Chapter 8
Missing a Sub-pulmonary Ventricle: The Fontan Circulation

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The "Fontan" Concept

A normal mammal cardiovascular system consists of a double circuit, pulmonary and systemic, connected in series and powered by a double chamber pump. In the absence of congenital heart disease, the right ventricle pumps through the pulmonary circulation and the left ventricle through the systemic circulation (Fig. 8.1a).

Many complex cardiac malformations are characterized by the existence of only one functional ventricle (Fig. 8.2). This "single" ventricle has to maintain both the systemic and the pulmonary circulations, which during fetal life and at birth are not connected in series but remain in parallel (Fig. 8.1b). Such a circuit has two major disadvantages: diminished oxygen saturation of the systemic arterial blood and a chronic volume load of the single ventricle. The chronic ventricular volume load leads to a progressive ventricular dysfunction and remodeled pulmonary vasculature, causing a gradual attrition due to congestive heart failure and pulmonary hypertension from the third decade of life, with few survivors beyond the fourth decade.

In 1971 Francis Fontan [1] from Bordeaux, France, reported a new approach to the operative treatment of these malformations, separating the systemic and pulmonary circulations. In a "Fontan circulation" the systemic venous return is connected to the pulmonary arteries without the interposition of a pumping chamber (Fig. 8.1c). In this construct, residual post-capillary transit energy is used to push blood through the lungs in a new portal circulation-like system [2]. Advantages of a Fontan circuit include (near-) normalization of the arterial oxygen saturation and abolishment of the chronic volume load on the single ventricle. However, because the pulmonary

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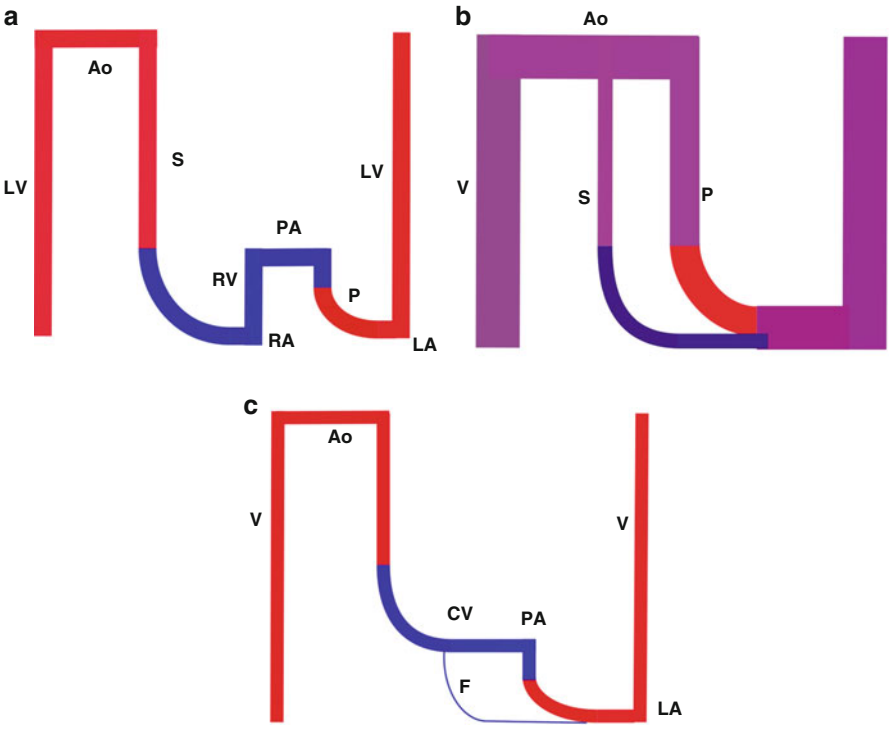


Fig. 8.1 Schematic representation of the normal cardiovascular circulation (**a**), shunted palliation (**b**), and Fontan circulation (**c**). (**a**) Normal circulation: the pulmonary circulation (P) is connected in series with the systemic circulation (S). The right ventricle maintains the right atrial pressure lower than the left atrial pressure, and provides enough energy for the blood to pass through the pulmonary resistance. (**b**) The systemic (S) and pulmonary (P) circuits are connected in parallel, with a considerable volume overload to the single ventricle (V). There is complete admixture of systemic and pulmonary venous blood, causing arterial oxygen desaturation. (**c**) Fontan circuit: the systemic veins are connected to the pulmonary artery (PA), without a subpulmonary ventricle or systemic atrium: the lungs are thereby converted into a neo-portal system which limits flow to the ventricle. In the absence of a fenestration, there is no admixture of systemic and pulmonary venous blood, but the systemic venous pressures are markedly elevated. A fenestration (F) allows the systemic venous blood to bypass the Fontan portal system and limits the damming effect, thereby increasing output and decreasing congestion, but also arterial saturation. *Ao* aorta, *CV* caval veins, *F* fenestration, *LA* left atrium, *LV* left ventricle, *PA* Pulmonary artery, *RV* right ventricle, *V* single ventricle. Line thickness reflects output, color reflects oxygen saturation

impedance hinders venous return through the pulmonary vasculature, this circulation creates a state of chronic "hypertension" and congestion of the systemic veins, and results in a decreased cardiac output, both at rest and during exercise [3, 4] (Fig. 8.3). These two features of the Fontan circulation, elevated systemic venous pressure and chronically low cardiac output, are the root cause of the majority of the physiologic impairments of this circulation.

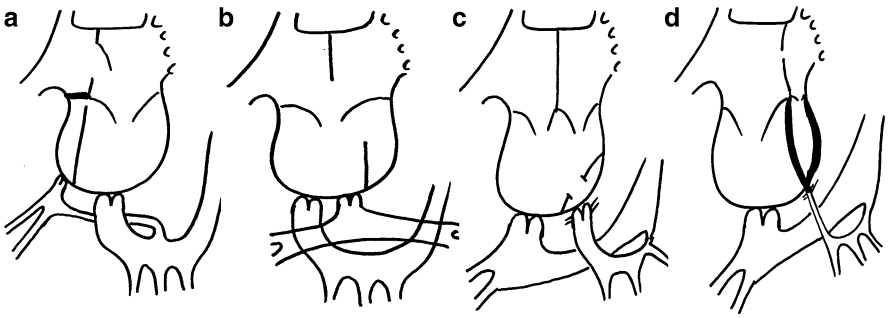


Fig. 8.2 Different examples of functional single ventricles: (**a**) tricuspid valve atresia with hypoplastic right heart, ductal flow to pulmonary artery; (**b**) double inlet right ventricle DIRV through an unbalanced atrioventricular septal defect with common atrioventricular valve, double outlet right ventricle DORV and hypoplasia of the left ventricle; (**c**) double inlet left ventricle DILV with left-sided hypoplastic right ventricle, restrictive ventricular septal defect VSD acting as subaortic stenosis, transposition of the great arteries TGA, small aortic arch and coarctation of aorta; (**d**) hypoplastic left heart syndrome HLHS due to aortic valve atresia

