Section Editor: **Peter J. Davis**

A Mathematical Model of Transitional Circulation Toward Biventricular Repair in Hypoplastic Left Heart Syndrome

Koichi Yuki, MD,*† Sitaram Emani, MD,†§ and James A. DiNardo, MD*†

BACKGROUND: Although the traditional surgical approach for left hypoplastic heart syndrome is to perform staged, palliative procedures as a single ventricle lesion, certain anatomical subsets of patients are candidates for a 2-ventricle repair either as a primary or as a staged procedure. The pulmonary blood flow (Q_P)/systemic blood flow (Q_S) range necessary to optimize systemic oxygen delivery (DO_2) and systemic venous oxygen saturation has been delineated for patients undergoing conventional interventions as a single ventricle physiology where the left ventricle is assumed to make no contribution to systemic cardiac output. However, in the transitional circulations created during staging to a 2-ventricle repair, the left ventricle does contribute to cardiac output. The Q_P/Q_S at which systemic DO_2 and systemic venous oxygen saturation are optimized in the latter circulations has not yet been evaluated. Using computer modeling, we investigated parameters to optimize systemic oxygen delivery.

METHODS: We designed model circulations after both modified stage I operation and modified bidirectional Glenn shunt with Sano shunt, which are transitional circulations created during staging to a 2-ventricle repair. Mathematical equations were derived to describe DO_2 in both models. Using a computer and an Excel spreadsheet, we used the equations to examine the relationships between DO_2 and arterial oxygen saturation (Sao_2), venous oxygen saturation (Svo_2), $Sao_2 - Svo_2$, Q_P/Q_S, and the oxygen excess factor $Sao_2/(Sao_2 - Svo_2)$.

RESULTS: In both circulations, Sao_2 or Svo_2 alone does not accurately predict DO_2 or Q_P/Q_S. The relationships between these variables are further altered by the degree of systemic cardiac output supplied by the left ventricle. To the contrary, DO_2 demonstrates the linear relationship with the oxygen excess factor $Sao_2/(Sao_2 - Svo_2)$ irrespective of the degree of systemic cardiac output supplied by the left ventricle.

CONCLUSIONS: Commonly obtained clinical values such as Sao_2 and Svo_2 alone are not accurate assessments of DO_2 or Q_P/Q_S. Therefore, these cannot be used in isolation to guide perioperative therapy. (Anesth Analg 2012;115:618–26)

In patients with hypoplastic left heart syndrome, hypoplasia of left-sided heart structures occurs as a continuum. The mitral valve, aortic valve, left ventricle (LV), left atrium (LA), and the ascending aorta and transverse aortic arch are variably affected. The presence of endocardial fibroelastosis (EFE) can adversely affect LV diastolic function and impede LV growth potential. As experience with hypoplastic left heart syndrome has accumulated, patients with borderline LV are considered candidates for a 2-ventricle repair either as a primary or staged procedure.[1–3] The current modified Norwood stage I surgical approach for patients deemed to be suitable candidates for a staged 2-ventricle repair can be summarized as follows:

- Percutaneous transcatheter or surgical aortic valvuloplasty EFE resection in the LV, LA, and mitral papillary muscles. This procedure is usually limited by the small mitral orifice through which the resection is performed.
- Magnetic resonance imaging (MRI) provides a better assessment of the extent of EFE and true LV volume than echocardiography.[4,5] EFE resection improves the size and compliance of LA and LV cavities. This promotes antegrade ejection of fully saturated pulmonary venous blood into the aortic valve.
- Mitral valvuloplasty.
- Damus-Kaye-Stansel anastomosis with arch augmentation and coarctation repair if necessary.
- Creation of a partially restrictive atrial septum. This may help "force" blood into the LV. However, it may produce LA and pulmonary venous hypertension leading to development of pulmonary vascular occlusive disease. Only mild restriction is usually created at this stage because LV diastolic compliance is poor.
- A right ventricle (RV) to pulmonary artery (PA) conduit (Sano shunt) rather than a modified Blalock-Taussig shunt for provision of pulmonary blood flow

From the Departments of *Anesthesiology, Perioperative and Pain Medicine, and ‡Cardiac Surgery, Children's Hospital Boston, Boston; and Departments of †Anaesthesia and §Surgery, Harvard Medical School, Boston, Massachusetts.

Accepted for publication April 10, 2012.

The authors declare no conflicts of interest.

Reprints will not be available from the authors.

Address correspondence to Koichi Yuki, MD, Department of Anesthesiology, Perioperative and Pain Medicine, Children's Hospital Boston, 300 Longwood Ave., Boston, MA. Address e-mail to koichi.yuki@childrens.harvard.edu.

DOI: 10.1213/ANE.0b013e31825d36a1

because the preservation of aortic diastolic blood pressure may improve coronary blood flow to the LV.

A bidirectional Glenn (BDG) shunt in conjunction with additional EFE resection and aortic and/or mitral valvuloplasty if necessary is performed at 3 to 6 months of age if insufficient LV growth precludes takedown of the modified stage I repair and conversion to a 2-ventricle repair. During the BDG procedure, the atrial septal defect (ASD) is aggressively restricted (4-mm fenestration). At 3 to 4 years of age, a Fontan procedure is performed if takedown of the BDG and conversion to a 2-ventricle repair is not feasible.

Both clinical investigations and computer modeling have delineated the pulmonary blood flow (Q_P)/systemic blood flow (Q_S) range necessary to optimize systemic oxygen delivery (DO_2) and systemic venous oxygen saturation (Svo_2) in single ventricle physiology.[6–9] In these models, the LV is assumed not to contribute to systemic cardiac output (CO). However, optimal circulatory variables in the transitional circulations created during staging to a 2-ventricle repair, in which the LV does contribute to CO, have not been previously evaluated. In this investigation, we sought to determine whether computer modeling could be used to facilitate evaluation of systemic DO_2 in these transitional circulations. In addition, we sought to determine whether indices derived from oxygen saturation measurements would be clinically useful in optimizing systemic DO_2.

METHODS

Model 1: Circulation After Modified Stage I Operation

Figure 1 illustrates the circulation of a newborn who has undergone stage I palliation with a Sano shunt in conjunction with EFE resection and creation of a partially restrictive intraatrial communication. A portion of pulmonary venous blood is ejected antegrade by the LV across the aortic valve into the aorta while the remaining blood crosses the atrial septum to mix with systemic venous blood in the right atrium (RA) and RV. Part of the blood in the RV is ejected antegrade into the aorta while the remaining is delivered across the conduit to the PA. All flow at the atrial septal level is left to right, and systemic and pulmonary venous blood in the RV is mixed before delivery to the PA.

