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 (Qp)/systemic blood flow (Qs) range necessary to optimize systemic oxygen delivery (DO2) 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 Qp/Qs at which systemic DO2 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 DO2 in both models. Using a computer and an Excel spreadsheet, we used the equations to examine the relationships between DO2 and arterial oxygen saturation (SaO2), venous oxygen saturation (SvO2), SaO2 – SvO2, Qp/Qs, and the oxygen excess factor SaO2/(SaO2 – SvO2).

RESULTS: In both circulations, SaO2 or SvO2 alone does not accurately predict DO2 or Qp/Qs. The relationships between these variables are further altered by the degree of systemic cardiac output supplied by the left ventricle. To the contrary, DO2 demonstrates the linear relationship with the oxygen excess factor SaO2/(SaO2 – SvO2) irrespective of the degree of systemic cardiac output supplied by the left ventricle.

CONCLUSIONS: Commonly obtained clinical values such as SaO2 and SvO2 alone are not accurate assessments of DO2 or Qp/Qs. Therefore, these cannot be used in isolation to guide perioperative therapy. (Anesth Analg 2012;115:618–26)
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 (Qp)/systemic blood flow (QS) range necessary to optimize systemic oxygen delivery (DO2) and systemic venous oxygen saturation (SvO2) in single ventricle physiology. 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 DO2 in these transitional circulations. In addition, we sought to determine whether indices derived from oxygen saturation measurements would be clinically useful in optimizing systemic DO2.

**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, we derived equations (DO2) as follows:

Arterial oxygen content (CaO2)(mL O2/dL)

\[ CaO2 = 1.38 \cdot \text{Hb} \cdot \text{SaO2} \]  

Accordingly, pulmonary arterial oxygen content (CpA\text{O}_2) = 1.38 \cdot \text{Hb} \cdot \text{pulmonary arterial oxygen saturation}, left ventricular oxygen content (C_L\text{O}_2) = 1.38 \cdot \text{Hb} \cdot \text{left ventricular oxygen saturation}, and right ventricular oxygen content (C_{RV}\text{O}_2) = 1.38 \cdot \text{Hb} \cdot \text{right ventricular oxygen saturation}.

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

\[ \text{SVO}_2 = \text{whole body oxygen consumption (CVO}_2) \]  

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

\[ \text{CaO}_2 \cdot \text{QS} - \text{CVO}_2 = \text{CVO}_2 \cdot \text{QS} \]  

Similarly,

\[ \text{C}_{PA}\text{O}_2 \cdot \text{Q}_p + \text{SVO}_2 = \text{C}_{PA}\text{O}_2 \cdot \text{Q}_p \]  

The combined output of the ventricular system is described as:
From Figure 1:

\[ CO = Q_p + Q_s \]  

\[ \text{C}_{LV}O_2 = \text{C}_{RV}O_2 \]
\[ \text{C}_{RV}O_2 = \text{C}_{PA}O_2 \]

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

\[ \text{DO}_2 = Q_s \cdot \text{CaO}_2 = (kQ_s \cdot \text{C}_{LV}O_2) + (1 - k) Q_s \cdot \text{C}_{RV}O_2 \]  

Equation (7) can be converted to:

\[ \text{DO}_2 = Q_s \cdot \text{CaO}_2 = kQ_s \cdot \text{C}_{PV}O_2 + (1 - k) Q_s \cdot \text{C}_{PA}O_2 \]  

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

\[ \text{DO}_2 = Q_s \cdot \text{CaO}_2 = [1/(1 + Q_p/Q_s)] \cdot \text{CO} \cdot \text{C}_{PV}O_2 \]
\[ - [(1 - k) \cdot \text{CVO}_{2}/(Q_p/Q_s)] \]  

At \( k = 1 \), LV provides all \( Q_s \). When \( Q_p/Q_s = 1 \), Equation (9) describes \( \text{DO}_2 \) in a normal 2-ventricle circulation:

\[ \text{DO}_2 = Q_s \cdot \text{CaO}_2 = Q_s \cdot \text{C}_{PV}O_2 \]