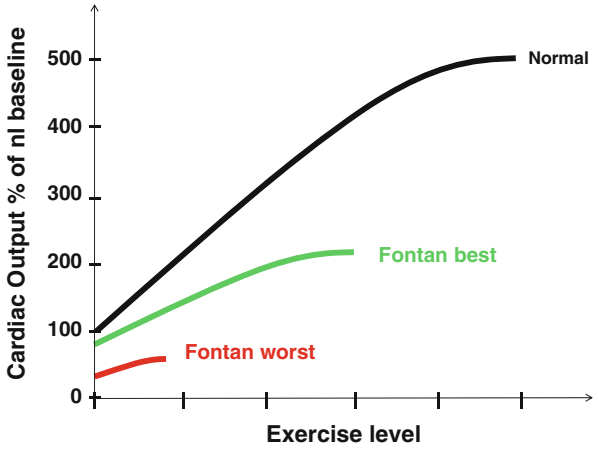


Fig. 8.3 Exercise and output: normal versus Fontan circulation: A normal subject with a biventricular circuit can increase his output by a factor of 5 (*black line*). In Fontan patients, output is significantly impaired both at rest and during exercise; at best (*green line*) the output is mildly decreased at rest, with moderate capacity to increase flow during moderate exercise. At worst (*red line*), the output is severely reduced at rest and barely augments during minimal exercise

Is Every Fontan Circuit the Same?

Since its original description, the Fontan circuit has undergone **numerous modifications**. Early on surgeons used valves (cavo-atrial, atrioventricular, or atrio-pulmonary) and created various connections between the right atrium and the pulmonary artery (anterior atrio-pulmonary connection, with or without inclusion

of a small hypoplastic right ventricle, posterior atrio-pulmonary connection), with different materials (valved conduits, homografts, patches, direct anastomosis). The very high incidence of late reoperations, reaching 40 % in some series, does reflect the poor design of the first Fontan circuits and the less than ideal surgical techniques used in the early series. Most of the older circuits are no longer created and considered obsolete; however, many patients still survive with such circuits. 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.

During the last decade, the **total cavo-pulmonary connection** (TCPC) has emerged as being superior [5]. The caval veins are connected to the pulmonary artery, bypassing not only the right ventricle but also the right atrium (Fig. 8.4a–c).

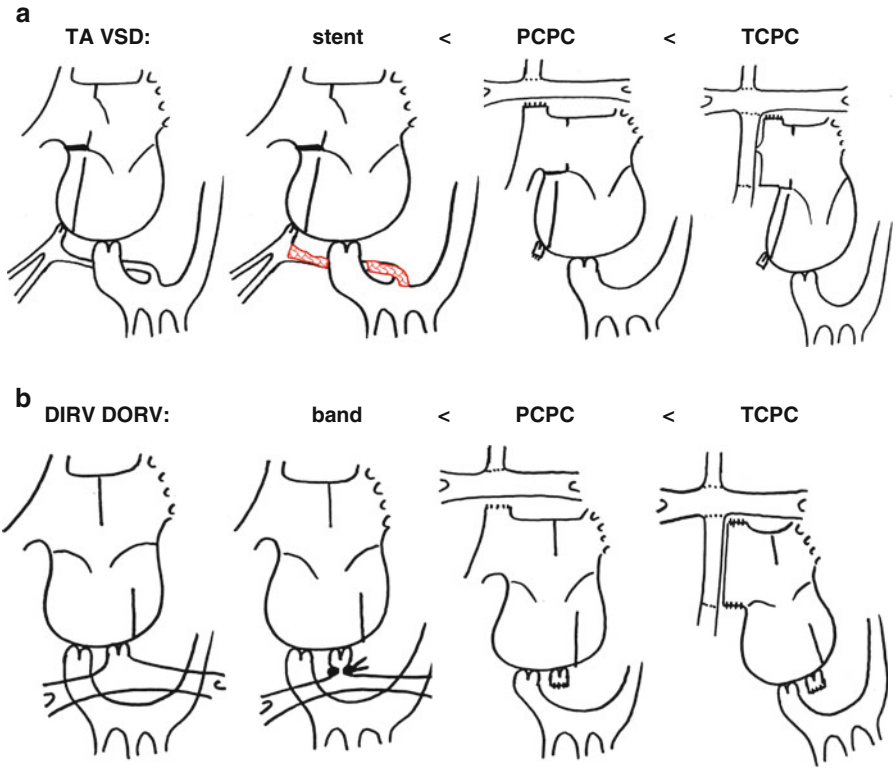
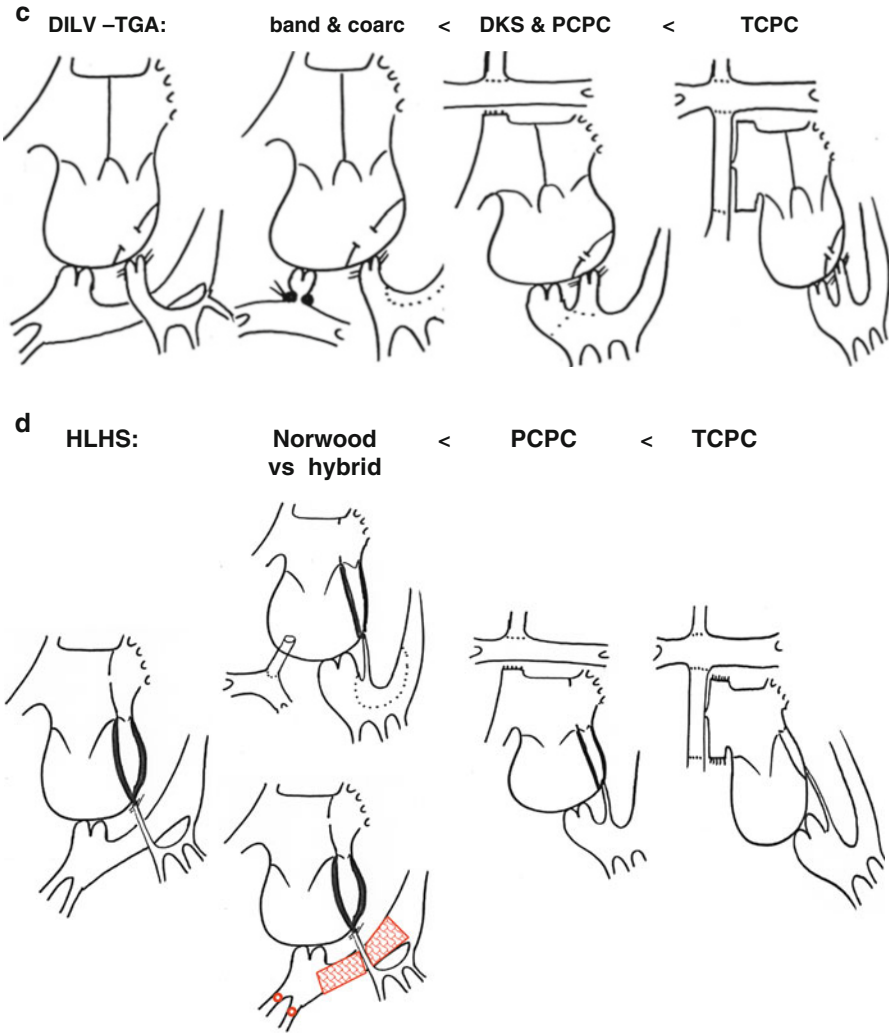


