Inclusion of oxygen consumption improves the accuracy of arterial and venous oxygen saturation interpretation after the Norwood procedure

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Objective: Management strategy for the postoperative Norwood neonate has been formulated from models that have estimated oxygen consumption ($\dot{V}O_2$). Superior vena caval oxygen saturation (SvO_2), systemic arterial and superior vena caval oxygen saturation difference ($Sa-vO_2$), and oxygen excess factor (Ω = arterial oxygen saturation/ $Sa-vO_2$) have been used as indirect indicators to estimate systemic blood flow (Q_s) and oxygen delivery (DO_2). We sought to examine the correlation of the indirect indicators to $\dot{V}O_2$ -derived measures of oxygen transport.

Methods: Respiratory mass spectrometry was used to continuously measure $\dot{V}O_2$ after the Norwood procedure ($n = 13$). Measured saturations and the direct Fick equation were used to obtain pulmonary blood flow, Q_s , DO_2 , and oxygen extraction ratio (ERO_2) values. Correlations to SvO_2 , $Sa-vO_2$, and Ω were sought.

Results: There was a close correlation of SvO_2 , $Sa-vO_2$, and Ω to ERO_2 ($r = 0.92$, 0.96 , and 0.97 , respectively; $P < .0001$). Correlation to Q_s and DO_2 was variable ($r = 0.39$ to 0.78 , respectively; $P < .0001$). Correlation to $\dot{V}O_2$ was poor but significant ($r = 0.24$ to 0.40 , $P < .0001$). Inclusion of $\dot{V}O_2$ improved the correlation to Q_s and DO_2 ($r = 0.66$ to 0.97 , $P < .0001$).

Conclusions: The close correlation of SvO_2 , $Sa-vO_2$, and Ω to ERO_2 indicates that each is a measure of the balance of DO_2 and extraction. The significant but less reliable correlation to DO_2 and $\dot{V}O_2$ indicates the values for SvO_2 , $Sa-vO_2$, and Ω do not discriminate between the contribution of DO_2 and $\dot{V}O_2$. Measured $\dot{V}O_2$ and hemodynamics may improve the optimization of postoperative management strategy in the individual neonate.

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Care of the postoperative Norwood patient continues to be challenging.¹⁻⁶ Performance requirements for the single ventricle with a parallel circulation are substantial and are made more physiologically stressful by the recent insult of cardiopulmonary bypass (CPB) and myocardial ischemia. Postoperative management strategies are predicated on balancing pulmonary (Q_p) and systemic (Q_s) blood flow⁶⁻⁸ and optimizing systemic oxygen delivery (DO_2).⁹⁻¹² These strategies have been designed on the basis of experimental models,^{13,14} theoretic models,¹⁵⁻¹⁷ and human studies^{3,5,11,18} that have intrinsic limitations. Experimental

Abbreviations and Acronyms

Do ₂	= oxygen delivery
ERo ₂	= oxygen extraction ratio
Ω	= oxygen excess factor
Qp	= pulmonary blood flow
Qs	= systemic blood flow
SaO ₂	= arterial oxygen saturation
Sa-vo ₂	= systemic arterial and venous oxygen saturation difference
Svo ₂	= systemic venous oxygen saturation
vo ₂	= oxygen consumption

animal models might not fully reflect human physiology. Mathematic models require assumptions that might differ from those seen clinically. To date, human models have used estimations of, rather than directly measured, oxygen consumption (vo₂) and pulmonary venous saturations.^{3,5,11,18}

Because of the difficulties in obtaining measured Qs, Do₂, and Qp values, decision making for postoperative management is based on reflectors of Do₂ and Qs, as well as an estimated pulmonary venous oxygen saturation. The reflectors of Do₂ and Qs are superior vena caval oxygen saturation (Svo₂),^{5,8,19} the difference between arterial and venous oxygen saturations (Sa-vo₂) and oxygen excess factor (Ω = arterial oxygen saturation [Sao₂]/Sa-vo₂).^{3-7,11,12,18}

Qp is generally accounted for by making an estimation that pulmonary venous saturation is greater than 95%.^{3,5,11,18,19} This estimation is not always correct.⁸

The above-outlined parameters can be obtained with minimal difficulty in clinical practice but have the limitation of not accounting for interindividual and intraindividual variability of vo₂.²⁰⁻²⁴ It has been increasingly realized that changes in vo₂ might have an important effect on hemodynamics and oxygen transport.²⁰⁻²⁴ Changes in vo₂ might not be fully reflected or understood for the commonly measured values Svo₂, Sa-vo₂, and Ω. We sought to examine the correlation of Svo₂, Sa-vo₂, and Ω to hemodynamics and oxygen transport parameters obtained by using vo₂ and the direct Fick equation.

