungs, high filling pressures will limit transpulmonary flow (and thus cardiac output). The clinician has, however, no tools or lusitropic drugs to enhance diastolic function, especially not in a chronically deprived ventricle. It is, therefore, essential that the intrinsic diastolic function remains preserved during growth by avoiding overgrowth, dilation, long-standing pressure or volume overload, and later disuse hypofunction by chronic deprivation (by the Fontan portal system itself). The volume requirements for optimal growth and development of the ventricle and the lungs during infancy are therefore different and opposed. Avoiding significant overload of the ventricle avoids damage, but excessive protection from volume overload may cause pulmonary vascular hypoplasia, which in turn will severely affect the outcome of the final Fontan circuit.

How to keep a Fontan circulation as good as possible?

A functional decline of a Fontan circuit can be expected and is observed. The chronic venous congestion and diminished output, typical for the Fontan physiology itself, may in time trigger a vicious downward spiral which will cause morbidity and mortality.

The Glenn and Fontan connections generate abnormal conditions for the pulmonary vascular bed. Longstanding diminished flow, desaturation, increased collateral flow, below normal mixing of inferior and superior caval flows, lack of pulsatile flow, endothelial dysfunction, and absence of periods of high flow and high pressure with vessel recruitment, influence function with increasing resistances. Moreover, the chronic volume deprivation results in ventricular remodelling, reduced compliance, and increasing filling pressures. A failing Fontan circuit is thus characterized by high and increasing pulmonary (and systemic) vascular resistance, increasing congestion, decreasing output, ventricular compliance and contractility, and neurohormonal activation.

As in many diseases, avoidance of problems is essential as treatment options are disappointing. In a complex circuit, many components can act as a bottleneck and may be improved. We will now discuss all potential bottlenecks in order of appearance in the circuit. However, when multiple bottlenecks are put in series, only changes at or immediately around the critical bottleneck will acutely improve overall flow; changes at a distance from the critical bottleneck usually will be irrelevant; at most they may influence the critical bottleneck with time.

◆ *Venous congestion*: chronic high venous pressures in excess of 18–20 mmHg are poorly tolerated in Fontan patients and result in symptoms such as congestion, oedema, ascites, thrombus formation, lymphatic failure, and progressive veno-venous collaterals with cyanosis. Diuretics control some of these, but at the risk of aggravating the long-term effects of ventricular deprivation.

◆ *Anticoagulation*: low flow and stasis in dilated veins predispose for clot formation, and liver dysfunction with protein loss may result in a prothrombotic state due to protein C deficiency, protein S deficiency, and antithrombin III deficiency[14] (Figure **17.29.4**). Thrombosis may complicate an infection, especially when associated with dehydration. A systemic venous thrombus may embolize to the pulmonary artery. Massive embolization may result in shock, arrhythmia, or death. It is the most common cause of sudden out-of-hospital death in patients with a Fontan circuit. Chronic multiple pulmonary microemboli may lead to pulmonary vascular obstructive disease, a late complication particularly lethal in a Fontan circulation. Some clinicians recommend anticoagulation for all patients with a Fontan circuit; however, there are clearly subgroups of patients with a very low risk. No difference in thromboembolic events was observed between aspirin and warfarin beyond the first year after the extracardiac conduit Fontan procedure.[15] Full anticoagulation should be prescribed in patients with previous thrombi, poor cardiac output (frequently associated with spontaneous contrast on echo), excessive congestion, dilation of venous or atrial structures, arrhythmia, and older age. The place of new oral anticoagulation therapies is being determined.[16] If coagulation abnormalities are present, oral contraceptives should not be prescribed without adequate anticoagulation.