Fig. 8.4 Schematic representation of treatment strategy from birth to Fontan circulation. (**a**) Patient of with tricuspid valve atresia and hypoplastic right heart (cf. Fig. 8.2a): first palliation consists of stenting the arterial duct, followed by partial cavo-pulmonary connection (PCPC); at the age of about 3 years the Fontan circulation or total cavo-pulmonary connection (TCPC) is completed by connecting the inferior caval vein through an extracardiac conduit to the pulmonary artery; a small fenestration is created between the conduit and the right atrium. (**b**) Patient of Fig. 8.2b (DIRV DORV AVSD): initial palliation consists of banding of the pulmonary artery at the age of 4–6



weeks; **Fig. 8.4** (continued) PCPC at 6 months; TCPC at 3 years. (**c**) Patient of Fig. 8.2c (DILV TGA coarctation): initial palliation consists of neonatal banding of the pulmonary artery with arch reconstruction; PCPC with Damus-Kaye-Stansel operation at 6 months; TCPC at 3 years. (**d**) Patient of Fig. 8.2d (HLHS): initial palliation consists of either Norwood operation (complex arch reconstruction, atrial septectomy, Sano shunt from RV to pulmonary artery) or hybrid procedure (stent in duct, bilateral banding branch pulmonary arteries); PCPC ± Norwood arch repair at 6 months; TCPC at 3 years

The superior caval vein is connected to the pulmonary artery (bidirectional Glenn shunt or partial cavo-pulmonary connection [PCPC]). There are two variants to connect the inferior caval vein: the lateral tunnel and the extra cardiac conduit. Introduced in the mid-1980s, **the lateral tunnel** provides a tubular path between the

inferior caval vein and the pulmonary artery, consisting of a prosthetic baffle and a portion of the lateral atrial wall. This circuit has growth potential and can therefore be created in children as young as 1 year; it leaves a minimal amount of atrial tissue exposed to high pressure, which over time may cause atrial arrhythmias. The **extra cardiac conduit** was introduced in 1990, and consists of a tube graft between the transected inferior caval vein and the pulmonary artery. This circuit leaves the entire atrium at a low pressure, has no or minimal atrial suture lines, and can be performed without aortic cross clamping or even cardiopulmonary bypass; however, this conduit has no growth potential and therefore will be offered to patients large enough to accept a graft adequate for an adult's inferior caval vein flow.

How to Build a Fontan Circuit?

At birth, it is impossible to create a Fontan circulation. The pulmonary vascular resistance (PVR) is still elevated for several weeks, and the vessels—caval veins and pulmonary arteries—are usually too small, making any cavo-pulmonary shunt impossible during that period. Even when resistance has fallen, a staged approach is preferred connecting the superior and inferior caval veins at separate occasions. Such a staged approach allows the body to adapt progressively to the different hemodynamic conditions, and reduces the overall operative morbidity and mortality. A staged approach also allows a better patient selection and intermediate preparatory interventions.

Initially in **the neonatal period**, management must focus on—if not provided to some degree by nature-unrestricted flow from the heart to the aorta (if required: coarctectomy, Damus-Kaye-Stansel, Norwood repair), a well-balanced limited flow to the lungs (if required: pulmonary artery banding, shunt (modified Blalock-Taussig, central), stent in duct), and unrestricted return of blood to the ventricle (if required: Rashkind balloon septostomy, atrial septectomy) (Fig. 8.4a–c). The infant is then allowed to grow for several months. During this time, the heart is submitted to a chronic volume overload which is beneficial for development of the pulmonary vasculature, but if excessive detrimental for ventricular function (see below). The infant will have mild oxygen desaturation which is inversely related to mild cardiac failure (Fig. 8.1b).

At the age of several months (4–12 months old), most centers will introduce **a partial cavopulmonary connection** (**PCPC**) **or bidirectional Glenn shunt**: the superior caval vein is connected to the pulmonary artery (bilateral if present). If no other blood flow is directed to the lungs, the volume load for the heart is significantly decreased to half or even less than normal for the body surface area (BSA). The patient at this stage will remain slightly cyanotic, as the desaturated blood from the inferior caval vein is still allowed to flow to the aorta.

At the age of several years (1–5 years, depending on the preference of the center, growth of vascular structures, and cyanosis at rest and during exercise), **the Fontan circuit** is completed by connecting the inferior caval vein to the pulmonary artery.

As mentioned above, two techniques are currently used: the lateral tunnel and the extra cardiac conduit. Frequently a small **fenestration** is created between the tunnel-conduit and the pulmonary atrium, either routinely or only in "high risk" patients [6]. Such fenestration will allow a residual right-to-left shunt, thereby limiting caval pressure and congestion, and increasing the preload of the systemic ventricle and cardiac output, at the expense of cyanosis. Such fenestration has been shown to reduce the operative mortality and morbidity associated with pleural drainage; the fenestration can later be closed percutaneously (weeks-months) after adaptation of the body to the new hemodynamic condition.

Cardiac Output in the Setting of a Fontan Circulation

By creating a TCPC, a new portal system is made. A portal system occurs when one capillary bed pools blood into another capillary bed through veins without passing through the heart, as for example in the hepatic portal system and the pituitary portal system. The Fontan neo-portal system dams off and pools the systemic venous blood. As a result, transit of blood through this neo-portal system is dependent on the pressure gradient from the systemic post-capillary vessels to the pulmonary post-capillary vessels (Fig. 8.1c). Since there is no pump to transmit energy to the system, small changes in the static resistances and dynamic impedances of the structures within this portal system have a profound impact on the blood flow.

Although the heart itself may function well, the inherent limitations of the Fontan neo-portal system determine the degree of circulatory compromise. It is this neo-portal system that is the major limiting factor of flow and the underlying cause of venous congestion and diminished cardiac output. The heart, 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 [7]. The heart therefore no longer controls cardiac output nor can it alter the degree of systemic venous congestion. However, in cases in which the systemic ventricle functions poorly, the heart can make an already compromised circulation worse. Figure 8.5a, b illustrates the relationship between output, ventricular contractility, and PVR in a normal and a Fontan circulation. In a normal subject, output at rest is minimally influenced by ventricular function, except when severely depressed; mild changes of the PVR will not influence the output as these changes are neutralized by the right ventricle. In Fontan patients, the PVR is the primary modulator of cardiac output: small changes have a profound impact; systolic performance will only impact output at rest when cardiac function is severely depressed. If the ventricular function is not severely depressed, squeezing harder will not result in more output.