Materials and Methods**Patients**

This study was approved by the Research Ethics Board at the Hospital for Sick Children, Toronto, Canada. Written informed consent was obtained from the parents of 13 of the 16 infants (12 boys; age range, 4-92 days; median, 7 days) undergoing a Norwood procedure between April and October 2004. The patient demographics are shown in Table 1. Three patients were not recruited for the study because of nonclinical issues.

Intraoperative Procedures

All patients were intubated with cuffed endotracheal tubes (Mallinckrodt Medical, Northampton, United Kingdom). General anesthesia was maintained with inhaled isoflurane, intravenous fentanyl, and pancuronium bromide. Low-flow CPB and selective cerebral perfusion were used in 12 of 13 patients. A standard Norwood procedure was used.²⁵ The aortic arch was reconstructed with a homograft patch. The 3.5-mm right modified Blalock-Taussig shunt was completed with anastomosis of the distal conduit to the central pulmonary artery. All patients received methylprednisolone (30 mg/kg) in the operating room at or before CPB. Phenoxybenzamine, 0.25 mg/kg, was administered

TABLE 1. Clinical data for the 13 patients

Patient	Age (d)	Weight (kg)	BSA (m ²)	CPB (min)	ACC (min)	Circulatory arrest (min)	Cerebral perfusion (min)	Diagnosis
1	55	3.8	0.24	69	38	6	30	DORV, AS, parachute MV
2	7	3.5	0.23	108	47	12	35	HLHS, AS, MS
3	4	3.7	0.25	151	100	35	53	HLHS, AS, MS
4	7	4	0.26	105	47	3	44	HLHS, AS, MS
5	16	3.5	0.24	133	39	34	0	HLHS, endocardial fibroelastosis of LV, AS, MS
6	7	4.2	0.27	122	62	3	60	HLHS, AS, MS
7	12	3.5	0.23	165	75	13	59	DILV, TGA
8	6	3.5	0.23	172	82	9	70	HLHS, AA, MA
9	92	4.1	0.26	105	58	30	17	DILV, TGA
10	16	3.9	0.25	170	60	1	60	HLHS, AS, MS
11	7	4	0.25	167	64	17	44	HLHS, AS, MS
12	6	2.9	0.2	142	62	1	62	HLHS, AS, MS
13	9	3.6	0.24	109	50	4	44	HLHS, AS, MS

BSA, Body surface area; CPB, cardiopulmonary bypass; ACC, aortic crossclamp; DORV, double-outlet right ventricle; AS, aortic stenosis; MV, mitral valve; HLHS, hypoplastic left heart syndrome; MS, mitral stenosis; LV, left ventricle; DILV, double-inlet left ventricle; TGA, transposition of the great arteries; AA, aortic atresia; MA, mitral atresia.

at initiation of CPB. A bolus of aprotinin, 50,000 KIU, was administered, followed by 100,000 KIU per 100 mL of prime. Our protocol was to administer milrinone ($100 \mu\text{g}/\text{kg}$) before termination of CPB and to initiate dopamine ($5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) for the immediate time around cessation of bypass. Dopamine was subsequently discontinued if the hemodynamics and ventricular function were satisfactory. Modified ultrafiltration was performed at the completion of CPB in all patients. A pulmonary venous line was inserted into the orifice of the right upper pulmonary vein. A direct oximetric catheter was inserted in the superior vena cava.

Postoperative Management

Our protocol for management is as follows. The central temperature (esophageal) is maintained between 36°C and 37°C . Postoperative monitoring includes heart rate, end-tidal carbon dioxide, and arterial, superior vena caval, and pulmonary venous pressures. Sedation consists of continuous intravenous infusion of morphine and intermittent injections of a muscle relaxant (pancuronium) and lorazepam. Infants are ventilated with volume control and pressure support. Ventilation volume and rate are adjusted to control PaCO_2 . Arterial oxygen saturation is maintained between 70% and 85%. Inotropic agents, vasoactive drugs (milrinone, dopamine, phenoxylbenzamine, and vasopressin), and volume infusions (5% albumin or blood) are administered according to our standard protocol.¹⁰ Hemoglobin is maintained between 14 and 16 mg/dL.

