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Single-ventricle physiology

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The term "single ventricle" applies to several congenital cardiac anomalies and their subsequent postoperative anatomy. Single-ventricle physiology presents a challenge to the intensive care physician because patients with these lesions often respond to common interventions such as supplemental oxygen, mechanical ventilation, and vasopressors differently than patients with conventional circulations. Furthermore, single-ventricle patients are commonly encountered in pediatric critical care medicine because they undergo multiple cardiac operations, may be more adversely affected by intercurrent illnesses, or have chronic cardiac problems that may require intensive care. A thorough understanding of the complexities of single-ventricle physiology is therefore imperative for the pediatric intensivist. This article addresses the important physiologic issues that arise in the care of patients with single-ventricle anatomy. Because there are important alterations in anatomy and physiology that are unique to each of the reconstructive stages of single-ventricle palliation, the physiology of the newborn (pre- and postoperative), bidirectional cavopulmonary anastamosis (bidirectional Glenn or hemi-Fontan), and total cavopulmonary anastamosis (Fontan) circulations are discussed.

The newborn

Anatomy

In congenital heart disease, anatomy dictates physiology. Single-ventricle physiology can result from a number of anatomic lesions that are associated with a variety of physiologic manifestations (Table 1). Although virtually all newborns with single-ventricle physiology have mixing of pulmonary and systemic venous

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Table 1
Anatomic diagnoses commonly associated with single-ventricle physiology in the newborn[a]

Physiology	Anatomy
Systemic outflow obstruction	Hypoplastic left heart syndrome
	Critical aortic stenosis
	Critical coarctation of the aorta
	Interrupted aortic arch
	Tricuspid atresia with transposition of the great arteries
	Double-inlet left ventricle
	Double-outlet right ventricle (some variations)
Pulmonary outflow obstruction	Tricuspid atresia with normally related great arteries
	Pulmonary atresia with intact ventricular septum
	Tetralogy of Fallot with pulmonary atresia
	Critical pulmonary stenosis
	Severe Ebstein's anomaly of the tricuspid valve
	Double-outlet right ventricle (some variations)

[a] Not all diagnoses listed are single-ventricle lesions.

return, the relative amounts of each vary substantially depending on the underlying anatomy. The most important anatomic issue that can affect data interpretation and intensive care management is the outflow to and from the systemic ventricle and lungs. The newborn may have either pulmonary or aortic obstruction or bilaterally unobstructed outflow. Additionally, either systemic or pulmonary venous return may also be obstructed in the single-ventricle circulation in the newborn.

Systemic outflow obstruction

Systemic outflow obstruction occurs in hypoplastic left heart syndrome (HLHS), tricuspid atresia with transposed great arteries, double inlet left ventricle, and other less common anatomic variations. Single-ventricle physiology with systemic outflow obstruction is also applicable to newborns with critical aortic stenosis, severe coarctation of the aorta, or interrupted aortic arch. The important features of this type of anatomy are complete mixing of systemic and pulmonary venous return and ventricular outflow directed primarily to the pulmonary artery. Systemic blood flow (Q_s) is provided largely by right-to-left ductal shunting and is dependent on the relative pulmonary and systemic vascular resistance. In general, systemic outflow obstruction is poorly tolerated, and in the face of single-ventricle anatomy is usually accompanied by signs or symptoms of shock.

Pulmonary outflow obstruction

Single-ventricle physiology with pulmonary outflow obstruction occurs in lesions such as tricuspid atresia, pulmonary atresia, and severe Ebstein's anomaly of the tricuspid valve, among others. The salient anatomic features are complete mixing of systemic and pulmonary venous return and ventricular outflow predominantly directed out the aorta. Low pulmonary blood flow (Q_p) in single-ventricle patients implies an obligate right-to-left shunt, generally at the

atrial level, and results in deoxygenated blood reaching the systemic circulation and the clinical finding of cyanosis. The clinical consequences of low Q_p are variable and depend on the severity of the lesion. Mild obstruction may permit an inordinate amount of the total cardiac output to go to the pulmonary circulation, sometimes at the expense of systemic cardiac output. Treatment is therefore directed at limiting, rather than increasing Q_p. Infants with this type of anatomy may be only minimally cyanotic and can have signs and symptoms of congestive heart failure. At the other end of the spectrum are those with severe pulmonary outflow obstruction or even atresia. These patients are profoundly cyanotic unless an alternate source of Q_p is quickly established.

The atrial septum

In the setting of a single-ventricle lesion, unobstructed pulmonary or systemic venous return often depends on an unrestrictive interatrial communication. When one of the atrioventricular (AV) valves is severely stenotic or atretic, as occurs in HLHS, tricuspid atresia, or pulmonary atresia with intact ventricular septum, a large atrial septal defect is required for decompression of the atrium with the inadequate AV valve. Obstruction of the systemic venous atrium causes increased central venous pressures, third spacing of fluid, and limited systemic cardiac output. Although a patent foramen ovale allows right-to-left shunting of blood across the atrial septum, it may be inadequate to permit unobstructed flow of all systemic venous return.

Obstruction of the pulmonary venous atrium causes elevated pulmonary venous pressure and pulmonary hypertension. This phenomenon can be helpful in the immediate newborn period, because it can limit Q_p and enhance systemic flow, thereby increasing systemic oxygen delivery (DO_2) even at the expense of arterial oxygen saturation (SaO_2). Nevertheless, the atrial septum must be opened at the time of the first palliative operation to avoid the long-term consequences of elevated pulmonary vascular resistance. A severely restrictive or intact atrial septum with pulmonary venous hypertension usually requires emergent creation of an atrial level shunt because of profound cyanosis. These procedures carry a high risk of morbidity and may imply a worse prognosis for further palliative surgery [1,2].