The components that make up the Fontan neo-portal system are thus critically important in the overall function of the Fontan circuit. These include the veno-arterial Fontan connection itself (atrio-pulmonary in older patients), pulmonary arteries, pulmonary capillary network (including precapillary sphincters), pulmonary veins,

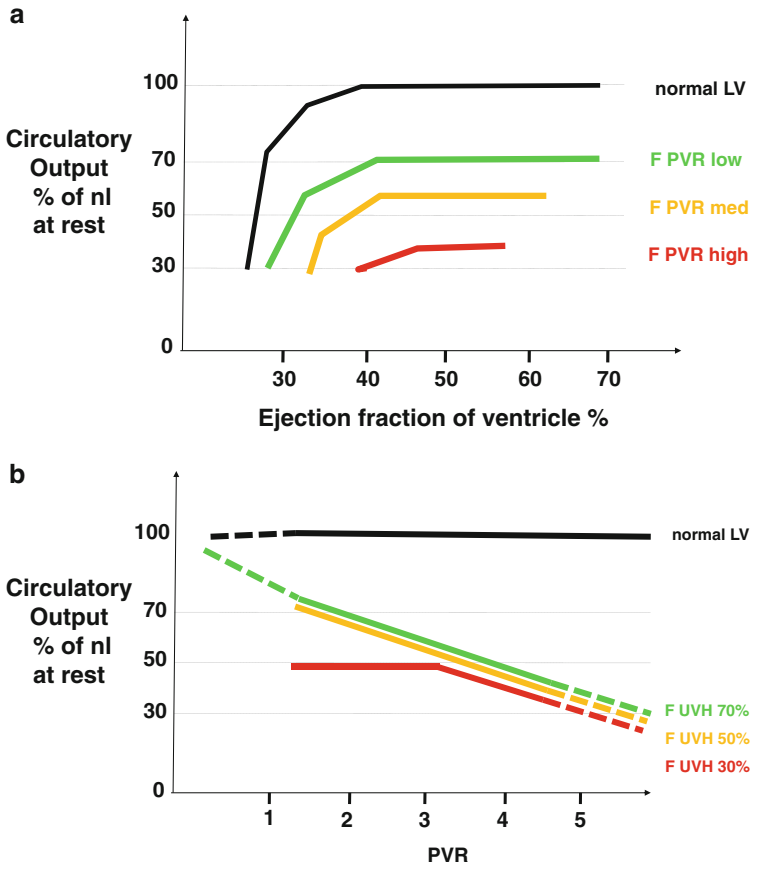


Fig. 8.5 Relationship of output at rest, ventricular function and PVR. (**a**) Modulation by PVR: in a normal subject (*black line*), output at rest is minimally influenced by ventricular function, except when severely depressed. In Fontan patients (colored lines), PVR is the primary modulator of cardiac output. As in a two-ventricle system, systolic performance will only impact output at rest when cardiac function is severely depressed. If ventricular function is not severely depressed, squeezing harder will not result in more output. (**b**) Modulation by ventricular function. In a normal subject (*black line*), cardiac output is not influenced by a mild increase of PVR up to 5 Woods Units. In all Fontan patients (colored lines), an increase in PVR is invariably associated with a decrease in cardiac output. If PVR is low, a reasonable output is achieved in patients with normal or moderately depressed ventricular function (*green* and *yellow lines*). However, severely depressed ventricular function invariably results in low output (*red*). *EF* ejection fraction, *F* Fontan, *LV* normal left ventricle, *PVR* pulmonary vascular resistance, *UVH* univentricular heart

and the veno-atrial 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 microvessels, turbulence and flow collision, flow mismatch and obstruction by external compression.

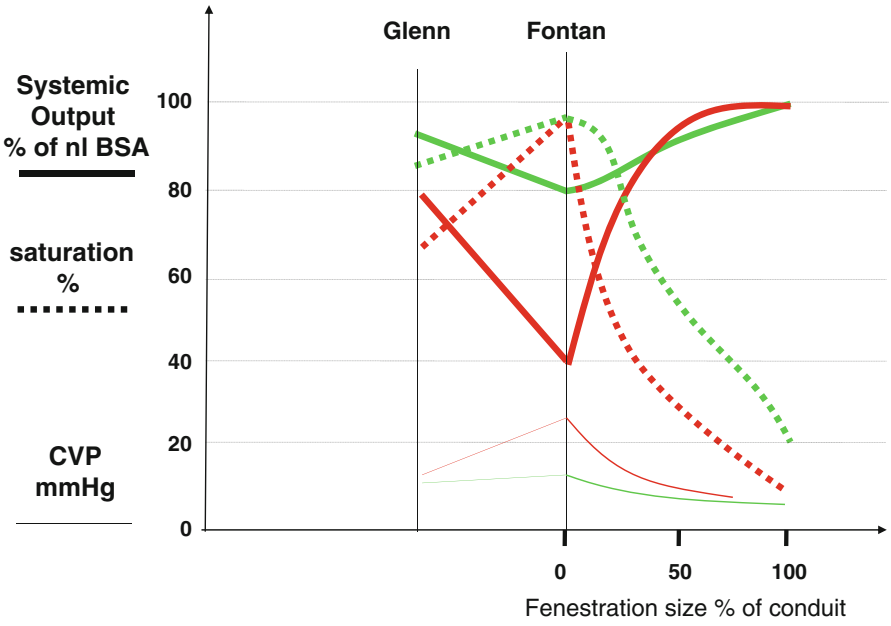


Fig. 8.6 Effect of various degrees of pulmonary bypassing in a Fontan circuit on systemic output, saturation, and systemic venous congestion. A "good Fontan" with low neo-portal resistance (*green lines*) has an output (*thick solid line*) of about 80 % of normal for BSA, with a high saturation (*dotted line*) and a mildly elevated CVP (*thin line*). The "bad Fontan" with a high portal resistance has an output with a similar saturation but with a very low to unacceptable output despite a high CVP. Partial bypassing of the Fontan portal system by a fenestration invariably increases systemic output and decreases systemic congestion, but in the "bad Fontan," this occurs at an unacceptable degree of cyanosis. *CVP* central venous pressure

The restriction of the cardiac output imposed by the neo-portal system can be partially reversed by bypassing the pulmonary vasculature. A Fontan fenestration allows flow to bypass the Fontan neo-portal system and results in an increase in cardiac output and a decrease in venous congestion. However, while a fenestration can increase the overall output, it does so at the expense of diminished arterial oxygen saturation. Nevertheless, in the setting of a fenestration, the increase in cardiac output can result in an increase in peripheral oxygen delivery even if the saturation is mildly diminished. Figure 8.6 shows the relationship between output, congestion, and arterial saturation in a successful and a failing Fontan circuit, and the effect of partial improvement by a fenestration. In a successful Fontan circuit, the low resistance portal system will cause a mild decrease of output with a modest increase in the systemic venous pressures, making a fenestration unnecessary. In a failing Fontan circuit, inclusion of a high vascular resistance portal system will decrease the cardiac output and create venous congestion of an unacceptable degree; a fenestration will attenuate these changes, but in patients with an increased PVR an acceptable compromise may not be possible.

Functional Impairment After the Fontan Operation

The restriction of the cardiac output and the inability to power the blood through the pulmonary vasculature results in a circulation in which the ability to perform exercise is reduced. Under resting conditions, the cardiac output in a patient with a Fontan circulation is approximately 70–80 % of normal. During exercise, the limitations of the Fontan circuit are substantially magnified such that the small difference in cardiac output at rest becomes a large difference during activity (Fig. 8.2). At peak exercise, a well-trained athlete with a normal heart can increase blood flow through the lungs by up to fivefold (see also Chap. 15). This is accomplished through a substantial increase in the right ventricular systolic pressure (up to 70 mmHg! [5]) as well as with pulmonary blood flow acceleration coupled with a decrease in the PVR. In a patient with Fontan physiology, there is no physiologic mechanism to allow for a similar increase in cardiac output. The maximal mean venous pressure rarely reaches 30 mmHg; there is no blood acceleration and the pulmonary vascular reactivity and the ability to recruit reserve vessels is attenuated or absent [8]. Together, these limitations result in a diminished ability to augment cardiac output in response to increased metabolic demand, and therefore limit the ability of a patient with a Fontan circulation to perform exercise.