Based on the previous model,[6] we derived equations (DO_2) as follows:

$$\text{Arterial oxygen content } (CaO_2)(\text{mL } O_2/\text{dL}) = [1.38\ (\text{mL/g}) \cdot \text{hemoglobin (Hb) (g/dL)} \cdot SaO_2\ (\%)/100] + [0.003\ (\text{mL } O_2/\text{mmHg/dL}) \cdot \text{arterial partial pressure of oxygen } (PaO_2)\ (\text{mmHg})] \quad (1)$$

Because $[0.003 \cdot Pao_2]/[1.38 \cdot Hb \cdot Sao_2] = 0.00014 \cdot [Pao_2/Sao_2]$, and $[Pao_2/Spo_2] < 1$ in this circulation, Equation (1) can be simplified to:

$$CaO_2 = 1.38 \cdot Hb \cdot SaO_2 \quad (2)$$

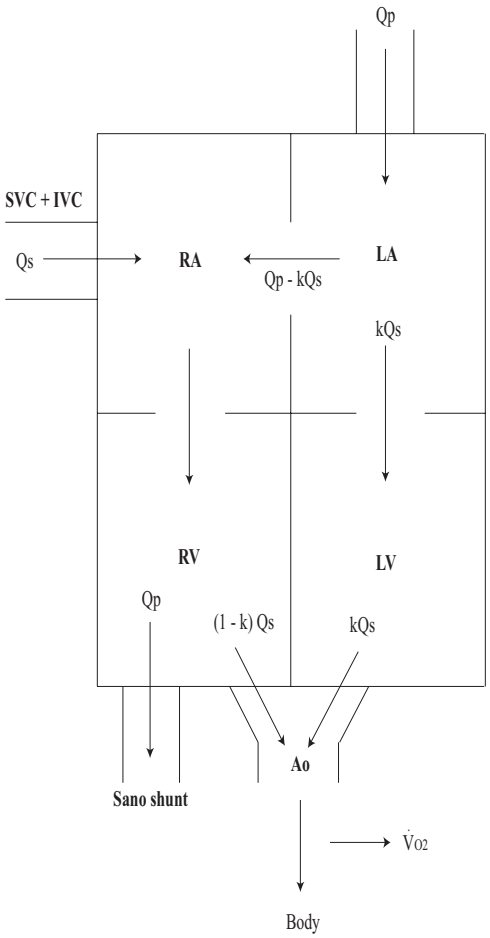

Figure 1. Circulation model following modified stage I operation. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle; SVC = superior vena cava; IVC = inferior vena cava; Ao = aorta; Q_P = pulmonary blood flow; Q_S = systemic blood flow; Vo_2 = oxygen consumption.

Accordingly, pulmonary arterial oxygen content $(C_{PA}O_2) = 1.38 \cdot Hb \cdot$ pulmonary arterial oxygen saturation, left ventricular oxygen content $(C_{LV}O_2) = 1.38 \cdot Hb \cdot$ left ventricular oxygen saturation, and right ventricular oxygen content $(C_{RV}O_2) = 1.38 \cdot Hb \cdot$ right ventricular oxygen saturation.

Because total body oxygen consumption equals lung oxygen uptake in the steady-state:

$$SVO_2 = \text{whole body oxygen consumption } (CVO_2) \quad (3)$$

The relation between systemic arterial and venous oxygen delivery is written as:

$$CaO_2 \cdot Q_S - CVO_2 = CVO_2 \cdot Q_S \quad (4)$$

Similarly,

$$C_{PA}O_2 \cdot Q_P + SVO_2 = C_{PV}O_2 \cdot Q_P \quad (5)$$

The combined output of the ventricular system is described as:

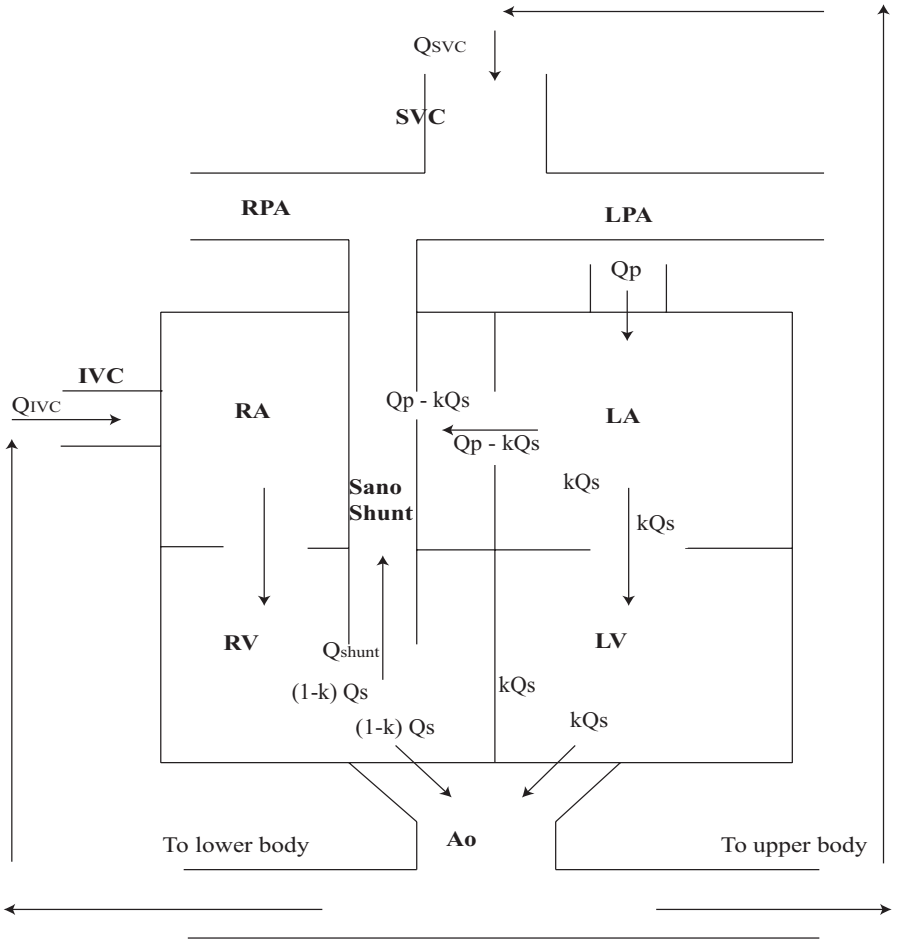

Figure 2. Circulation model following creation of modified bidirectional Glenn shunt with retained Sano shunt. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle; SVC = superior vena cava; IVC = inferior vena cava; Ao = aorta; LPA = left pulmonary artery; RPA = right pulmonary artery; Q_P = pulmonary blood flow; Q_S = systemic blood flow; Q_{shunt} = blood flow through Sano shunt.

$$CO = Q_P + Q_S \quad (6)$$

From Figure 1:

$$C_{LV}O_2 = C_{PV}O_2$$

$$C_{RV}O_2 = C_{PA}O_2$$

Using k, fraction of pulmonary vein (PV) blood entering the LV:

$$DO_2 = Q_S \cdot CaO_2 = (kQ_S \cdot C_{LV}O_2) + (1 - k)\, Q_S \cdot C_{RV}O_2 \quad (7)$$