Methods of Measurements

Svo_2 , Sa-vo_2 and Ω . Blood samples were taken from arterial, superior vena caval, and pulmonary venous catheters for measurements of oxygen saturation. Arterial blood gas analysis and lactate measurements were obtained. Systemic-mixed venous saturation was taken as superior vena caval saturation. Sa-vo_2 was the difference between the arterial and superior vena caval oxygen saturations. Ω was calculated as $\text{Sao}_2/\text{Sa-vo}_2$.

vo_2 . vo_2 was measured continuously with an AMIS2000 mass spectrometer (Innovision A/S, Odense, Denmark). This is a sensitive and accurate method that allows simultaneous measurements of multiple gas fractions. The details are described elsewhere.²⁰

Hemodynamics and oxygen transport and arterial lactate. Qp and Qs were calculated by using the direct Fick method. DO_2 and the oxygen extraction ratio (ERO_2) were calculated by using standard equations (Table 2). All values were indexed to body surface area. Arterial lactate levels were measured.

Study Protocol

This study was performed during the first 72 hours after arrival in the intensive care unit. Values of hemodynamics, oxygen transport, and arterial, superior vena caval, and pulmonary venous saturation were collected at 2-hour intervals during the first 24 hours and at 4-hour intervals from hours 25 through 72. Sampling was avoided if a change in sedation, paralysis, ventilation, or hemodynamic management was made within 15 minutes.

TABLE 2. Equations using systemic oxygen consumption to calculate hemodynamics and oxygen transport parameters

Parameters	Equations
Qp ($\text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$)	$\text{vo}_2/(\text{Cpvo}_2 - \text{CaO}_2)$
Qs ($\text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$)	$\text{vo}_2/(\text{CaO}_2 - \text{CvO}_2)$
DO_2 ($\text{mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$)	$\text{Qs} \times \text{CaO}_2$
ERO_2	vo_2/DO_2

Qp , pulmonary blood flow; vo_2 , systemic oxygen consumption; Cpvo_2 , pulmonary venous oxygen content; CaO_2 , arterial (equals to pulmonary arterial) oxygen content; Qs , systemic blood flow; CvO_2 , superior vena caval oxygen content; DO_2 , systemic oxygen delivery; ERO_2 , oxygen extraction ratio.

Data Analysis

Data are expressed as means $\pm$ standard deviation. The generalized linear model for repeated measures was used to determine the nature of any time trend of the measures over the 72-hour study period. Where appropriate for given measures, logarithmic and polynomial transformations were tested for the best fit over time. Correlations between the indirect indicators Svo_2 , Sa-vo_2 , and Ω and the direct measures of hemodynamics and oxygen transport were sought by using the generalized linear model for repeated measures without regard to time. Logarithmic transformations of both variables being compared was used when necessary to model nonlinear relationships. All data analysis was performed with SAS statistical software version 8 (SAS Institute, Inc, Cary, NC).

Results

Patients

During the study period, 16 patients underwent the Norwood procedure. There was no incidence of circulatory collapse or death during the study period. All patients survived to hospital discharge. Extubation occurred between 2 and 16 days (median, 7 days) after the procedure, except in one child who had vocal cord complications. Extubation for that infant occurred at 90 days and after the stage 2 procedure. The neonate extubated on day 2 had the study terminated at that time. One child had sudden hemodynamic collapse subsequent to the study and required resuscitation with extracorporeal membrane oxygenation. That child survived and was discharged home after the stage 2 procedure.

Changes of Svo_2 , Sa-vo_2 , and Ω Over Time

Figure 1 shows the profiles of Svo_2 , Sa-vo_2 , Ω , hemodynamics, and oxygen transport in 13 patients during the first 72 hours after arrival in the intensive care unit after the Norwood procedure. All measures showed broad interindividual variations.

Analogous trends over time, although in different directions, were seen with Svo_2 , Sa-vo_2 , and Ω . There were wide fluctuations within individuals. Svo_2 and Ω showed an initial rapid increase in the first 12 hours, a subsequent slow increase peaking around 28 to 32 hours, and thereafter a slow decrease in a complex polynomial function ($P <$

Figure 1. Mean $\pm$ standard deviation values of superior vena caval oxygen saturation (SvO_2), the difference between arterial and superior vena caval oxygen saturations ($Sa-vO_2$), oxygen excess factor ($\Omega = SaO_2/Sa-vO_2$), and the direct measures of hemodynamics and oxygen transport, including pulmonary (Q_p) and systemic (Q_s) blood flows, systemic oxygen delivery (DO_2), systemic oxygen consumption (VO_2), oxygen extraction ratio (ERO_2), and arterial lactate level in 13 patients during the first 72 hours after arrival in the intensive care unit (ICU) after the Norwood procedure. The slope of change is highest for SvO_2 , $Sa-vO_2$, and Ω in the first 12 hours of recovery. The change is explained by changes in VO_2 during the same time frame. There are parallel or mirror-imaged changes with respect to ERO_2 . *Data were entered after polynomial transformation, with *time* indicating the early trend, and *time*² indicating the later trend. **After logarithmic transformation.