Through childhood and until puberty, the mean maximal exercise capacity for patients with a Fontan circulation is in the range of 65 % predicted for gender and age [9]. While successful Fontan patients may remain stable for many years, poor Fontan patients suffer an accelerated increase of PVR, and increasing filling pressures of the ventricle as a result of chronic preload deprivation and disuse dysfunction. Longitudinal studies of late adolescents and young adults demonstrate this point well; as patients progress to late adolescence and early adulthood, exercise capacity tends to continue to decline by about 2.6 % per year [10–12].

There are several reasons why adults with a Fontan circuit in the current era do not represent the current cohort of patients. Many of the original candidates for a Fontan operation, the now adult cohort, were suboptimal for this type of surgery from a hemodynamic standpoint, with many significant residual lesions and sequelae related to the original cardiac malformation and palliative procedures. A shunt procedure performed during the period from the 1960s to the 1980s was evaluated based on the goal of the long-term relief of cyanosis: “the pinker the better.” Often a second aortapulmonary shunt was created to augment pulmonary blood flow after the first shunt was deemed inadequate. The potential that these shunts could induce pulmonary vascular disease, ventricular hypertrophy and dysfunction, or pulmonary artery distortion was not—as it is now—a principal concern of the surgeon. Currently, the success of a shunt is evaluated by obtaining acceptable relief of cyanosis without significant volume overload of the ventricle and by the induction of adequate pulmonary growth without causing changes of the PVR. In addition, in the modern era of palliation, the systemic to pulmonary shunt is designed to last 4–6 months, enough time for the PVR to drop such that a PCPC can safely be created.

Figure 8.7a–c illustrates the different loading conditions of the single ventricle at the various stages of palliation, highlighting the differences in management before the 1990s (typically two aortapulmonary shunts prior to the full Fontan circulation) and after (typically one shunt, then partial and later complete Fontan circulation). However, with the current staged strategy for functionally single ventricle, only a limited period of controlled pulmonary "overflow" is allowed to stimulate pulmonary arterial growth. The only time of significant pulmonary overflow is immediately after birth when a shunt or band is placed. In many situations the systemic to pulmonary shunt is made as small as possible to avoid volume overload of the ventricle and potential cardiac damage. If flow to the lungs is too low for too short a period, it may lead to inadequate development of the pulmonary vascular bed, high PVR and, eventually a poorly functioning Fontan circulation (Fig. 8.8). Similarly, hybrid procedures involving neonatal banding of branch pulmonary arteries may cause distortion and inadequate growth or even loss of the distal pulmonary arteries.

The Heart and Pulmonary Vasculature in the Fontan Circulation

The Heart

In the Fontan construct, the heart is exposed to a number of stressors that can change structure and impair function. Chronic preload deprivation and increased systemic vascular resistance create a milieu, which favors the development of both systolic and diastolic dysfunction. The effects of chronic preload deprivation are significantly aggravated by the fact that the ventricle is overgrown by the time it reaches the Fontan state [4]. This combination leads to a situation in which the optimal point for systolic contractility and diastolic suction according to the Frank Starling preload-contractility curve cannot be achieved: the ventricle has evolved from stretched and overloaded while shunted to overgrown and underloaded or even collapsed, at the time of completion of the Fontan circulation [13]. Figure 8.9 depicts the pressure-volume loops of the ventricle at the different phases of palliation, clearly showing the effect of unloading on an overgrown ventricle. Moreover the single ventricle may also exhibit systolic dysfunction as a result of the malformation itself (right versus left ventricle and fiber disarray) or as a result of dilation and damage by the volume or pressure overload state that had been present early during the palliative phase.

Diastolic function after the Fontan procedure is also typically abnormal, and the impairment is unfortunately progressive. The unloading of the ventricle at the time of the Fontan procedure results in less recoil, impaired compliance, and decreased suction in the acute phase [14]. Due to persistent preload deprivation, the pressure-volume curve may show a "reversed creep" with an upward shift and increasing filling pressures (Fig. 8.10). The ventricle may now enter a vicious cycle whereby

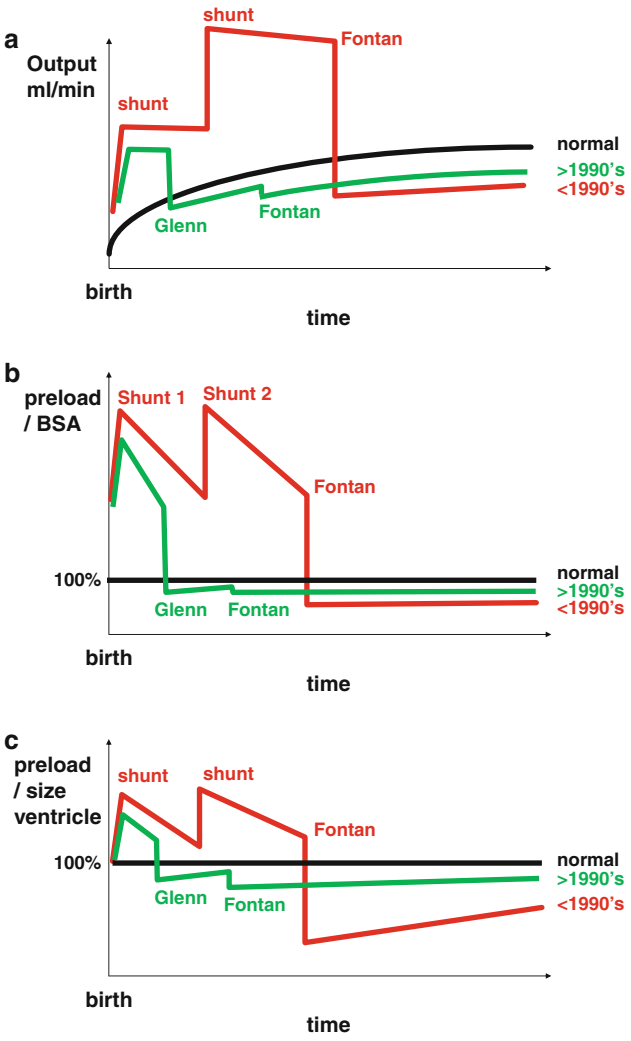


Fig. 8.7 Cardiac output versus time in the normal left ventricle and the univentricular heart (UVH) managed before and after the 1990s: the same story but expressed with different reference frame: in absolute value (**a**), related to BSA (**b**), and to ventricular size (**c**). (**a**) Cardiac output expressed in absolute value: The *black line* shows output of a normal ventricle which increases proportional to growth. At birth the volume load to the UVH is about 250–300 % of that of a normal left ventricle. Prior to the 1990s, a neonatal and infant large shunt was created with significant increase in output (*red line*); the shunts were abolished at the time of the Fontan operation, and the Fontan portal dam reduced even further preload. After the 1990s, a small neonatal shunt is created for a short time, and the ventricle is progressively unloaded both at the Glenn and the Fontan operation (*green line*). (**b**) Cardiac output related to BSA. *Black line*: output of normal remains at 100 % for BSA. This representation assumes only dilation and stretch without any overgrowth of the ventricle.