Equation (7) can be converted to:

$$DO_2 = Q_S \cdot CaO_2 = kQ_S \cdot C_{PV}O_2 + (1 - k)\, Q_S \cdot C_{PA}O_2 \quad (8)$$

Combining Equations (3), (4), (5), (6), and (8) yields:

$$DO_2 = Q_S \cdot CaO_2 = [1/(1 + Q_P/Q_S)] \cdot CO \cdot C_{PV}O_2 - [(1 - k) \cdot CVO_2/(Q_P/Q_S)] \quad (9)$$

Of note at k = 0, when there is no LV contribution to Q_S, Equation (9) simplifies to the equation previously used to describe DO_2 in univentricular physiology (6):

$$DO_2 = Q_S \cdot CaO_2 = [1/(1 + Q_P/Q_S)] \cdot CO \cdot C_{PV}O_2 - [CVO_2/(Q_P/Q_S)]$$

At k = 1, LV provides all Q_S. When $Q_P/Q_S = 1$, Equation (9) describes DO_2 in a normal 2-ventricle circulation:

$$DO_2 = Q_S \cdot CaO_2 = Q_S \cdot C_{PV}O_2$$

The RV stroke volume/LV stroke volume ratio is described as follows:

$$\text{RV/LV stroke volume ratio} = [Q_P + (1 - k)\, Q_S]/kQ_S = (1/k) \cdot Q_P/Q_S + (1 - k)/k \quad (10)$$

Model 2: Circulation After Creation of Modified BDG Shunt with Sano Shunt

Figure 2 illustrates the circulation of a child who has undergone creation of a BDG shunt with retention or upsizing of Sano shunt in conjunction with additional EFE resection and retention of a partially restrictive intraatrial communication. The circulation is as described for the modified stage I procedure except that all superior vena cava (SVC) return is directed to the PA such that Q_P is determined by the combination of SVC and RV to PA conduit flow.

Referring to the previous model,[10] we derived additional equations to describe DO_2. If p is the fraction of CVO_2 consumed by the upper body and (1 − p) is the fraction consumed by the lower body, then:

$$CVO_2 = p \cdot CVO_2 + (1 - p) \cdot CVO_2 \quad (1a)$$

Upper body DO_2 minus upper body oxygen consumption results in reduced DO_2 to the SVC:

$$CaO_2 \cdot Q_{SVC} - p \cdot CVO_2 = C_{SVC}O_2 \cdot Q_{SVC} \quad (2a)$$

Likewise, lower body DO_2 minus lower body oxygen consumption results in reduced oxygen delivery to the inferior vena cava (IVC):

$$CaO_2 \cdot Q_{IVC} - (1 - p) \cdot CVO_2 = C_{IVC}O_2 \cdot Q_{IVC} \quad (3a)$$

CO is the combination of SVC, IVC, and Sano shunt flow:

$$CO = Q_{SVC} + Q_{IVC} + Q_{shunt} \quad (4a)$$

Pulmonary blood flow is a combination of SVC and Sano shunt flow:

$$Q_p = Q_{SVC} + Q_{shunt} \quad (5a)$$

Systemic blood is a combination of SVC and IVC blood flow:

$$Q_S = Q_{SVC} + Q_{IVC} \quad (6a)$$

If upper and lower body oxygen consumption is coupled to SVC and IVC flow respectively, then:

$$Q_{SVC} = p \cdot Q_S \quad (7a)$$

$$Q_{IVC} = (1 - p) \cdot Q_s \quad (8a)$$

From Figure 2:

$$Q_{Shunt} = Q_{IVC} + (Q_P - kQ_S) - (1 - k)\, Q_S \quad (9a)$$

In addition, the fraction of total RV blood (IVC blood and PV blood that crosses the atrial septum) that is ejected into the aorta versus the Sano shunt is determined by the ratio:

$$[(1 - k)\, Q_S]/[Q_{IVC} + (Q_P - kQ_S)] \quad (10a)$$

From Equation (6a) is derived:

$$DO_2 = CaO_2 \cdot Q_S = CaO_2 \cdot (Q_{SVC} + Q_{IVC}) \quad (11a)$$

Recalling that k is the fraction of PV blood entering the LV and that 1 − k is the fraction of PV crossing the atrial septum and combining Equations (10a) and (11a):

$$CaO_2 \cdot Q_S = C_{PV}O_2 \cdot k\, Q_S + [C_{IVC}O_2 \cdot Q_{IVC} + C_{PV}O_2 \cdot (Q_P - k\, Q_S)] \cdot [(1 - k)\, Q_S/Q_{IVC} + (Q_P - k\, Q_S)] \quad (12a)$$

Using Equations (3a), (8a), and (12a) yields:

$$CaO_2 \cdot Q_S = C_{PV}O_2 \cdot k\, Q_S + [CaO_2 \cdot (1 - p)Q_s - (1 - p)CVO_2 + C_{PV}O_2 \cdot (Q_P - kQ_S)] \cdot [(1 - k)\, Q_S/(1 - p)Q_s + (Q_P - kQ_S)] \quad (13a)$$

Equation (13a) can be simplified to:

$$CaO_2 = C_{PV}O_2 - (1 - K)(1 - p) \cdot CVO_2/(Q_P - kp\, Q_S) \quad (14a)$$

Using Equations (11a) and (14a):

$$DO_2 = C_{PV}O_2 \cdot Q_S - (1 - p)(1 - k) \cdot [1/(Q_P/Q_S - kp)] \cdot CVO_2 \quad (15a)$$

Of note, when k = 0 and there is no output from the LV, Equation (17a) simplifies to the equation previously used to describe DO_2 in BDG circulation[6]:

$$DO_2 = C_{PV}O_2 \cdot Q_S - [(Q_S/Q_P) \cdot (1 - p) \cdot CVO_2]$$

where $Q_S/Q_P = (1 + Q_{SVC}/Q_{IVC})/(Q_{SVC}/Q_{IVC})$.