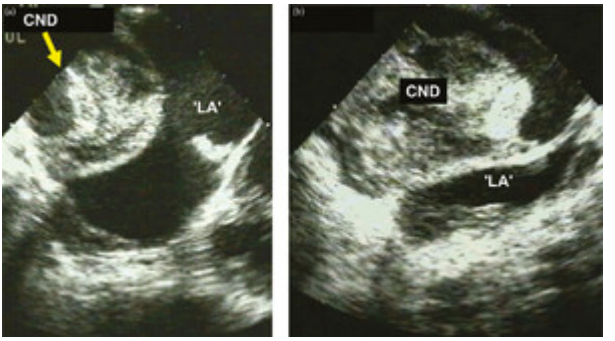

Figure 17.29.4
Intra-atrial conduit (CND) in total cavopulmonary connection visualized from two parasternal views (a, b), suspected large thrombogenic formation confirmed later on angiogram.

◆ The Fontan connection should be optimized by alleviating turbulence and gradients. Conversion to a more streamlined cavopulmonary connection appears a good investment when the patient becomes symptomatic, or even earlier.[17,18] This, however, involves a major operation.

◆ *Pulmonary vasculature:* pulmonary artery stenosis, hypoplasia, distortion, flow collision, or excessive collateral flow should be detected early and managed. Regular exercise and adapted breathing patterns may play a role in the ability to increase transiently central venous pressure, but especially to lower the pulmonary vascular impedance by repeated vessel recruitment and vasodilation.[19] Pulmonary vasodilators have been studied (oxygen at altitude, sildenafil, bosentan, inhaled iloprost); however, as only few pulmonary vascular lesions are amenable to dilation, the haemodynamic improvements have been modest, with modification of pulmonary vascular resistance in the region of 0–8%.[20,21,22,23] Such amelioration can critically improve a failing Fontan patient, but further studies are required to determine to what extent these agents can affect the long-term outcomes in the overall Fontan population.

◆ *Ventricular function*: we currently have no lusitropic drugs that can significantly lower ventricular filling pressures, especially not in a preload deprived ventricle. Moreover, ageing and sustained ‘disuse hypofunction’ remodelling may further reduce ventricular compliance.[24] The effects on ventricular filling pressure by agents which alter contractility, heart rate, or afterload are frequently negligible. Making the Fontan ventricle contract harder, faster, or against a lower afterload will not increase output as the ventricle has no preload reserve. Angiotensin-converting enzyme inhibitors have repeatedly been shown to have no acute effect; it still needs to be determined if such drugs can influence long-term ventricular diastolic

function. Resynchronization may be helpful if desynchronization impairs diastolic and systolic function (Figure **17.29.5**).

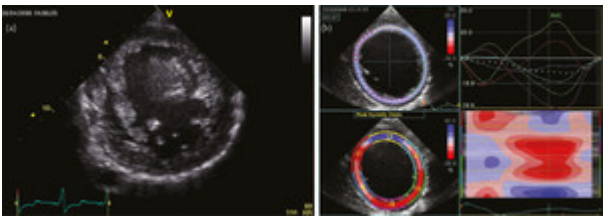

Figure 17.29.5
Failing Fontan circulation demonstrated grossly dilated ventricle (a) with significant mechanical dyssynchrony on speckle tracking strain echocardiography (b).