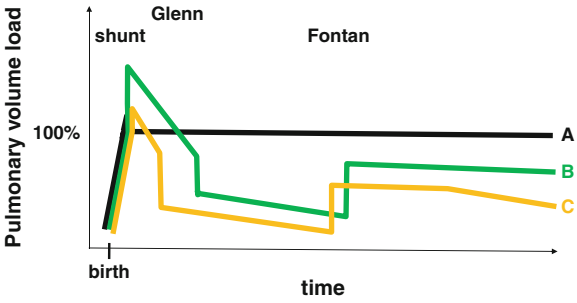


Fig. 8.8 Pulmonary volume load (and outcome) of Fontan since 1990s. In the normal circulation, pulmonary blood flow increases at birth and remains at 100 % of normal for BSA (*A*, *black line*). In a univentricular heart, a phase of significant pulmonary overflow exists immediately after birth until a shunt or band is placed to limit blood flow. With adequate pulmonary growth (*B*, *green line*), pulmonary blood flow is reduced to about 50 % of normal for BSA after the superior cavopulmonary connection (stage 2 palliation). Pulmonary flow is then increased by completion of the total cavo-pulmonary connection (the Fontan operation). If flow to the lungs is too low after the initial palliation, this may result in inadequate growth (*C*, *orange line*). The cyanosis from low pulmonary blood flow may lead to early referral for superior cavopulmonary connection, which may further reduce flow and growth. When the Fontan circuit is created, the Fontan portal system will have a high impedance, resulting in a poor Fontan circulation irrespective the ventricular function, with low cardiac output and a progressive functional impairment

Fig. 8.7 (continued) The patient with a UVH is born with a large ventricle (volume load of 250 % of normal for BSA). Prior to the 1990s (*red line*), the preload to the ventricle is augmented shortly after birth by a shunt procedure to ±350 % of normal for BSA. The patient slowly outgrows his shunt, thereby gradually reducing the volume overload. A second shunt was created, augmenting the volume overload again. As this patient again outgrows his shunt, a Fontan circuit is made, reducing the volume load to <80 %. After the 1990s (*green line*), a small neonatal shunt was created for a short time; the patient slowly outgrows his shunt; the ventricle is progressively unloaded both at the Glenn and Fontan operation (*green line*). (**c**) Cardiac output related to ventricular size in univentricular heart (UVH) managed before and after the 1990s. This representation assumes adapted overgrowth of the ventricle in every stage in function of chronic preload, *A*: output of normal remains at 100 % for ventricular size. The patient with a UVH is born with an appropriate ventricle for volume load (100 % of normal for ventricular size). Prior to the 1990s (*red line*), the preload to the ventricle was augmented shortly after birth by a shunt procedure to ±150 %. The patient slowly outgrows his shunt, and adapts his ventricle, thereby gradually reducing the volume overload to ±100 % for its size. A second shunt was created, augmenting the volume overload again to 150 %. As this patient again outgrows his shunt, a Fontan circuit is made, reducing the volume load to 25 % of its "due" preload. After the 1990s (*green line*), a small neonatal shunt was created for a short time; the patient slowly outgrows his shunt; the ventricle is progressively unloaded both at the Glenn and Fontan operation in much milder steps avoiding acute unloading and severe deprivation (*green line*)

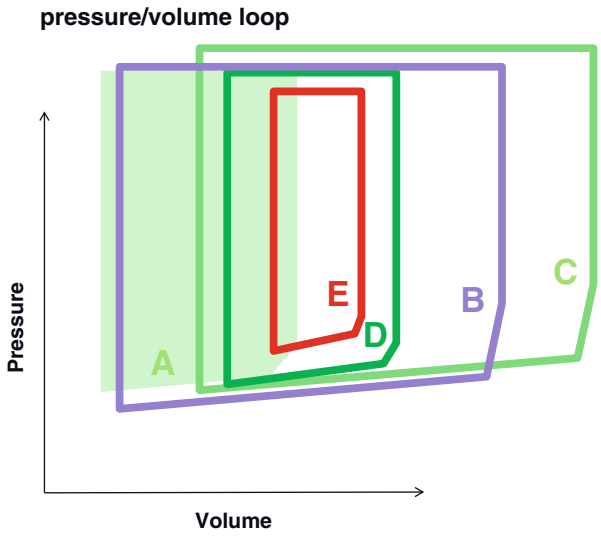


Fig. 8.9 Pressure-volume loops: normal left ventricle (*A*) versus single ventricle at various stages of palliation (*B*–*E*). *A*: PV loop of normal LV. At birth, the neonatal ventricle (*B*) of the UVH had an intrauterine volume overload of approximately 250 of normal for BSA. In the first months a systemic to pulmonary shunt is necessary to maintain oxygen saturations of above 85 %; the ventricle will now have a volume overload of about 250–350 % of a normal for BSA (*C*: large stroke volume with increasing filling pressures). When a "Fontan" type procedure is performed, all systemic to pulmonary shunts are removed, and the volume preload of the ventricle is acutely reduced to levels that may vary between at best 80 % of normal for BSA (*D*) down to the worst end of 30 % (*E*: small stroke volume, elevated filling pressure). If the Fontan ventricle is compared to a normal LV it will be called "stretched & dilated" (*E* versus *A*), but when compared to the pre-Fontan state it is "collapsed and deprived" (*E* versus *C*)

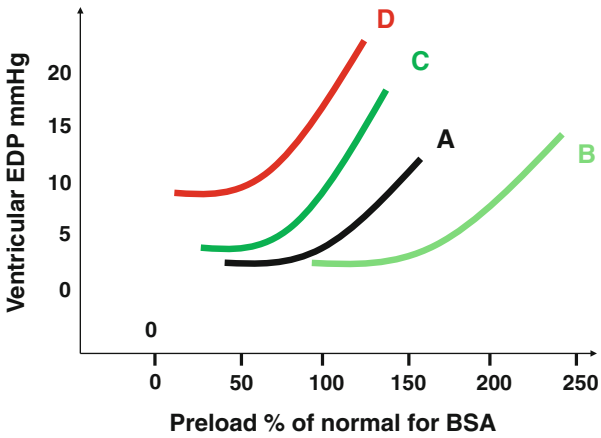


Fig. 8.10 Ventricular end-diastolic pressure in various phases of ventricle. *A*: normal ventricle; *B*: shunted ventricle with chronic volume overload leading to enhanced compliance; *C*: Fontan ventricle after acute phase: mild preload deprivation of the overgrown ventricle; *D*: Fontan ventricle with low output as result of severe chronic preload deprivation leading to elevated filling pressures

the chronic low preload results in remodeling, reduced compliance with increasing diastolic pressures, poor ventricular filling, and eventually progressively declining cardiac output. This phenomenon of progressive "disuse hypofunction" occurs at a chronic preload of less than 70 % of the preload expected for ventricular size [15].

The response of the heart to the stressors associated with the Fontan operation appears to be variable. In some patients the heart can appear quite normal for many years and cardiac function may be relatively well preserved, while in other patients the ventricle appears heavily trabeculated and "overgrown" even before the time of the Fontan surgery. The variability may be related in part to the native anatomy or myocardial structural disarray due to changes resulting from the palliative surgeries preceding the Fontan procedure, but there may also be a genetic heterogeneity in the response to the stressors associated with the single ventricle physiology. Polymorphisms in the renin-angiotensin-aldosterone system have been shown to have a measureable impact on ventricular hypertrophy and on the response of the myocardium to treatment with angiotensin converting enzyme inhibitors [16]. It is possible that these and other unknown genetic variants are in part responsible for the variable response of the heart to the Fontan circulation.