The RV stroke volume/LV stroke volume ratio is described as follows:

$$\text{RV/LV stroke volume ratio} = [Q_{IVC} + (Q_P - k\, Q_S)]/k\, Q_S = (1/k) \cdot Q_{IVC}/Q_S + (1/k) \cdot Q_P/Q_S - 1 \quad (16a)$$

Combining Equations (8a) and (16a) yields:

$$\text{RV/LV stroke volume ratio} = (1 - p - k)/k + (1/k) \cdot Q_P/Q_S \quad (17a)$$

Using a computer and an Excel spreadsheet, we used these equations to examine the relation between DO_2 and Sao_2, Svo_2, $Sao_2 - Svo_2$, Q_P/Q_S, and the oxygen excess factor $Sao_2/(Sao_2 - Svo_2)$ for models 1 and 2. Physiologically relevant solutions to the equations for both models exist only when $Q_P \geq k\, Q_S$ or $Q_P/Q_S \geq k$. In both models, we assumed CVO_2 = 9 mL/kg/min, Hb = 15 g/dL, and pulmonary venous saturation = 96% as has been previously described.[6] For models 1 and 2, CO (the combined output of both ventricles) is assumed to be 300 mL/kg/min. These values for CVO_2 and CO are consistent with those used in previous models[6] and with values measured in patients at our own and other institutions.[9] In model 2, p = 0.6 was chosen, consistent with the value previously reported in children with a superior cavopulmonary anastomosis.[10]

RESULTS

Model 1

Figure 3 demonstrates the relationship of DO_2 with Q_P/Q_S at a fixed biventricular output of 300 mL/kg/min. The Q_P/Q_S of maximal DO_2 at k = 0 is 0.64, which is compatible with the previous modeling.[6] Maximum DO_2 of k = 0.25 and k = 0.5 are at Q_P/Q_S of 0.51 and 0.5, respectively. As Q_P/Q_S increases, DO_2 of k = 0.25, 0.5 and 0.75 become

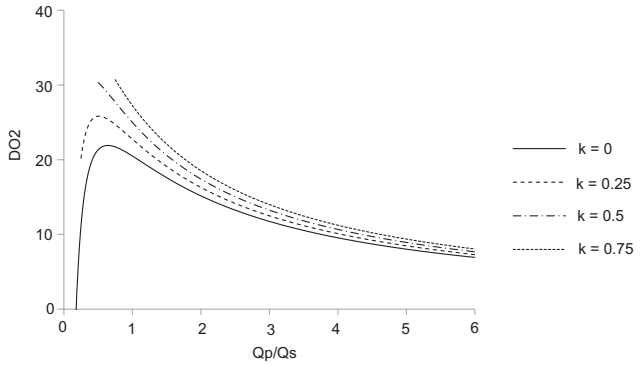

Figure 3. Systemic oxygen delivery (DO_2) versus Q_P/Q_S.

indistinguishable from that of single ventricle physiology (k = 0). This is the result of "excess" oxygenated pulmonary venous blood crossing the atrial septum to be recirculated into the pulmonary circulation. With a fixed biventricular output, this increases RV stroke volume, decreases LV stroke volume, and increases the RV/LV volume ratio (Fig. 4).

Maximum Svo_2, which may be a better indicator of tissue oxygenation than maximum DO_2,[7] occurs at a Q_P/Q_S of 1 when k = 0 (Fig. 5). Maximum Svo_2 at k = 0.25 and 0.5 is at Q_P/Q_S of 0.87 and 0.71, respectively. The use of

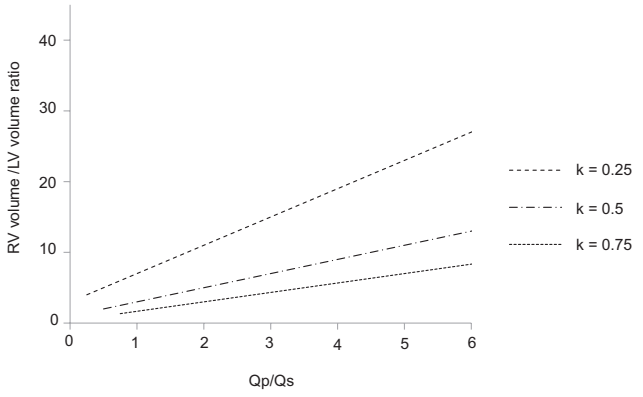

Figure 4. Right ventricle (RV) volume/left ventricle (LV) volume ratio versus Q_P/Q_S.

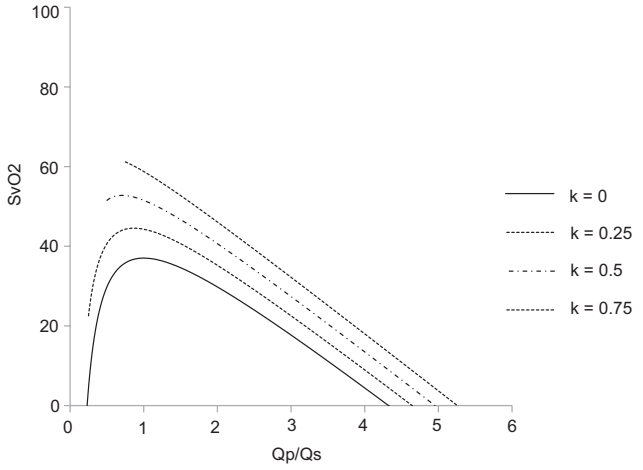

Figure 5. Systemic venous oxygen saturation (Svo_2) versus Q_P/Q_S.

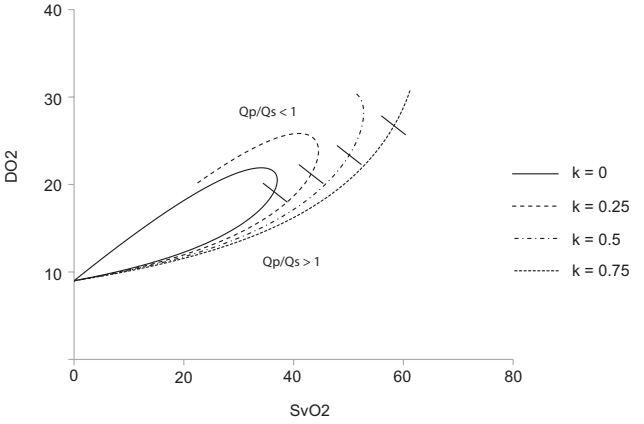

Figure 6. Systemic venous oxygen saturation (Svo_2) versus systemic oxygen delivery (DO_2).

absolute Svo_2 as a surrogate assessment of Q_P/Q_S is limited at lower values of k because equal values of Svo_2 exist at both high and low Q_P/Q_S as Q_P/Q_S varies above and below unity. For lower values of k, peak Svo_2 does not occur at peak DO_2 (Fig. 6). At lower values of k, peak Svo_2 is achieved at a higher Q_P/Q_S than that necessary to maximize DO_2. However, maximum DO_2 and Svo_2 at k = 0.75 are at Q_P/Q_S of k (= 0.75). As k increases toward 1, the Q_P/Q_S necessary to maximize both Svo_2 and DO_2 converge toward k. Use of absolute Svo_2 as a surrogate assessment of DO_2 is limited at lower values of k because equal values of Svo_2 exist at both high and low DO_2.

The Q_P/Q_S necessary to bring Sao_2 to a plateau value decreases as k increases (Fig. 7). Once this plateau is reached, neither changes in Sao_2 nor the absolute value of Sao_2 provides an accurate assessment of Q_P/Q_S for any value of k. For k = 0, it will be the case at $Q_P/Q_S \geq 1.5$. At lower values of k, comparable values of Sao_2 exist at both low and high states of DO_2 (Fig. 8). For any k, once a maximum value of DO_2 is achieved, clinically imperceptible increases in Sao_2 are associated with precipitous decreases in DO_2. A nonlinear relationship exists between DO_2 and $Sao_2 - Svo_2$ (Fig. 9). As Q_P/Q_S increases from values slightly above 1, DO_2 decreases as $Sao_2 - Svo_2$ increases. DO_2 peaks at a value of Q_P/Q_S just below 1 and for k = 0 and 0.25, DO_2 rapidly decreases as $Sao_2 - Svo_2$ continues to decrease.