Postoperative anatomy

There are three primary surgical options for the newborn with single-ventricle anatomy. The goal of any initial palliative surgery is to establish unobstructed pulmonary and systemic venous return, unobstructed systemic outflow, and limited Q_p and pulmonary artery pressure. Typically, this goal is accomplished by a stage I Norwood type procedure, a modified Blalock-Taussig shunt, or a pulmonary artery band. Although variations on each of these operations exist, they represent the spectrum of postoperative anatomy the intensive care physician is likely to encounter. Because each anatomic arrangement establishes similar

physiology, the important differences between them are in the means by which each operation accomplishes its goals. The Norwood operation requires cardiopulmonary bypass, cardioplegia, and a period of deep hypothermic circulatory arrest, although newer techniques can limit circulatory arrest time [3–5]. The heart, kidneys, brain, and other organs including the systemic and pulmonary endothelium undergo a period of ischemia followed by reperfusion often followed by a defined period of myocardial, renal, and perhaps endothelial dysfunction in the postoperative period. A Blalock-Taussig shunt, either alone or as part of a stage I Norwood procedure, often results in low diastolic arterial pressure, which may compromise coronary perfusion. Unlike a Blalock-Taussig shunt, a pulmonary artery band is not associated with diastolic systemic arterial run-off. Some investigators have suggested a pulmonary artery band may increase the risk of subaortic obstruction and ventricular hypertrophy [6], although this assertion has also been disputed [7]. Both shunts and bands carry the risk of unilateral pulmonary artery obstruction, and this possibility should be included in the differential of late cyanosis after either of these procedures.

Physiology

Ratio of pulmonary blood flow to systemic blood flow

Regardless of underlying anatomy, the newborn with single-ventricle physiology has mixing of systemic and pulmonary venous return, and the total cardiac output is partitioned into Q_p and Q_s based on the amount of anatomic obstruction or vascular resistance to flow in the respective circuits. It is generally assumed that Sa_{O_2} reflects the ratio of Q_p to Q_s (Q_p/Q_s) in the unoperated, shunted, or banded newborn single-ventricle patient. This assumption is based on manipulation of the Fick principle. The Fick equation for Q_s is

$$Q_s = VO_2/(CaO_2 - CmvO_2) \quad (1)$$

and for Q_p is

$$Q_p = VO_2/(CpvO_2 - CpaO_2) \quad (2)$$

where VO_2 = oxygen consumption, CaO_2 = arterial oxygen content, $CmvO_2$ = mixed venous oxygen content, $CpvO_2$ = pulmonary venous oxygen content, and $CpaO_2$ = pulmonary artery oxygen content.

By substituting the equations for oxygen content into equations 1 and 2, and because arterial and pulmonary artery saturations are identical in this type of single ventricle physiology, one can derive a simplified Fick equation for Q_p/Q_s

$$Q_p/Q_s = (SaO_2 - SmvO_2)/(SpvO_2 - SaO_2) \quad (3)$$

where $SmvO_2$ = oxygen saturation of mixed venous blood, SaO_2 = oxygen saturation of arterial blood, and $SpvO_2$ = oxygen saturation of pulmonary venous blood.

Equation 3 can be further simplified because the lungs are relatively healthy in most infants with congenital heart disease. The oxygen saturation of pulmonary venous blood can therefore be assumed to be normal at approximately 95% in room air. If one also assumes that the systemic arterial-venous oxygen saturation (A-VO_2) difference ($SaO_2 - SmvO_2$) is normal, at approximately 25%, equation 3 can be simplified to

$$Q_p/Q_s = 25/(95 - SaO_2) \quad (4)$$

This simplified version of the Fick equation allows estimation of Q_p/Q_s based on SaO_2. Given the ease with which SaO_2 can be obtained in clinical practice, equation 4 has clear advantages. Specifically, it allows the clinician to estimate DO_2 simply by looking at SaO_2. Thus, one can theoretically assess the effectiveness of any intervention designed to alter Q_p/Q_s by observing the change in SaO_2.

This simplified approach to estimating Q_p/Q_s is based on assumptions regarding $SmvO_2$ and $SpvO_2$. The assumption regarding the systemic A-VO_2 difference is accurate only if DO_2 is normal. In shock, which often occurs in neonates with ductal dependent Q_s, or in the face of myocardial dysfunction following surgery, $SmvO_2$ will be low, and therefore $SaO_2 - SmvO_2$ will be substantially higher than 25%. When the decrease in $SmvO_2$ is offset by an increase in the amount of well-saturated blood returning from the lungs (increased Q_p/Q_s) SaO_2 will remain unchanged. Clinical data suggest that this occurrence may be common [8–11]. Many centers have begun to monitor $SmvO_2$ routinely following Norwood palliation for HLHS using a sample from the superior vena cava (SVC) as representative of mixed-venous blood (in single ventricle anatomy, there is no site of true systemic mixed-venous blood). Fig. 1 shows simultaneous SaO_2, $SmvO_2$, and mean arterial blood pressure (MAP) in a subject in the first 3 to 4 hours following Norwood palliation. The SaO_2 remains relatively constant, but $SmvO_2$ plummets starting at about 17:00 and is accompanied by a slight increase in MAP. The only plausible explanation for this phenomenon is that Q_p/Q_s increases dramatically, and the decrease in $SmvO_2$ is offset by the larger amount of well-saturated blood returning to the heart from the lungs, the result of the increase in Q_p/Q_s. In this situation, estimation of Q_p/Q_s from SaO_2 alone would lead the clinician to the erroneous conclusion that the Q_p/Q_s is well balanced when Q_s is actually critically low. Several studies suggest the average systemic A-VO_2 difference is about 25% to 30% [8,10] as predicted by the assumption inherent in equation 4, but the range of values is quite broad, limiting the applicability of equation 4 to any particular patient.