◆ *Arrhythmia:* patients with a Fontan circulation are predisposed to develop atrial arrhythmias. In many older circuits, the atrial wall is incorporated in the circuit, causing atrial dilatation and hypertrophy; furthermore, most patients have had an atriotomy, possible injury to the sinus node, or its arterial supply or innervation. The incidence of late atrial tachycardia has decreased with the use of cavopulmonary connections.[25] Clinically, tachycardias are more common after Fontan in patients with a suboptimal haemodynamic result, especially if the right atrium is dilated and the pulmonary vascular resistance is increased. The prognosis, therefore, remains worrying even if the patient can be reconverted to sinus rhythm. The most common atrial tachycardia is intra atrial reentry tachycardia or atypical atrial flutter. Such tachycardia can quickly lead to severe haemodynamic deterioration. Survival depends on the ventricular contractility and the vascular resistance, which can be critically altered by most antiarrhythmic drugs. The safest option is therefore immediate direct current cardioversion. During the subsequent work-up, the clinician should obtain a complete haemodynamic evaluation in every patient with a new tachycardia, as this may be the late but first clinical manifestation of pathway obstruction and/or thrombi. Full anticoagulation should be considered in every Fontan patient with atrial arrhythmias, in view of the significant risk of a right atrial thrombus. Long-term treatment of atrial arrhythmia can involve medication and ablation. Progression of the arrhythmia and functional decline is frequently observed. The best long-term investment for these patients may be conversion of the old Fontan circuit to an extra cardiac cavopulmonary connection, together with a right atrial Maze and a reduction plasty (combined with a DDD epicardial pacemaker if indicated).[26] Ventricular arrhythmias are rare in patients with a Fontan circulation. If present, they are probably related to very poor Fontan haemodynamics or severe ventricular dysfunction.

◆ *Fenestration:* creation of a fenestration (Figure **17.29.6**) between the systemic veins and the pulmonary atrium improves cardiac output and relieves congestion at the price of arterial saturation. Primary fenestration at the time of the Fontan operation speeds up postoperative recovery, is usually well tolerated, and may be functional for a long period—up to several years. Closing the fenestration typically results in improved oxygen saturations, both at rest and during exercise, leading to improved exercise ability. The discussion is still open whether the increased exercise tolerance outweighs the long-term benefit of decreased congestion which might delay late hepatic and lymphatic dysfunction. Secondary fenestration, late in a failing but 'pink' Fontan, results in a degree of cyanosis that is typically not well tolerated. In such a patient, achieving a balance between cyanosis, decreased congestion, and increased output is quite difficult and may not be possible. Nevertheless, percutaneous fenestration in the failing Fontan may have a place while waiting for a cardiac transplant.

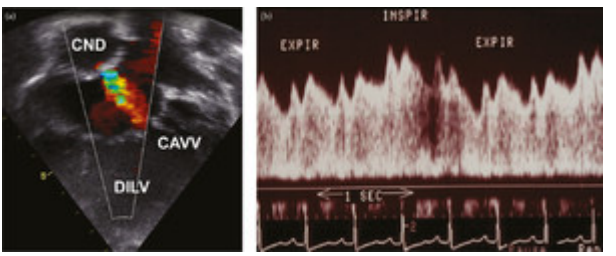

Figure 17.29.6
Total cavopulmonary connection with fenestration indicated by colour flow mapping (a), Doppler flow profile demonstrated continuous flow with marked respiratory variation (b). CAVV, common atrioventricular valve; CND, conduit; DILV double-inlet left ventricle.

◆ *Lymphatic failure*: optimization of the Fontan circuit is of upmost importance, preferably well before any complication develops. Both plastic bronchitis and protein-losing enteropathy can be lethal. Symptoms can be alleviated by diuretics, protein infusions, and bronchial cast dissolvers.[27] Additionally, local intestinal steroids (budesonide),[28] heparin, high-dose spironolactone,[29] somatostatin, super-selective embolization of the lymphatic leak,[30,31] secondary fenestration,[32] thoracic duct decompression,[33] and heart transplantation[34] have all had a role in the management of this insidious complication.

◆ *Mechanical support:* mechanical support for the failing single ventricle is still under development. The usual ventricular assist devices are designed to aid a failing systemic ventricle. In the failing Fontan circulation, where the problem is not ventricular performance

but rather the neo-portal system, the interposition of a subpulmonary assist device or biventricular assist may be needed.[35,36,37]

◆ *Heart transplantation:* in many cases of Fontan circulation failure, heart transplantation is likely to be the final outcome. Heart transplantation in Fontan patients is associated with a higher risk than that in patients without congenital heart disease, and may be even higher in those patients with Fontan circulation failure but preserved ventricular function.[38]

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