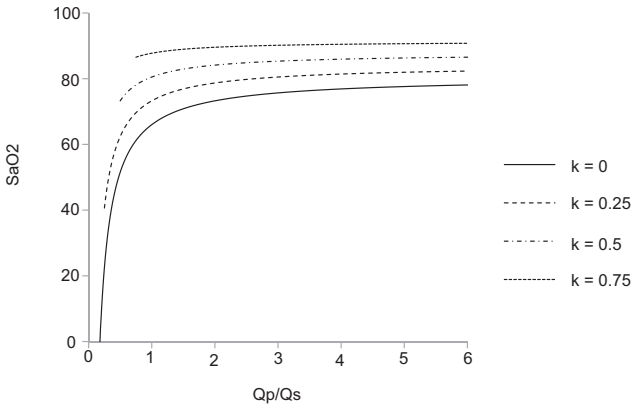

Figure 7. Systemic arterial oxygen saturation (Sao_2) versus Q_P/Q_S.

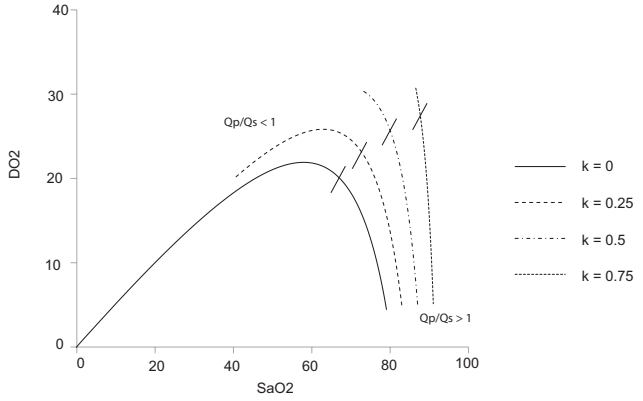

Figure 8. Systemic arterial oxygen saturation (Sao_2) versus systemic oxygen delivery (DO_2). The short line on each curve represents the point at which $Q_P/Q_S = 1$.

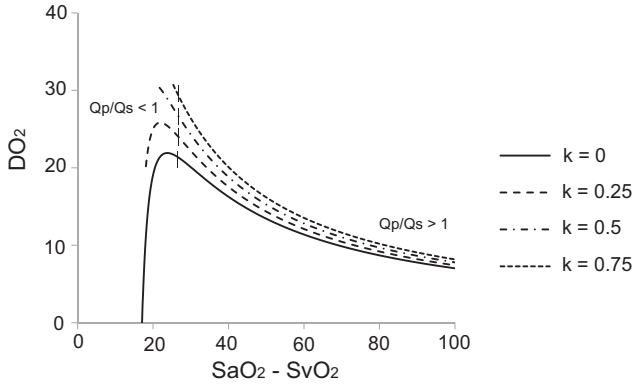

Figure 9. Systemic oxygen delivery (DO_2) versus $Sao_2 - Svo_2$. The short line on each curve represents the point at which $Q_P/Q_S = 1$.

$Sao_2/(Sao_2 - Svo_2)$ has been defined as the oxygen excess factor reflective of the ratio of oxygen delivery to oxygen consumption.[6] The relationship between $Sao_2/(Sao_2 - Svo_2)$ and DO_2 is uniquely linear. Its slope is constant for all values of k as is illustrated in Figure 10. Because $DO_2 = CVO_2 \cdot [Sao_2/(Sao_2 - Svo_2)]$, only changes in CVO_2 will alter this slope. Increases in CO will be reflected by values upward and to the right along this same line. Although the absolute value of $Sao_2/(Sao_2 - Svo_2)$ may not be clinically useful, changes in this value can be used to assess the adequacy of interventions designed to improve DO_2.

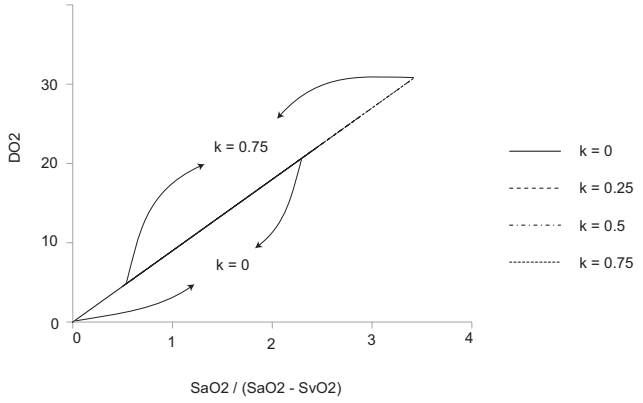

Figure 10. Systemic oxygen delivery (DO_2) versus $Sao_2/(Sao_2 - Svo_2)$. The lines corresponding to k = 0 and k = 0.75 are illustrated with arrows.

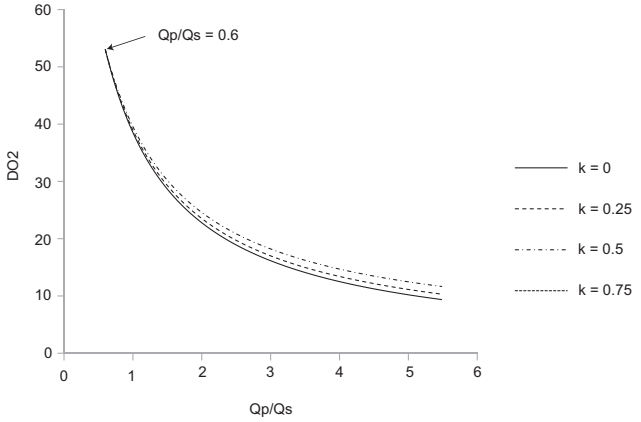

Figure 11. Systemic oxygen delivery (DO_2) versus Q_P/Q_S.

Model 2

From Equations (5a) and (7a), $Q_P/Q_S = [p + (Q_{shunt}/Q_S)]$, therefore $Q_P/Q_S \geq p$. For any value of k, DO_2 is maximal when $Q_P/Q_S = p$ (= 0.6) (Fig. 11). As Q_P/Q_S increases above p, a larger portion of IVC is delivered to the pulmonary vascular bed and returned to the LA. As a consequence, a larger portion of the fixed biventricular CO is composed of a physiological left-to-right shunt. This increases RV stroke volume, decreases LV stroke volume, and increases the RV/LV volume ratio as seen in Figure 12. This in turn reduces effective systemic blood flow and DO_2. This is readily apparent in Figure 13 where Svo_2 is seen to decrease as Q_P/Q_S increases, DO_2 decreases, and the Sao_2 Svo_2 difference widens for a fixed CVO_2. Because upper and lower body oxygen consumption are coupled to SVC and IVC flow, respectively, $Svo_2 = S_{SVC}O_2 = S_{IVC}O_2$.