Although $SpvO_2$ is likely to be normal in the absence of clinical or radiographic evidence of pulmonary parenchymal disease, there are conditions under which this assumption is also false. Taeed and colleagues [10] placed catheters in the left lower pulmonary vein at the time of the Norwood operation in infants with HLHS and found unexpected pulmonary venous desaturation occurred commonly, particularly with a fraction of inspired oxygen (FiO_2) below 0.3

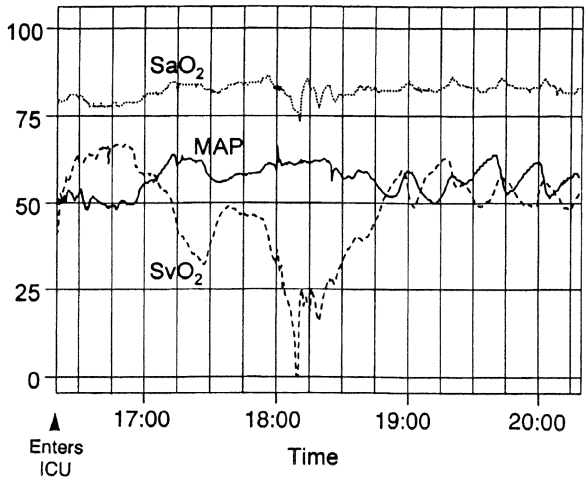

Fig. 1. Arterial oxygen saturation (SaO_2), mean arterial blood pressure (MAP), and mixed venous oxygen saturation ($SmvO_2$) over time in a patient following Norwood palliation. The $SmvO_2$ falls precipitously, whereas MAP and SaO_2 do not change significantly. This phenomenon can be explained by a rise in systemic vascular resistance associated with an increase in pulmonary blood flow and a decrease in systemic blood flow. (*From* Tweddell JS, Hoffman GM, Fedderly RT, et al. Phenoxybenzamine improves systemic oxygen delivery after the Norwood procedure. Ann Thorac Surg 1999;67:161–7; discussion 167–8; with permission.)

(Fig. 2). Failure to account for decreased $SpvO_2$ results in a falsely low calculation of Q_p/Q_s using equation 4. As shown in Fig. 3, small errors in estimation of $SpvO_2$ can result in gross inaccuracy in calculated Q_p/Q_s [12]. The important clinical implication of this principle is that maneuvers that decrease $SpvO_2$ rather than Q_p/Q_s result in lower SaO_2 and reduced DO_2 because there is no increase in Q_s.

The importance of accurately estimating Q_p/Q_s can be seen when one considers the relationship between Q_p/Q_s, DO_2, and total cardiac output (Fig. 4) [13]. Using mathematical modeling and keeping $SpvO_2$ constant at 96%, one can generate a series of curves showing DO_2 as a function of Q_p/Q_s. Because the total cardiac output pumped by the single ventricle is $Q_p + Q_s$, an increase in Q_p is accompanied by a decrease in Q_s, and vice versa, unless the total cardiac output also increases. Fig. 4 shows that the maximum DO_2, represented by the dashed line, occurs between a Q_p/Q_s of approximately 0.5 and 1 and depends on the total cardiac output. The slope of each isobar for a given cardiac output is steepest on either side of the maximum DO_2, suggesting that small changes in Q_p/Q_s can be associated with large changes in DO_2. Fig. 4 also suggests DO_2 can be improved to a far greater degree by increasing total cardiac output than by altering Q_p/Q_s. One limitation to this type of model for DO_2 is the use of SaO_2 and Q_s as interchangeable components of DO_2. Although newborns tolerate cyanosis well, the oxyhemoglobin dissociation curve dictates that once SaO_2 becomes critically low, further decreases can no longer be compensated for by increases in Q_s [14].

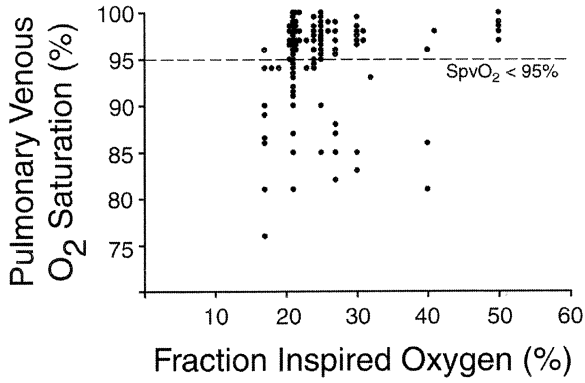

Fig. 2. Pulmonary venous oxyhemoglobin saturation ($SpvO_2$) plotted as a function of fractional inspired oxygen (FiO_2) demonstrates that pulmonary venous desaturation occurs frequently following the Norwood operation. Pulmonary venous oxyhemoglobin saturation lower than 95% (points below the dashed line) most often occurs at FiO_2 below 0.21 but can also occur at an FiO_2 as high as 0.40 (*From* Taeed R, Schwartz SM, Pearl JM, et al. Unrecognized pulmonary venous desaturation early after Norwood palliation confounds Q_p:Q_s assessment and compromises oxygen delivery. Circulation 2001;103:2699–704; with permission.)