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

\[ \text{RV/LV stroke volume ratio} = [Q_p + (1 - k) Q_s]/kQ_s \]
\[ = (1/k) \cdot Q_p/Q_s + (1 - k)/k \]  

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,\textsuperscript{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:

\[
CVO_2 = p \cdot CVO_2 + (1 - p) \cdot CVO_2 \tag{1a}
\]

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

\[
CaO_2 \cdot Q_{SVC} - p \cdot CVO_2 = C_{SVC}O_2 \cdot Q_{SVC} \tag{2a}
\]

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

\[
CaO_2 \cdot Q_{IVC} - (1 - p) \cdot CVO_2 = C_{IVC}O_2 \cdot Q_{IVC} \tag{3a}
\]

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

\[
CO = Q_{SVC} + Q_{IVC} + Q_{shunt} \tag{4a}
\]

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

\[
Q_p = Q_{SVC} + Q_{shunt} \tag{5a}
\]

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

\[
Q_s = Q_{SVC} + Q_{IVC} \tag{6a}
\]

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

\[
Q_{SVC} = p \cdot Q_s \tag{7a}
\]

\[
Q_{IVC} = (1 - p) \cdot Q_s \tag{8a}
\]

From Figure 2:

\[
Q_{shunt} = Q_{IVC} + (Q_r - kQ_3) - (1 - k)Q_s \tag{9a}
\]

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:

\[
[(1 - k)Q_s]/[Q_{IVC} + (Q_r - kQ_3)] \tag{10a}
\]

From Equation (6a) is derived:

\[
DO_2 = CaO_2 \cdot Q_s = CaO_2 \cdot (Q_{SVC} + Q_{IVC}) \tag{11a}
\]

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):

\[
CaO_2 \cdot Q_s = C_{PV}O_2 \cdot kQ_3 + [CaO_2 \cdot (1 - p)Q_s - (1 - p)CVO_2 + C_{PV}O_2 \cdot (Q_r - kQ_3)] \tag{12a}
\]

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

\[
CaO_2 \cdot Q_s = C_{PV}O_2 \cdot kQ_3 + [CaO_2 \cdot (1 - p)Q_s - (1 - p)CVO_2 + C_{PV}O_2 \cdot (Q_r - kQ_3)] \tag{13a}
\]

Equation (13a) can be simplified to:

\[
CaO_2 = C_{PV}O_2 - (1 - k)(1 - p) \cdot CVO_2/(Q_r - kpQ_3) \tag{14a}
\]

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

\[
DO_2 = C_{PV}O_2 - (1 - p)(1 - k) \cdot [1/(Q_r/Q_3) - kp)] \cdot CVO_2 \tag{15a}
\]

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:\textsuperscript{9}

\[
DO_2 = C_{PV}O_2 - [(Q_r/Q_3) \cdot (1 - p) \cdot CVO_2] \tag{16a}
\]

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

\[
RV/LV stroke volume ratio = (Q_{SVC} + (Q_r - kQ_3))/kQ_3 \tag{17a}
\]

Combining Equations (15) and (16a) yields:

\[
RV/LV stroke volume ratio = (1 - p - k)/k \tag{18a}
\]

Using a computer and an Excel spreadsheet, we used these equations to examine the relation between \(DO_2\) and \(Sa_o_2, Svo_2, Sao_2, Swo_2, Q_r/Q_s,\) and the oxygen excess factor \(Sa_o_2/(Sa_o_2 - Svo_2)\) for models 1 and 2. Physiologically relevant solutions to the equations for both models exist only when \(Q_r \geq kQ_3\) or \(Q_r/Q_3 \approx k\). 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.\textsuperscript{9} 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\textsuperscript{6} and with values measured in patients at our own and other institutions.\textsuperscript{7} In model 2, \(p = 0.6\) was chosen, consistent with the value previously reported in children with a superior cavopulmonary anastomosis.\textsuperscript{10}