The clinician will thus observe many abnormal features in the Fontan ventricle: a large cavity, thick wall, decreased systolic and diastolic function, not responsive to classic measures that should increase the cardiac output. Many of these abnormalities are "secondary" and not the primary cause for the low flow observed in the Fontan circuit. When a ventricle is large, our management will however differ whether we consider this a stretched ventricle, or rather a collapsed underloaded but overgrown pump. Similarly, when a ventricle is hypocontractile, our management will differ whether we contribute this dysfunction to a damaged burned-out ventricle, or rather to underfilling of an overgrown chronically deprived pump with disuse hypofunction. Assessing the contribution of ventricular overgrowth, dilation, hypertrophy, dysfunction due to intrinsic myopathy or due to relative underfilling (controlled by pulmonary vasculature) is difficult. Due to this complexity, most if not all analyses are based on simplified and incomplete models.

The Pulmonary Vasculature

Abnormal growth and development of the pulmonary vasculature are a hallmark of single ventricle congenital heart disease. Decreased flow to the pulmonary arterial tree may begin during fetal life, depending on the specific lesion, and will certainly exist by necessity after the first stage of palliation during partial or complete cavopulmonary connection (Fig. 8.8). 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 creates for the pulmonary vasculature a condition with chronically decreased flow, mild desaturation, increased collateral flow, suboptimal mixing of inferior and superior caval

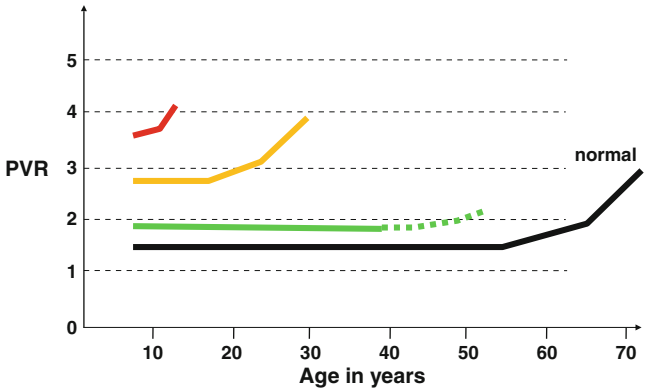


Fig. 8.11 Evolution of PVR with age. In normal subjects (*black line*), PVR remains low for many decades, and will increase only at old age without significant cardiovascular limitation. In "good" Fontan patients with low PVR (*green line*), resistance remains low for many decades, but is expected to increase at older age (*dotted line*). In "poor or bad" Fontan patients with increased PVR (*orange* and *red line*), PVR trends to increase faster with poor clinical outcome at resistances beyond four units

flow, absence of pulsatility, endothelial dysfunction, absence of episodes of high flow and high pressure as is normally seen during exercise. These changes can further alter the vasculature, which underwent abnormal growth and development both during fetal and postnatal life.

The chronic low flow conditions will induce an overall state of pulmonary (and systemic) vasoconstriction, causing the whole circuit to fail (Fig. 8.11). Failing Fontan circuits typically have a high and increasing PVR, although this is often reversible after transplantation (higher output of pulsatile flow) [17].

Complications after Fontan repair are common and related to the continuously increased venous pressure and congestion, and chronic low cardiac output. Complications include early and late mortality, exercise intolerance, ventricular dysfunction, rhythm and conduction disturbances, hepatomegaly with secondary fibrosis and cirrhosis [18, 19], lymphatic dysfunction with protein losing enteropathy [20] and bronchial casts [21, 22], systemic venous thrombi, ascites, and peripheral edema.

Treatment of Circulatory Failure in Fontan Circulation

In the world of "classical cardiology" with primary myocardial disease, such as ischemic heart disease or cardiomyopathy, ventricular function is most frequently the limiting factor of the cardiac output; typically ventricular preload is abundant. Most cardiac algorithms and treatment strategies have focused on augmenting systolic performance. However in some conditions the systemic ventricle is not the

limiting factor but the preload of that ventricle: obstructed inflow is a problem after Mustard repair, in primary pulmonary hypertension, constrictive pericarditis, supravalvar and valvular mitral stenosis, and in the setting of the Fontan circuit.

The circulatory problem in a Fontan circuit is primarily created by the dam effect of the Fontan neo-portal system and the subsequent limited cardiac preload. It has become clear that once created, the Fontan circuit runs on "autopilot" and allows little modulation. The ventricular enlargement and dysfunction are initially epiphenomena secondary to the previous palliation and Fontan physiology itself; the state of volume deprivation—when sufficiently profound or long-lasting—may aggravate ventricular dysfunction and circulatory failure. As such, strategies aimed at maximizing the efficiency of this portal system will conceptually be more effective than "traditional" heart failure therapies. Such modulation may consist of increasing the pressure before the dam (systemic venous pressure), lowering the height (resistance of Fontan neo-portal system) of the dam, enhancing the runoff after the dam (ventricular suction), or bypassing the dam (fenestration).

Elevated Systemic Venous Pressure (Increasing Pressure Before the Dam)

An acute increase of systemic venous pressure, as is achieved during exercise (up to 30 mmHg), can temporarily increase output [23]. However, such an elevation cannot be maintained for a long time. A chronic elevation of venous pressures above 18–20 mmHg, as in patients with a high resistance Fontan portal circuit, will result in unacceptable side effects such as vascular congestion, edema, ascites, and lymphatic failure. Diuretics can partially control these complications of congestion, but may further increase the problems of chronic low output. General aerobic fitness may play a role in the transient ability to increase central venous pressure, but even then, the venous pressure cannot sustain the driving pressure that can be achieved by a sub-pulmonary ventricle.

Impedance and Pulmonary Vascular Resistance (Lowering the Height of the Dam)

In the current era, the surgical technique used to create a TCPC is usually quite good with minimal focal stenosis, reduced turbulence, and flow of the inferior caval vein blood to both lungs [5, 24]. Previous connections, including valved pathways and atrioventricular pulmonary connections, are now considered obsolete. For those patients who received older style Fontan operations, conversion to cavo-pulmonary connection should be considered when the patient becomes symptomatic, or as a prevention strategy, to limit any energy loss in the Fontan portal system [25, 26] and to avoid recurrent atrial arrhythmias. Furthermore, even in patients who are

"doing well," care should be taken to ensure that focal areas of stenosis, hypoplasia, distortion, or abundant collateral flow are repaired when possible.

The total cross-sectional area of the pulmonary vascular bed and the impedance both at rest and during exercise are important factors for the efficiency of the Fontan circulation. The first palliative procedure is probably the most important and crucial intervention in the development of the pulmonary vasculature in patients with single ventricle physiology (Fig. 8.8). It is during these early days that pulmonary vascular arterial development and "catch-up" growth occurs. The volume requirements for optimal growth and development of the ventricle and the lungs during infancy are different and opposed. Avoiding significant overload of the ventricle is important, but excessive protection from volume overload may cause pulmonary vascular hypoplasia, which in turn will severely affect the outcome of the final Fontan circuit. Current strategies place much emphasis on preserving cardiac function, which is important in the short term whereas for a good long-term outcome, adequate growth and development of the lungs are more important.