Nevertheless, when cardiac output is maximized, optimization of Q_p/Q_s is still important for improvement of marginal DO_2.

Cardiac output

Low total cardiac output ($Q_p + Q_s$) in single-ventricle physiology causes both low Q_s and low SaO_2 and thus recognition is of critical importance to allow rapid diagnosis and treatment. In the absence of $SmvO_2$ monitoring, low SaO_2 with clinical signs of low cardiac output such as anuria, poor capillary refill, high ventricular filling pressure, or metabolic acidosis out of proportion to the degree of cyanosis suggests poor cardiac function. Single-ventricle physiology places the newborn at an increased risk of ventricular dysfunction [15–17]. The single ventricle is volume loaded compared with an anatomically normal heart in which the left ventricle needs only to supply Q_s. Low Q_s, particularly with low diastolic blood pressure (as seen in the newborn with a large patent ductus arteriosus) or a high end-diastolic ventricular pressure (as occurs in a volume-loaded heart or after cardiopulmonary bypass) can cause coronary perfusion pressure to become critically low. This development can compromise systolic ventricular function and further raise end-diastolic pressure and lower systemic arterial pressure. If not rapidly corrected, this situation can result in profound hemodynamic decompensation.

Manipulation of delivered oxygen

The goal of management in single-ventricle physiology is to ensure adequate DO_2, not to maximize SaO_2. Optimization of DO_2 requires maintenance of

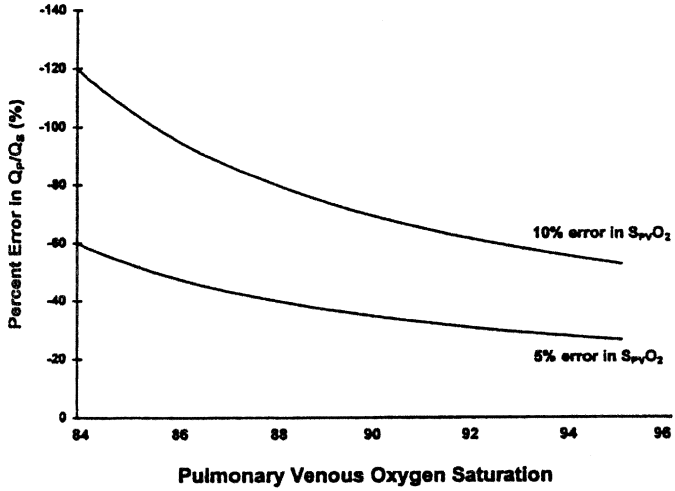

Fig. 3. The percent error in pulmonary/systemic blood flow ratio (Q_p/Q_s) as a function of pulmonary venous oxyhemoglobin saturation ($SpvO_2$). Arterial oxyhemoglobin saturation (SaO_2) is assumed to be 77%, and mixed venous oxyhemoglobin saturation is assumed to be 45%. The relationship is plotted for both a 5% and 10% error in $SpvO_2$. (*From* Barnea O, Austin EH, Richman B, et al. Balancing the circulation: theoretic optimization of pulmonary/systemic flow ratio in hypoplastic left heart syndrome. J Am Coll Cardiol 1994;24:1376–81; with permission.)

cardiac inotropy while balancing Q_p and Q_s and maintaining adequate blood pressure and SaO_2. Clinically, this task is challenging because of the inherent interrelationships between these hemodynamic variables. Furthermore, blood pressure and SaO_2 may not reflect moment-to-moment alterations in underlying physiology and may remain constant over a wide range of Q_p/Q_s [10,11]. Although management of newborn single-ventricle physiology has traditionally focused on manipulation of Q_p/Q_s by manipulation of pulmonary vascular resistance (PVR), newer data suggest management of total cardiac output and systemic vascular resistance (SVR) may be more effective [11]. In all instances, maintenance of oxygen-carrying capacity by keeping hemoglobin in the range of 13 to 15 mg/dL can have a positive influence on DO_2. Increased hemoglobin concentration increases $SmvO_2$ and SaO_2 and decreases Q_p/Q_s in single-ventricle physiology [18,19].

Most commonly, differential manipulation of PVR and SVR is through the use of oxygen, CO_2, and acid-base status (Table 2) [20,21]. Subatmospheric oxygen (FiO_2 0.17–0.19) or induction of respiratory acidosis can effectively raise PVR, decrease SVR, and thus decrease Q_p/Q_s in infants with unrestricted Q_p. Subatmospheric oxygen should be used with caution because it may be associated with pulmonary venous desaturation and thus have a less beneficial effect on DO_2, particularly in the postoperative patient [10]. Furthermore, use of inhaled CO_2 in newborns with HLHS has been associated with increased cerebral or systemic DO_2 compared with subatmospheric oxygen [22,23] and after the stage I