**RESULTS**

**Model 1**

Figure 3 demonstrates the relationship of \(DO_2\) with \(Q_r/Q_3\) at a fixed biventricular output of 300 mL/kg/min. The \(Q_r/Q_3\) of maximal \(DO_2\) at \(k = 0\) is 0.64, which is compatible with the previous modeling.\textsuperscript{6} Maximum \(DO_2\) of \(k = 0.25\) and \(k = 0.5\) are at \(Q_r/Q_3\) of 0.51 and 0.5, respectively. As \(Q_r/Q_3\) increases, \(DO_2\) of \(k = 0.25, 0.5\) and 0.75 become
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 SvO2, which may be a better indicator of tissue oxygenation than maximum DO2, occurs at a Qp/Qs of 1 when k = 0 (Fig. 5). Maximum SvO2 at k = 0.25 and 0.5 is at Qp/Qs of 0.87 and 0.71, respectively. The use of absolute SvO2 as a surrogate assessment of Qp/Qs is limited at lower values of k because equal values of SvO2 exist at both high and low Qp/Qs as Qp/Qs varies above and below unity. For lower values of k, peak SvO2 does not occur at peak DO2 (Fig. 6). At lower values of k, peak SvO2 is achieved at a higher Qp/Qs than that necessary to maximize DO2. However, maximum DO2 and SvO2 at k = 0.75 are at Qp/Qs of k (= 0.75). As k increases toward 1, the Qp/Qs necessary to maximize both SvO2 and DO2 converge toward k. Use of absolute SvO2 as a surrogate assessment of DO2 is limited at lower values of k because equal values of SvO2 exist at both high and low DO2.

The Qp/Qs necessary to bring SaO2 to a plateau value decreases as k increases (Fig. 7). Once this plateau is reached, neither changes in SaO2 nor the absolute value of SaO2 provides an accurate assessment of Qp/Qs for any value of k. For k = 0, it will be the case at Qp/Qs ≥1.5. At lower values of k, comparable values of SaO2 exist at both low and high states of DO2 (Fig. 8). For any k, once a maximum value of DO2 is achieved, clinically imperceptible increases in SaO2 are associated with precipitous decreases in DO2. A nonlinear relationship exists between DO2 and SaO2 = SvO2 (Fig. 9). As Qp/Qs increases from values slightly above 1, DO2 decreases as SaO2 = SvO2 increases. DO2 peaks at a value of Qp/Qs just below 1 and for k = 0 and 0.25, DO2 rapidly decreases as SaO2 = SvO2 continues to decrease.

---

**Figure 3.** Systemic oxygen delivery (DO2) versus Qp/Qs.

**Figure 4.** Right ventricle (RV) volume/left ventricle (LV) volume ratio versus Qp/Qs.

**Figure 5.** Systemic venous oxygen saturation (SvO2) versus Qp/Qs.

**Figure 6.** Systemic venous oxygen saturation (SvO2) versus systemic oxygen delivery (DO2).

**Figure 7.** Systemic arterial oxygen saturation (SaO2) versus Qp/Qs.
SaO2/(SaO2 - SvO2) has been defined as the oxygen excess factor reflective of the ratio of oxygen delivery to oxygen consumption. The relationship between SaO2/(SaO2 - SvO2) and DO2 is uniquely linear. Its slope is constant for all values of k as is illustrated in Figure 10. Because DO2 = CVO2 - [SaO2/(SaO2 - SvO2)], only changes in CVO2 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 SaO2/(SaO2 - SvO2) may not be clinically useful, changes in this value can be used to assess the adequacy of interventions designed to improve DO2.