Sao_2 plateaus at a Q_P/Q_S at or slightly more than 1 (Fig. 14). As a result, neither changes in Sao_2 nor the absolute value of Sao_2 provides an accurate assessment of Q_P/Q_S. By the time Sao_2 has reached a plateau, DO_2 has begun to decrease precipitously (Fig. 15). Again, neither changes in Sao_2 nor the absolute value of Sao_2 provides an accurate assessment of DO_2 for any value of k. Although not linear,

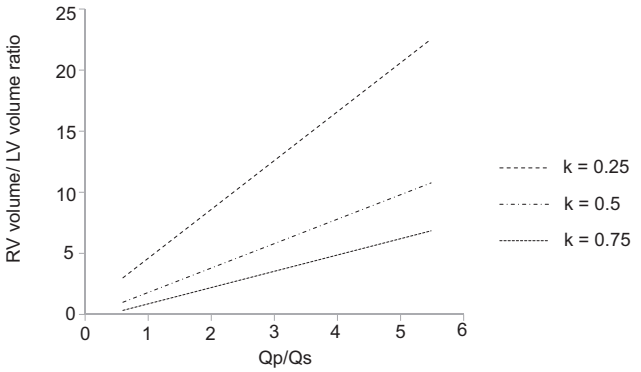

Figure 12. Right ventricle (RV) volume/left ventricle (LV) volume ratio versus Q_P/Q_S.

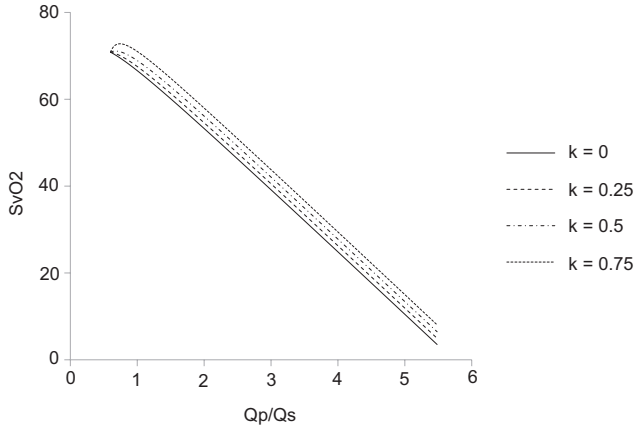

Figure 13. Superior (or inferior) vena cava oxygen saturation (Svo_2) versus Q_P/Q_S. In this model, $Svo_2 = S_{SVC}O_2 = S_{IVC}O_2$.

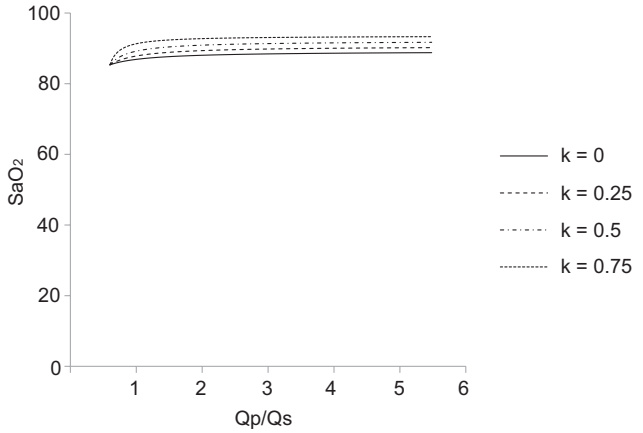

Figure 14. Systemic arterial oxygen saturation (Sao_2) versus Q_P/Q_S.

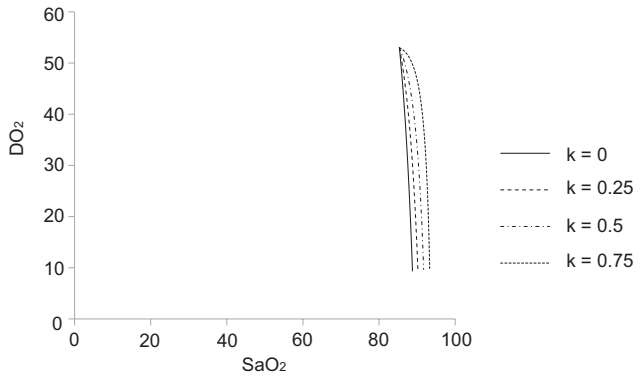

Figure 15. Systemic arterial oxygen saturation (Sao_2) versus systemic oxygen delivery (DO_2).

the relationships between $Sao_2 - S_{SVC}O_2$ and DO_2 at various k are comparable (Fig. 16). As $Sao_2 - S_{SVC}O_2$ decreases, DO_2 increases.

As is true for model 1, the relationship between $Sao_2/(Sao_2 - Svo_2)$ and DO_2 is unique in that it is linear. The slope of this relationship is constant for all values of k as is illustrated in Figure 17. As is true for model 1, only changes in CVO_2 will alter the slope of this line. Increases

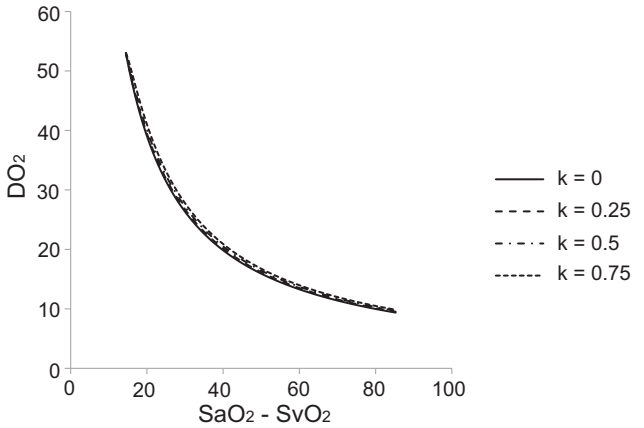

Figure 16. Systemic oxygen delivery (DO_2) versus $Sao_2 - Svo_2$. In the figure, $Svo_2 = S_{SVC}O_2 = S_{IVC}O_2$.

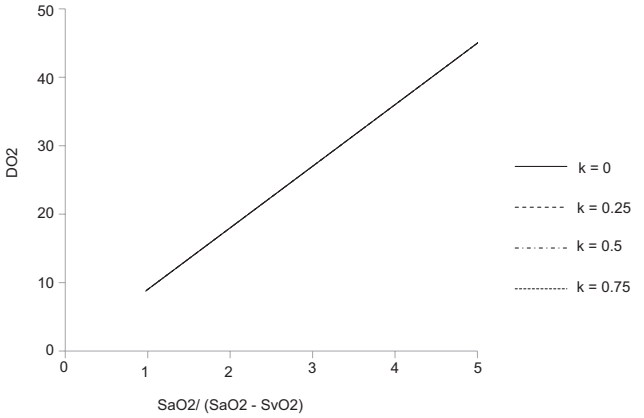

Figure 17. Systemic oxygen delivery (DO_2) versus excess oxygen factor $Sao_2/(Sao_2 - Svo_2)$. In the figure, $Svo_2 = S_{SVC}O_2 = S_{IVC}O_2$.

in CO will be reflected by values upward and to the right along this same line.