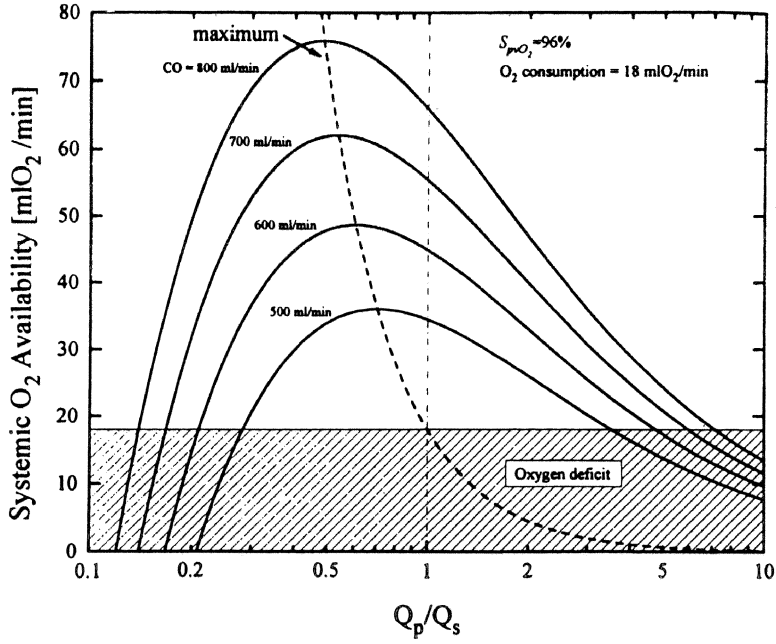

Fig. 4. Systemic oxygen availability (mLO_2/min) as a function of pulmonary/systemic blood flow ratio (Q_p/Q_s)at different levels of cardiac output. Pulmonary venous oxyhemoglobin saturation ($SpvO_2$) is assumed to be 96%, and oxygen consumption (VO_2) is assumed to be 18 mLO_2/min. (*From* Barnea O, Austin EH, Richman B, et al. Balancing the circulation: theoretic optimization of pulmonary/systemic flow ratio in hypoplastic left heart syndrome. J Am Coll Cardiol 1994;24:1376–81; with permission.)

Norwood procedure [24]. It is less clear that manipulation of PVR is useful in altering Q_p/Q_s in infants with low PVR and anatomically restricted pulmonary blood flow. One study has demonstrated no significant changes in Q_p/Q_s with subatmospheric oxygen following Norwood palliation [10]. It is likely that Q_p becomes limited by the size of the systemic-to-pulmonary artery shunt or pulmonary artery band and further decreases in downstream resistance are of minimal consequence.

Table 2
Effects of respiratory maneuvers on pulmonary and systemic vascular resistance

Treatment	PVR	SVR	Q_p/Q_s
Increase FiO_2	Decrease	Increase	Increase
Increase CO_2	Increase	Decrease	Decrease
Increase pH	Decrease	Increase	Increase
PEEP	Increase	No effect	Decrease

Abbreviations: FiO_2, fraction of inspired oxygen; PEEP, positive end-expiratory pressure; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance.

Pulmonary vascular resistance can also be increased independently of SVR by positive end-expiratory pressure (PEEP) [21]. When lung compliance is normal, PEEP increases PVR by compressing the interalveolar pulmonary arterioles. To accomplish this compression, the level of PEEP must result in an end-expiratory lung volume greater than functional residual capacity (FRC) because the nadir of PVR occurs at FRC rather than at zero PEEP. The initial application of PEEP above zero applies radial traction forces to the pulmonary vasculature and aids vascular recruitment. Further increases in PEEP above FRC compress the vessels. Increased PEEP may also prevent pulmonary venous desaturation by optimizing lung gas exchange and therefore decrease Q_p/Q_s while simultaneously maximizing $SpvO_2$ [10].

Another approach to differential regulation of PVR, SVR, and Q_p/Q_s is pharmacologic manipulation of SVR. Although intravenous vasodilators tend to have similar effects on the pulmonary and systemic vasculature, in the setting of poor systemic perfusion and low PVR, they may have a relatively greater effect on the systemic vasculature. Specifically, nitroprusside, phenoxybenzamine, inamrinone, and milrinone have been used as systemic afterload-reducing agents and to block the α-adrenergic receptor–mediated vasoconstriction that occurs with drugs such as epinephrine. Phenoxybenzamine lowers SVR, decreases Q_p/Q_s and improves DO_2 after the Norwood operation, even though it is associated with a decrease in systemic blood pressure [11]. β-Adrenergic stimulation of the myocardium in conjunction with vasodilation can further increase total cardiac output ($Q_p + Q_s$) without associated vasoconstriction. Other vasodilating agents can potentially be used to accomplish the same goal, although they involve different receptor mechanisms and cellular pathways. Systemic vasodilation may be particularly valuable after operations that require deep hypothermic circulatory arrest such as the Norwood operation. Following conventional cardiopulmonary bypass, during which the lungs are exposed to a period of ischemia and subsequent reperfusion, the pulmonary endothelium may be significantly impaired in its ability to produce nitric oxide [25]. Although the possibility has not been systematically evaluated, it is plausible that there is systemic endothelial dysfunction following circulatory arrest. An inappropriate increase in SVR in single-ventricle physiology is capable of increasing Q_p at the expense of Q_s while maintaining blood pressure and SaO_2 and thus masking potential warning signs of low Q_s. The utility of manipulating SVR has not been studied in newborns with unrestricted Q_p.