In the last few years, the pulmonary vasculature itself has emerged as a therapeutic target to improve output. In the Fontan circuit, PVR is generally mildly elevated at baseline but, in the absence of pulsatile flow, it does not decrease normally with increased cardiac output. Treatment effects of several agents have been reported (oxygen at altitude, sildenafil, bosentan, inhaled ilosprost); however, the short-term improvements have been modest [27–30]. Longer-term studies with pulmonary vasodilators are needed to understand whether these agents can impact the long-term outcomes of patients after Fontan surgery, and impact on what is characteristically a slow, downward slope of exercise capacity and cardiovascular functionality.

Ventricular Suction (Enhancing Runoff Past the Dam)

In order to minimize the hemodynamic effect of the Fontan portal system, the ventricle must keep pulmonary venous atrial pressure as low as possible. However, in mammals ventricular filling is a nearly passive phenomenon and no ventricle will generate adequate suction, let alone build up the negative pressures required to pull the blood through the neo-portal Fontan system. Moreover, the Fontan ventricle is already in a state of chronic severe preload restriction, making it work at the low end of its pressure–volume relationship. Aging [31] and the progressive "disuse hypofunction" remodeling may further reduce its compliance as on diastolic pressures.

The effect on the pulmonary venous atrial pressure of agents which alter contractility, heart rate, and afterload is frequently minimal:

- **Contractility**: The contraction of the ventricle itself has a role in helping blood flow through the pulmonary vascular bed. As the atrioventricular annulus contracts toward the apex of the heart, a vacuum is created to "pull" blood into the pulmonary atrium; as the ventricular myocardium relaxes and the atrioventricular valve opens, blood is further pulled into the ventricle. The total contribution of this "suction" is hard to quantify, but is clearly lost in the setting of atrioventricular

dyssynchrony or in the setting of an enlarged previously overgrown atrium. Inotropic agents can make the Fontan ventricle squeeze harder, but in the setting of an already preload deprived ventricle, will not effectively change the pulmonary atrial pressure, and hence will not result in a clinically significant cardiac output increase! Only in the Fontan patient with extreme ventricular dysfunction (not due to underloading), or if enhanced contractility results in decreased pulmonary venous pressure (and thus transpulmonary flow) some increase in the cardiac output may be observed after application of inotropic agents.

- **Heart rate**: in a ventricle with preload reserve, an increase of heart rate will result in increased output. In a Fontan circuit with no ventricular preload reserve, an increase in heart rate will result in a proportional decrease of stroke volume, and subsequently no change in output [32]. If there is excessive bradycardia, pacing to drive the heart rate into the physiologic range will increase the cardiac output and decrease congestion [33]. Fontan patients exhibit what is called "chronotropic incompetence" during exercise with a heart rate consistently lower than normal controls; this has typically been attributed to an abnormal reflex control of heart rate or adrenergic dysfunction. However, adequate ventricular preload during exercise is crucial and a major determinant of an increase in heart rate. The "chronotropic incompetence" is probably not detrimental, or perhaps lifesaving: tachycardia out of proportion to the cardiac output is poorly tolerated in patients with limited preload, such as in patients with a Mustard or Fontan circuit.
- **Afterload**: Any patient who is in a chronically low cardiac output state will invariably generate an increased systemic vascular resistance in order to maintain blood pressure. In a failing but normally connected biventricular circulation with a hypocontractile ventricle and preload reserve, a decrease of afterload results in an increase in the cardiac output. The increase in output will counter the tendency for hypotension, thus resulting in a favorable clinical response. In a Fontan patient a decrease of afterload without preload reserve will not result in an increased cardiac output, but may be detrimental by causing severe hypotension. Whether there is a role for chronic low dose afterload reduction in an attempt to modulate ventricular diastolic function, remains unknown. In the only randomized trial of enalapril in patients with the circulation Fontan, no beneficial effect was observed [34]. However, the duration of this trial was only 10 weeks; it is still possible that the benefit of afterload reducing agents may be a chronic impact on diastolic function as opposed to a short-term impact on systemic, vascular resistance.

Fenestration (Bypassing the Dam)

A proven strategy to improve cardiac output in patients with the Fontan procedure is to create a bypass of the pulmonary circuit in the form of a small fenestration. This concept had originally been reported as a means to aid the physiologic adjustment in the perioperative state following the Fontan surgery itself [6]. Following the establishment of the fenestration, the incidence of prolonged pleural effusions and

long hospitalizations decreased significantly. In addition, a limited bypass of the Fontan portal system also results in chronic improvement of congestion and circulatory output. The downside of a fenestration is decreased arterial oxygen saturation (Fig. 8.6). Nevertheless, the improved cardiac output may result in a better overall oxygen delivery, and will also help to alleviate the congestive symptoms, particularly of the liver.

While a fenestration at the time of the Fontan surgery is well tolerated and may be viable for years or decades after surgery, the creation of a fenestration late in a patient who has not previously had a fenestration is not well tolerated. These patients are referred for fenestration creation because of the failure of their Fontan circuit, often characterized by elevated PVR and a high transpulmonary gradient. In this setting, achieving the proper balance in the creation of a fenestration is quite difficult and may not be possible. A small fenestration will not generate the degree of decompression necessary to alleviate symptoms, and a larger fenestration might alleviate congestion and augment cardiac output, but in so doing will result in an unacceptable level of cyanosis. Nevertheless, fenestration creation may have a role in a failing Fontan as a bridge to heart transplantation and to avoid cardiac cachexia.

Mechanical Support and Heart Transplantation

Mechanical support for the failing single ventricle is still in its infancy. The usual ventricular assist devices are designed to aid a failing systemic ventricle. In the failing Fontan circulation, the problem is typically not systolic performance, but rather the physiology as it relates to the neo-portal system and chronic preload deprivation. In this setting, the interposition of a sub-pulmonary assist device is needed. This has been reported in one instance as a bridge to transplantation [35].

In many cases of Fontan circulation failure, heart transplantation is likely to be the final outcome. Heart transplantation in the 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 [4, 36].

Summary

The Fontan construct has allowed the survival of countless children born with congenital heart disease. However, this palliation creates a form of man-made circulation failure characterized by a neo-portal system that leads to chronic preload deprivation resulting in a low cardiac output and systemic venous congestion. The careful attention to pulmonary blood flow and pulmonary arterial growth in the initial stages of palliation are crucial, as are the technical details of the geometry of

the Fontan connections. Avoiding overload of the systemic ventricle during initial palliation is important, while excessive protection from volume overload may result in pulmonary vascular hypoplasia [37]. Nevertheless, even in a "perfect" Fontan, it is difficult to predict how durable this man-made form of circulation failure will be over the long term.

The overall treatment options for circulatory failure of a Fontan circuit are disappointing; avoidance of problems is most important, because once the Fontan circuit is created it runs on "auto-pilot," and allows little modulation. However, clinical trials are underway to evaluate the potential benefits of modulators of PVR and to determine whether aerobic training may help to forestall the insidious onset of circulatory failure.

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