**Model 2**

From Equations (5a) and (7a), Qp/Qs = [p + (Qshunt/Qs)], therefore Qp/Qs = p. For any value of k, DO2 is maximal when Qp/Qs = p (= 0.6) (Fig. 11). As Qp/Qs 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 DO2. This is readily apparent in Figure 13 where SvO2 is seen to decrease as Qp/Qs increases, DO2 decreases, and the SaO2 - SvO2 difference widens for a fixed CVO2. Because upper and lower body oxygen consumption are coupled to SVC and IVC flow, respectively, SvO2 = S SVC O2 = S IVC O2.

SaO2 plateaus at a Qp/Qs at or slightly more than 1 (Fig. 14). As a result, neither changes in SaO2 nor the absolute value of SaO2 provides an accurate assessment of Qp/Qs. By the time SaO2 has reached a plateau, DO2 has begun to decrease precipitously (Fig. 15). Again, neither changes in SaO2 nor the absolute value of SaO2 provides an accurate assessment of DO2 for any value of k. Although not linear,
the relationships between \( \text{SaO}_2 - \text{SvO}_2 \) and \( \text{DO}_2 \) at various \( k \) are comparable (Fig. 16). As \( \text{SaO}_2 - \text{SvO}_2 \) decreases, \( \text{DO}_2 \) increases.

As is true for model 1, the relationship between \( \text{SaO}_2/(\text{SaO}_2 - \text{SvO}_2) \) and \( \text{DO}_2 \) 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 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 stroke 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 \( \mu \)g/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 13. Superior (or inferior) vena cava oxygen saturation (\( \text{SvO}_2 \)) versus \( \text{Qp/Qs} \). In this model, \( \text{SvO}_2 = \text{S}_{\text{SvC}}\text{O}_2 = \text{S}_{\text{SvC}}\text{O}_2 \).

Figure 14. Systemic arterial oxygen saturation (\( \text{SaO}_2 \)) versus \( \text{Qp/Qs} \).

Figure 15. Systemic arterial oxygen saturation (\( \text{SaO}_2 \)) versus systemic oxygen delivery (\( \text{DO}_2 \)).

Figure 16. Systemic oxygen delivery (\( \text{DO}_2 \)) versus \( \text{SaO}_2 - \text{SvO}_2 \). In the figure, \( \text{SvO}_2 = \text{S}_{\text{SvC}}\text{O}_2 = \text{S}_{\text{SvC}}\text{O}_2 \).

Figure 17. Systemic oxygen delivery (\( \text{DO}_2 \)) versus excess oxygen factor \( \text{SaO}_2/(\text{SaO}_2 - \text{SvO}_2) \). In the figure, \( \text{SvO}_2 = \text{S}_{\text{SvC}}\text{O}_2 = \text{S}_{\text{SvC}}\text{O}_2 \).
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 DO2 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. 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

![Diagram](image-url)
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. 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 DO2 and systemic venous oxygen saturation. Clearly, the RV/LV stroke volume ratio and the proportion of pulmonary venous return delivered to the LV affect DO2. As we have demonstrated, isolated measurements of SaO2 and SvO2 alone do not accurately reflect DO2 or Qp/Qs because the relationships between these variables are not linear, which is consistent with a previous model. These relationships are further altered by variations in the proportion of systemic CO supplied by the LV. To the contrary, the relationship between DO2 and the oxygen excess factor SaO2/(SaO2 – SvO2) is linear irrespective of the proportion of the systemic CO supplied by the LV. The slope does not depend on CO or SpvO2. Thus, DO2 will increase in a predictable, linear manner as SaO2/(SaO2 – SvO2) increases. Because SaO2/(SaO2 – SvO2) can be easily measured in the clinical setting, it can be used to direct therapy to improve DO2, 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 CVO2 increases. Thus, as CVO2 increases, a given value of DO2 will be represented by a lower value of SaO2/(SaO2 – SvO2). From a clinical perspective, as CVO2 increases, each incremental increase in SaO2/(SaO2 – SvO2) will effectuate a smaller improvement in DO2.

There are limitations to our model. Measurement of true SvO2 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, SvO2 has been used as surrogate for SvO2 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 DO2. 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**