Inotropic support that increases Q_s may also increase SaO_2 simply by increasing $SmvO_2$. The use of particular inotropic agents may also be associated with a change in Q_p/Q_s in addition to increases in total cardiac output. Riordan et al [26] studied the effects of epinephrine, dobutamine, and dopamine in an animal model of single-ventricle physiology. They found that dobutamine (5 and 15 μg/kg/min) increased Q_p/Q_s, epinephrine (0.05 and 0.1 μg/kg/min) decreased Q_p/Q_s, and dopamine (5 and 15 μg/kg/min) had a minimal effect on Q_p/Q_s. The use of low-dose epinephrine (0.05 μg/kg/min) was associated with the greatest increase in PVR/SVR ratio, largely because of a decrease in SVR. This increase

probably reflects the predominance of vascular β-receptor stimulation at this dose compared with α-adrenergic activation at a higher dose and illustrates the importance of using vasodilating drugs as an accompaniment to inotropic agents with prominent vasoconstrictor properties. The importance of maximizing inotropic function can be seen in Fig. 4. The DO_2 is increased dramatically by increasing total cardiac output and is optimized by adjusting Q_p/Q_s; thus, the combination of inotropic support and decreasing SVR is potentially the optimal strategy to maximize DO_2.

Not all single-ventricle patients demonstrate pulmonary overcirculation. Elevated PVR can easily persist in the newborn with single-ventricle physiology and can cause severe cyanosis. When Q_p is very low ($PaO_2 < 30$ mm Hg), it can effectively increase pulmonary dead space and impair minute ventilation. The occurrence of respiratory acidosis in this setting is of grave concern, because this condition will further increase PVR, limiting the ability to hyperventilate or alkalinize the patient. Treatment of high PVR in the single-ventricle patient is much the same as in any other population. Alveolar recruitment strategies of ventilation are appropriate when there is atelectasis or pulmonary disease, but otherwise airway pressures should be kept to a minimum. High-frequency jet ventilation may be effective in inducing hyperventilation at low mean airway pressure [27], a desirable combination in pulmonary hypertension. Use of supplemental inspired oxygen, hyperventilation, and alkalosis may all be effective. Inhaled nitric oxide and infusion of prostaglandin E have also been used in these patients to lower PVR selectively [28]. Raising systemic blood pressure by vasoconstriction may increase Q_p and will usually increase SaO_2 but does so at the expense of some systemic perfusion.

Bidirectional cavopulmonary anastomosis

Anatomy

The second stage of single-ventricle palliation is the creation of a bidirectional cavopulmonary anastomosis in which the SVC is connected directly to the pulmonary artery and other sources of Q_p are either eliminated or severely restricted. Anatomic variations include the bidirectional Glenn and the hemi-Fontan anastomoses. These procedures differ in that the hemi-Fontan anastomosis includes the attachment of the proximal stump of the SVC to the underside of the pulmonary artery, but this connection is then patched to avoid flow of deoxygenated blood into the right atrium from the pulmonary artery. The bidirectional cavopulmonary anastomosis has been remarkable for the relatively low level of associated morbidity and mortality. Numerous reviews suggest an overall mortality rate of 3% to 5% [29–31].

Physiology

Three significant aspects separate the physiology of the bidirectional cavopulmonary anastomosis from that of a normal circulation or newborn single-

ventricle physiology. First, the driving force for Q_p is SVC pressure. Second, Q_p must pass through two separate and highly regulated vascular beds: the cerebral vasculature and the pulmonary vasculature. Finally, compared with newborn single-ventricle physiology, the bidirectional cavopulmonary anastomosis removes the left-to-right shunt and thus the volume load from the single ventricle. The clinical physiology of the bidirectional cavopulmonary anastomosis therefore centers on issues regarding central venous/pulmonary artery pressure, pulmonary and cerebral vascular resistance, and alterations in ventricular loading and geometry.

Because Q_p is supplied by upper body systemic venous return, one consequence of conversion to a bidirectional cavopulmonary anastomosis is an acute rise in SVC pressure. Selection of patients with low PVR as candidates for the bidirectional cavopulmonary anastomosis minimizes the risk of clinical complications arising from elevated SVC pressure [32], but SVC syndrome can occur nonetheless. Failure to maintain low SVC pressure following the bidirectional cavopulmonary anastomosis can also lead to problems maintaining an adequate SaO_2. Small veno-venous collateral vessels (such as a persistent left SVC or vein of Marshall) may enlarge in size following a bidirectional cavopulmonary anastomosis and allow a route for desaturated blood in the SVC to bypass the lungs and thus contribute to arterial desaturation [33]. When the anastomosis is performed as part of a hemi-Fontan procedure rather than a bidirectional Glenn procedure, a right-to-left shunt may occur if there is a persistent communication between the SVC and right atrium.

To minimize SVC pressure, it is desirable to minimize use of positive pressure, including PEEP, following surgery [34–37]. Setting the ventilator to maintain the PEEP at zero, however, may result in atelectasis and an increase in PVR. Favorable hemodynamics are most likely maintained by using ventilator settings that allow the end-expiratory lung volume to approximate FRC, because PVR is lowest at FRC. In the patient with healthy lungs, minimal mean airway pressure and early extubation are often beneficial, because negative-pressure ventilation is associated with increased Q_p in this type of circulation. When lung disease such as pneumonia or acute respiratory distress syndrome occurs in the patient with a cavopulmonary anastomosis, higher airway pressures may actually promote Q_p and minimize pulmonary artery pressure if the higher airway pressure helps maintain FRC. Use of aprotinin and modified ultrafiltration have also been associated with a decreased transpulmonary pressure gradient, less pleural drainage, and improved SaO_2 [38,39].