Patient Data

Figure 18 provides cardiac MRI (cMRI) and cardiac catheterization data from a patient staged to a 2-ventricle repair. At birth, cMRI demonstrated a mildly hypoplastic, nonapex-forming LV with severely depressed systolic function. LV stoke volume was 2.2 mL; RV stroke volume was 11.1 mL and the combined 2-ventricle CO was 660 mL/kg/min with a dopamine infusion at 5 to 10 μg/kg/min. A stage I procedure with a 5-mm Sano shunt in association with LV EFE resection, mitral valvotomy, and tricuspid valvuloplasty was performed on day 6 of life. At 6 months of age, a BDG procedure, replacement of the 5-mm RV to PA conduit, restriction of the ASD, mitral valvotomy, and LV EFE resection were performed. Postoperative cMRI showed LV stroke volume 9.9 mL, RV stroke volume 13.0 mL, and the combined 2-ventricle CO 392 mL/kg/min (k = 0.43). At 2.5 years of age, a biventricular repair consisting of takedown of RV-PA conduit, Damus-Kaye-Stansel anastomosis, and BDG anastomosis were performed. In addition, subaortic membrane resection, aortic valvotomy, mitral valvotomy, and creation of a 4-mm ASD were performed. One year later, cMRI revealed an LV stroke volume of 29.4

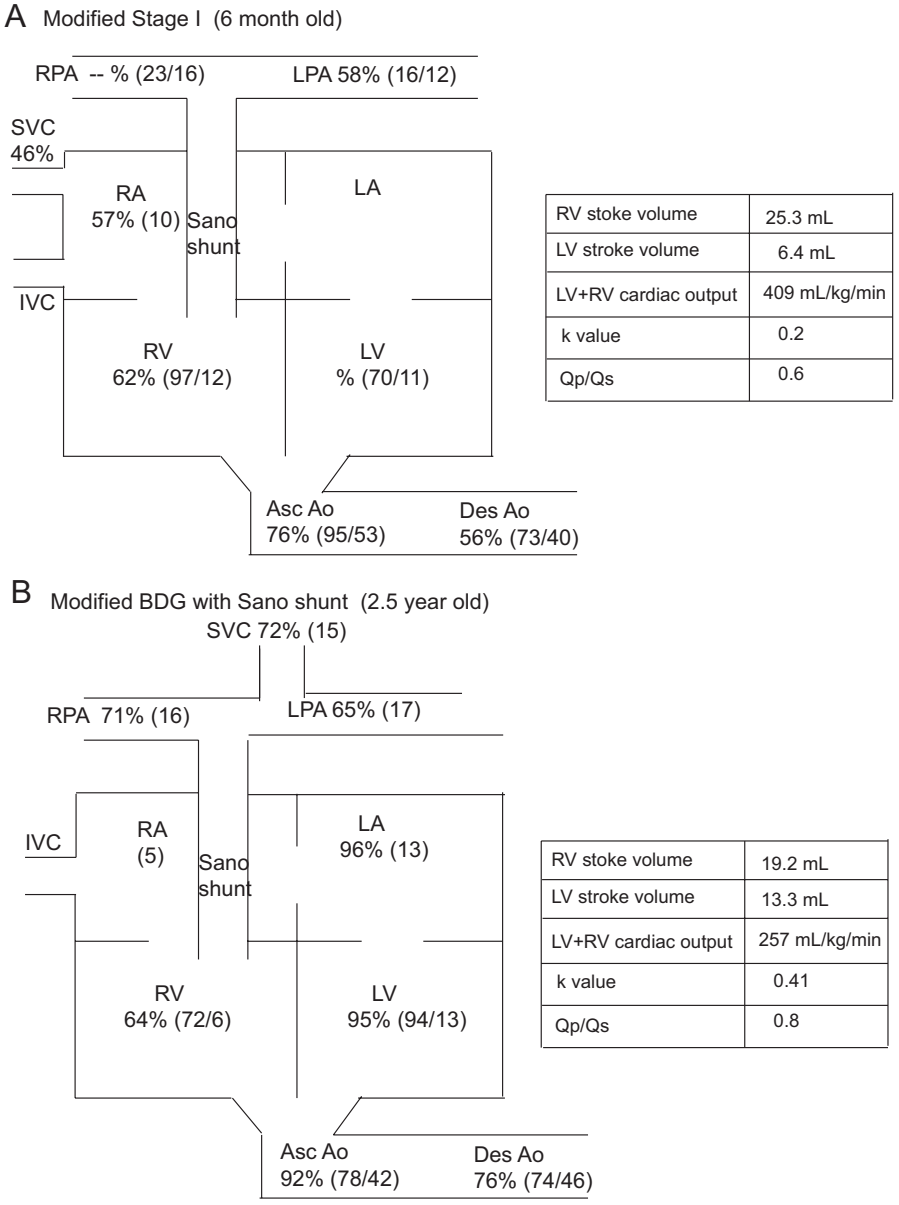

Figure 18. Hemodynamic data of a patient who underwent 2-ventricle repair. A, Hemodynamic data after modified stage I at the age of 6 months. B, Hemodynamic data after modified bidirectional Glenn (BDG) shunt with Sano shunt at the age of 2.5 years. In both A and B, pressure measurements are shown within parentheses. RA = right atrium; LA = left atrium; RV = right ventricle; LV = left ventricle; Asc Ao = ascending aorta; Des Ao = descending aorta; SVC = superior vena cava; IVC = inferior vena cava; RPA = right pulmonary artery; LPA = left pulmonary artery. In A, RPA saturation was not obtained.

mL and an RV stroke volume of 35.4 mL, an LV output of 289 mL/kg/min and an RV CO of 349 mL/kg/min. The increased RV CO was secondary to a left-to-right shunt through the 4-mm ASD.

Figure 18 illustrates that selective delivery of oxygenated pulmonary venous blood to the proximal aorta occurs as a consequence of LV ejection. Conversely, mixed pulmonary and systemic venous blood is delivered to the distal aorta. This results in differential proximal and distal aortic saturations.

DISCUSSION

The dynamics of systemic DO_2 in 2 complicated transitional circulations can be mathematically modeled. In the circulation depicted by model 1, the RV delivers all pulmonary blood flow in addition to all (k = 0) or a fraction (k = 0.75) of the systemic CO whereas the LV delivers none (k = 0) or a substantial portion (k = 0.75) of the systemic CO. In the circulation depicted by model 2, the RV delivers none (Q_P/Q_S = 0.6) or a portion (Q_P/Q_S > 0.6) of the IVC blood to the pulmonary bed in addition to all (k = 0) or a fraction (k = 0.75) of the systemic CO whereas the LV delivers none (k = 0) or a substantial portion (k = 0.75) of the systemic CO. k is a conglomerate variable that depends on the size of intraatrial communication, the mitral valve, the aortic valve, and LV compliance. It provides an assessment of the proportion of the system CO provided by the LV and as such is useful to assessing progress toward a 2-ventricle circulation.