Another unique aspect of the physiology of the bidirectional cavopulmonary anastomosis is that Q_p is largely dependent on the resistance of two highly but differentially regulated vascular beds. The cerebral and pulmonary vasculatures have opposite responses to changes in carbon dioxide, acid-base status, and oxygen. This difference can make treatment of elevated PVR or low SaO_2 particularly challenging. Hyperventilation and alkalosis, for example, may have limited utility in this setting. Although they are effective pulmonary vaso-

dilators, hyperventilation and alkalosis cause cerebral vasoconstriction [40,41]. Because Q_p is dependent on venous return through the SVC (largely made up of cerebral blood flow), maneuvers that limit cerebral blood flow may decrease Q_p and exacerbate hypoxemia. Hyperventilation following bidirectional cavopulmonary anastomosis does, in fact, impair cerebral blood flow and decrease SaO_2 [42]. Other frequently used techniques for decreasing PVR, such as deep sedation or anesthesia, may also reduce cerebral blood flow and therefore fail to increase Q_p even if they successfully reduce PVR. Inhaled nitric oxide, which acts selectively on the pulmonary vasculature, has been reported to be effective in reducing the transpulmonary pressure gradient for patients after the bidirectional cavopulmonary anastomosis and may therefore be the best treatment for high PVR and low SaO_2 [43]. When the degree of cyanosis is not prohibitive, expectant management with good hemodynamic support and maintenance of hemoglobin will often suffice. Arterial oxygen saturation tends to improve slowly in the first few days following surgery and again at the time of extubation as long as there are no intervening airway or pulmonary issues.

The real hemodynamic advantage of the bidirectional cavopulmonary anastomosis compared with shunted or banded single-ventricle physiology is in the reduction of the volume load on the ventricle. This reduction occurs because the right-to-left shunt is eliminated and all Q_p is effective pulmonary flow. The ventricle now only pumps Q_s, not $Q_p + Q_s$ [44]. Some of the Q_s (the portion distributed to the upper body) passes through the lungs before reaching the ventricle again, and thus all blood reaching the lungs is deoxygenated. The advantageous consequences of this volume reduction go beyond simply lowering the amount of blood the ventricle needs to pump to maintain adequate systemic cardiac output. An acute increase in wall thickness and decrease in cavity dimension has been associated with improved tricuspid valve function [45]. Preload and afterload are both decreased, although there is not a measurable increase in ventricular contractile state [46]. Coronary blood flow decreases, probably in response to the lower metabolic demand of the myocardium, but coronary flow changes from predominantly systolic to both systolic and diastolic [47].

When a significant left-to-right shunt persists following bidirectional cavopulmonary anastomosis because of additional sources of Q_p or aortopulmonary collateral blood vessels, persistent pleural effusions, high central venous pressures, and low cardiac output may result [48,49]. It is also important to recognize that the changes in ventricular geometry that occur with volume reduction place infants with certain types of anatomy at risk for systemic outflow obstruction. Specifically, when systemic outflow is dependent on flow through a ventricular septal defect or bulboventricular foramen, acute decreases in ventricular dimension may precipitate effective subaortic stenosis. The appearance of an ejection murmur in a patient with susceptible anatomy following bidirectional cavopulmonary anastomosis should prompt a complete assessment for this phenomenon.

Total cavopulmonary anastomosis

Anatomy

The Fontan operation has several commonly used anatomic variants, all designed to achieve optimal fluid dynamics and minimize the risk of long-term complications. Although one may still encounter older individuals with direct right atrial-to-pulmonary artery connections, the most common current approaches to the Fontan operation are the creation of either an intracardiac lateral tunnel or extracardiac conduit. The lateral tunnel involves placement of a semicircular tube, usually Gore-Tex (WL Gore & Associates, Flagstaff, AZ), along the lateral wall of the right atrium from the inferior vena cava to the SVC. Patients with a prior bidirectional Glenn anastomosis then need to have the proximal portion of the SVC reconnected to the pulmonary artery, whereas those who have had a prior hemi-Fontan anastomosis need only to have the patch between the pulmonary artery and right atrium taken down. The extracardiac conduit uses a complete circular tube of Gore-tex or pericardium to connect the inferior vena cava to the pulmonary artery. The conduit is placed along the outer surface of the right atrium and thus creates a connection incapable of dilating over time, unlike the classic Fontan procedure, or even potentially the lateral tunnel. Either variation on the Fontan procedure can be fenestrated by leaving a hole of known size in the baffle. In the case of the extracardiac Fontan procedure, fenestration requires connection of the conduit to the atrial wall.

The different approaches to the Fontan connection may have implications for postoperative physiology, although no consensus on which technique is preferable has yet been reached. The arguments in favor of the lateral tunnel are that it is less thrombogenic, can be done in patients at a younger age, and retains the possibility for growth without the likelihood of severe dilation. Those who favor the extracardiac approach argue that it preserves kinetic energy better, that it can be performed without cardioplegia (thereby reducing the incidence of postoperative myocardial dysfunction [50,51]), and that it is less arrhythmogenic [52] because there is no atrial suture line. Some laboratory work supports the contention that fluid dynamics are better with the extracardiac conduit, but real effects on patient outcome other than incidence of arrhythmia [52] have not been identified [53]. In the absence of a conclusive study, the differences between Fontan techniques remain largely theoretical.

Physiology

Fontan physiology is a hybrid of bidirectional cavopulmonary anastomosis and normal cardiovascular physiology. As with a bidirectional cavopulmonary anastomosis, Q_p is dependent on systemic venous pressure, and all Q_p is effective. If the Fontan baffle is fenestrated, there may still be a right-to-left shunt causing some mild systemic arterial desaturation, but the systemic and pulmonary circulation are largely separated, as with a normal heart. Important issues for the intensive care physician arise when there is elevated pulmonary

artery pressure. This elevation can occur either because the PVR is high (or there is mechanical pulmonary artery obstruction) or when myocardial dysfunction raises pulmonary venous atrial pressure. Numerous studies demonstrate that elevated pulmonary artery pressure (>10–15 mm Hg) is associated with poor outcome in Fontan patients [54–56], largely because it is difficult to maintain central venous pressure in this range without large third-space losses of fluid. As these fluid losses progress, patients often develop pleural effusions, ascites, and peripheral edema. It then becomes necessary to increase ventilator pressures to maintain adequate FRC and tidal volume in the face of a full abdomen, heavy chest wall, and smaller effective pleural cavities. Increased airway pressure, particularly in the absence of parenchymal lung disease, effectively raises PVR and thus necessitates even higher venous pressures to maintain cardiac output. Furthermore, as central venous and intra-abdominal pressures rise, renal perfusion pressure decreases, especially in the face of low cardiac output and borderline hypotension, as is often the case in this scenario. In general, Fontan fenestration can lower the risk of some of these complications by providing a source of Q_s that is not dependent on passing through the pulmonary circulation [57]. Fenestration can also decrease pulmonary artery pressure enough to reduce third-space losses of fluid [57–59]. A randomized trial of a fenestrated versus nonfenestrated Fontan connection has shown that fenestration decreases the duration of pleural effusions and is associated with a shorter hospital stay; however, the effect on acute postoperative hemodynamics was less clear [60].

When an individual with Fontan physiology is in a low cardiac output state, it is essential to determine and treat the underlying cause. Obstruction to Q_p should be considered as the cause of low output when left atrial pressure is low and central venous pressure is high. If central venous pressure is not monitored, large third-space fluid losses with a low or normal left atrial pressure should raise the suspicion of this diagnosis. Even in the presence of a fenestrated Fontan, the capability of the fenestration to preserve cardiac output in the face of anatomic or physiologic obstruction to pulmonary blood flow is significantly limited compared with the situation after the bidirectional cavopulmonary anastomosis. Therefore, limited Q_p can result in low cardiac output and, when a fenestration is present, in significant cyanosis. Cyanosis can also result from intrapulmonary arteriovenous malformations or ventilation-perfusion mismatch related to low cardiac output [61,62].

If high PVR is responsible for the elevation of central venous pressure, institution of the standard therapies of supplemental oxygen, hyperventilation, and alkalosis is indicated. As in the patient with bidirectional cavopulmonary anastomosis, the use of high positive pressures to achieve these ends may be counterproductive. Negative pressure ventilation can augment stroke volume and cardiac output, and high-frequency jet ventilation may lower $PaCO_2$ at low mean airway pressures [27,63,64]. Intravenous vasodilators such as prostacyclin or prostaglandin E should be used with caution because of the risk of systemic vasodilation with limited cardiac output. Inhaled nitric oxide has been reported to be effective in lowering the transpulmonary pressure gradient [65,66].

Low cardiac output with high left atrial and central venous pressures indicates myocardial dysfunction in the patient with Fontan physiology. Myocardial dysfunction can occur from ischemia-reperfusion injury if aortic cross-clamping and cardioplegia are used to create the Fontan baffle. It may also be related to poor preoperative myocardial function. Several studies demonstrate better outcome for the Fontan operation in patients under 4 years of age or when a bidirectional cavopulmonary anastomosis has been performed as the second stage in univentricular heart palliation [67,68], suggesting long-standing ventricular volume overload is detrimental to myocardial function. The only effective long-term therapy for low cardiac output with ventricular dysfunction following a Fontan operation is to improve cardiac output and reduce left atrial pressure. The use of inotropic agents that do not increase ventricular afterload, such as phosphodiesterase inhibitors, dobutamine, and low-dose epinephrine (≤ 0.05 μg/kg/min) may be helpful. If systemic blood pressure will tolerate it, aggressive afterload reduction with vasodilating agents may also lower left atrial pressure significantly. If there is good reason to believe the insult to ventricular function is reversible, mechanical circulatory support can also be effective therapy. Because persistent aortopulmonary collateral vessels can be associated with hemodynamics similar to those of ventricular dysfunction, aggressive assessment and embolization of these vessels may be useful in this situation [69,70].

Summary

The patient with single-ventricle physiology presents a significant challenge to the intensive care team at all stages of management. An integrated approach that applies a working knowledge of cardiac anatomy, cardiopulmonary physiology, and the basic principles of intensive care is essential to guide management for each individual patient. This management requires cooperative and constructive involvement of surgeons, cardiologists, and intensivists, as well as a nursing and respiratory care team experienced in the management of single-ventricle patients. The outcome of each stage of palliation for single-ventricle lesions should continue to improve as new ideas are developed and as older ideas are subjected to rigorous scientific analyses.

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