The use of 300 mL/kg/min as the combined biventricular output in model 1 is supported by in vivo data.[9] In utero, the RV alone generates an output of approximately 330 mL/kg/min compared with the LV output of 170 mL/kg/min. In normal neonates at birth, the RV and the LV each eject an output of approximately 350 mL/kg/min.[11] In the case presented herein, the combined CO after modified stage I was 409 mL/kg/min. As experience with the staged 2-ventricle repair accumulates, we

will be able to better define the expected range of outputs for each stage.

The BDG shunt is typically performed at 3 to 6 months of age. Previous analysis of the BDG circulation assumed a systemic, single ventricle output of 200 mL/kg/min based on the clinical observations of other investigators.[6] For our analysis, we chose a combined biventricular output of 300 mL/kg/min consistent with the anticipated increased capacity of the enlarging LV to contribute to total CO at this stage. In the case presented, CO was 392 and 257 mL/kg/min on 2 different occasions, which is close to our assumed value.

This investigation was designed to determine whether indices derived from oxygen saturation measurements would be useful in optimizing DO_2 and systemic venous oxygen saturation. Clearly, the RV/LV stroke volume ratio and the proportion of pulmonary venous return delivered to the LV affect DO_2. As we have demonstrated, isolated measurements of Sao_2 and Svo_2 alone do not accurately reflect DO_2 or Q_P/Q_S because the relationships between these variables are not linear, which is consistent with a previous model.[6] These relationships are further altered by variations in the proportion of systemic CO supplied by the LV. To the contrary, the relationship between DO_2 and the oxygen excess factor $Sao_2/(Sao_2 - Svo_2)$ is linear irrespective of the proportion of the systemic CO supplied by the LV. The slope does not depend on CO or $Spvo_2$. Thus, DO_2 will increase in a predictable, linear manner as $Sao_2/(Sao_2 - Svo_2)$ increases. Because $Sao_2/(Sao_2 - Svo_2)$ can be easily measured in the clinical setting, it can be used to direct therapy to improve DO_2, the variable that is arguably the most physiologically relevant, but is not measurable in a routine clinical setting. It is important to point out that the slope increases as CVO_2 increases. Thus, as CVO_2 increases, a given value of DO_2 will be represented by a lower value of $Sao_2/(Sao_2 - Svo_2)$. From a clinical perspective, as CVO_2 increases, each incremental increase in $Sao_2/(Sao_2 - Svo_2)$ will effectuate a smaller improvement in DO_2.

There are limitations to our model. Measurement of true Svo_2 in patients with complex cardiac lesions is problematic because there is no true mixed venous sample site. Weighted averages of SVC and IVC saturations are theoretically possible but accurate sampling of IVC is unreliable to streaming of blood with different saturations. Typically, $S_{SVC}O_2$ has been used as surrogate for Svo_2 in neonates, infants, and small children. We did not include the concept of useable oxygen in our model as has been done by others. This concept is based on the fact that the oxygen carried by Hb with a saturation at or below a defined threshold such as 30% is unusable by mitochondria and should therefore not be included in calculations of DO_2.[7]

As the future step, our mathematical models need to be critically evaluated by applying accumulating patient data. This will include quantification of differential aorta saturation based on k. This will allow us to evaluate the validity of our model as well as to develop optimal clinical management strategies in this unique population, thereby hopefully improving patient survival.

DISCLOSURES

Name: Koichi Yuki, MD.
Contribution: This author helped design the study, conduct the research, analyze the data, and prepare the manuscript.
Name: Sitaram Emani, MD.
Contribution: This author helped prepare the manuscript.
Name: James A. DiNardo, MD.
Contribution: This author helped design the study, analyze the data, and prepare the manuscript.
This manuscript was handled by: Peter J. Davis, MD.

REFERENCES

1. Emani SM, Bacha EA, McElhinney DB, Marx GR, Tworetzky W, Pigula FA, del Nido PJ. Primary left ventricular rehabilitation is effective in maintaining two-ventricle physiology in the borderline left heart. J Thorac Cardiovasc Surg 2009;138:1276–82
2. Brown SC, Boshoff D, Eyskens B, Gewillig M. Hybrid approach as bridge to biventricular repair in a neonate with critical aortic stenosis and borderline left ventricle. Eur J Cardiothorac Surg 2009;35:1080–2
3. Tchervenkov CI, Tahta SA, Jutras LC, Beland MJ. Biventricular repair in neonates with hypoplastic left heart complex. Ann Thorac Surg 1998;66:1350–7
4. Tworetzky W, del Nido PJ, Powell AJ, Marshall AC, Lock JE, Geva T. Usefulness of magnetic resonance imaging of left ventricular endocardial fibroelastosis in infants after fetal intervention for aortic valve stenosis. Am J Cardiol 2005;96:1568–70
5. Grosse-Wortmann L, Yun TJ, Al-Radi O, Kim S, Nii M, Lee KJ, Redington A, Yoo SJ, van Arsdell G. Borderline hypoplasia of the left ventricle in neonates: insights for decision-making from functional assessment with magnetic resonance imaging. J Thorac Cardiovasc Surg 2008;136:1429–36
6. Barnea O, Santamore WP, Rossi A, Salloum E, Chien S, Austin EH. Estimation of oxygen delivery in newborns with a univentricular circulation. Circulation 1998;98:1407–13
7. Francis DP, Willson K, Thorne SA, Davies LC, Coats AJ. Oxygenation in patients with a functionally univentricular circulation and complete mixing of blood: are saturation and flow interchangeable? Circulation 1999;100:2198–203
8. Photiadis J, Sinzobahamvya N, Fink C, Schneider M, Schindler E, Brecher AM, Urban AE, Asfour B. Optimal pulmonary to systemic blood flow ratio for best hemodynamic status and outcome early after Norwood operation. Eur J Cardiothorac Surg 2006;29:551–6
9. Li J, Zhang G, McCrindle BW, Holtby H, Humpl T, Cai S, Caldarone CA, Redington AN, Van Arsdell GS. Profiles of hemodynamics and oxygen transport derived by using continuous measured oxygen consumption after the Norwood procedure. J Thorac Cardiovasc Surg 2007;133:441–8
10. Salim MA, Case CL, Sade RM, Watson DC, Alpert BS, DiSessa TG. Pulmonary/systemic flow ratio in children after cavopulmonary anastomosis. J Am Coll Cardiol 1995;25:735–8
11. Kiserud T. Physiology of the fetal circulation. Semin Fetal Neonatal Med 2005;10:493–503