.0001). $Sa-vO_2$ showed the same trend but as a mirror image, with a rapid initial decrease in the first 12 hours and a slow decrease until 28 to 32 hours. Thereafter, there was a slow increase ($P < .0001$).

Changes of Direct Measures of Hemodynamics and Oxygen Transport

Changes of direct measures of hemodynamics and oxygen transport were highly variable, on an individual basis, as

Figure 2. The correlations between superior vena caval oxygen saturation (SvO_2), the difference between arterial and superior vena caval oxygen saturations ($Sa-vO_2$), and oxygen excess factor ($\Omega = SaO_2/SvO_2$) and oxygen extraction ratio (ERO_2), systemic blood flow (Q_s), oxygen delivery (DO_2), oxygen consumption (VO_2), pulmonary blood flow (Q_p), and Q_p/Q_s in 13 patients during the first 72 hours after arrival in the intensive care unit (ICU) after the Norwood procedure.

demonstrated by the broad standard deviations. Qp and Qs showed a small but significant linear increase over time ($P < .001$ for Qp, $P < .0001$ for Qs). Qs was significantly lower during the first 12 hours compared with the following 60 hours ($P < .001$). The same analysis for Qp was not significant ($P = .62$). Do₂ showed a significant change over time ($P < .0001$), with a slow increase peaking around 28 to 32 hours, followed by a slow decrease. Do₂ was significantly lower during the first 12 hours compared with the following 60 hours ($P < .001$). vo₂ was related to time after logarithmic transformation ($P < .0001$). There was a significant decrease in the first 12 hours, as there was with arterial lactate levels ($P < .0001$). ERo₂ was related to time after logarithmic transformation, with a rapid decrease in the first 12 hours ($P < .0001$). Central temperature was relatively stable ($36.6^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$), with a small linear increase over time ($P = .0002$).

Correlations Among Svo₂, Sa-vo₂, Ω and Direct Measures of Hemodynamics and Oxygen Transport

Figure 2 and Table 3 show the generalized linear model correlation among Svo₂, Sa-vo₂, and Ω and the direct measures of hemodynamics and oxygen transport. For significant correlations ($P < .05$), we have classified an r value of less than 0.30 to be a poor correlation, an r value of 0.31 to 0.70 to be a variable or moderate correlation, and an r value of greater than 0.70 to be a close correlation.

Over the entire study period, there was a close correlation of Svo₂, Sa-vo₂, and Ω with ERo₂ ($r = 0.92, 0.96$, and 0.97 , respectively; $P < .0001$ for all). Svo₂, Sa-vo₂, and Ω were variably correlated with Qs ($r = 0.39, -0.65$, and 0.66 , respectively; $P < .0001$ for all) and variably or closely correlated with Do₂ ($r = 0.57, -0.70$, and 0.78 , respectively; $P < .0001$ for all). Svo₂, Sa-vo₂, and Ω were significantly but poorly to moderately correlated with Qp/Qs ($r = 0.21, 0.34$, and 0.35 , respectively; $P < .0001$ for all). Inclusion of Qp and Qs as separate variables in the Qp/Qs correlation demonstrated no correlation ($P > .05$ for all). Svo₂, Sa-vo₂, and Ω were poorly and variably correlated with vo₂ ($r = 0.40, 0.24$, and 0.25 , respectively; $P < .0001$ for all). Inclusion of vo₂ to the Qs and Do₂ analysis significantly improved the correlations with Svo₂ (increased r from 0.39 to 0.66 for Qs and increased r from 0.57 to 0.84 for Do₂), Sa-vo₂ (increased r from -0.65 to -0.86 for Qs and from -0.70 to -0.88 for Do₂), and Ω (increased r from 0.66 to 0.87 for Qs and from 0.78 to 0.97 for Do₂). All P values for the inclusion of vo₂ were less than .0001. Svo₂ and Sa-vo₂ were poorly correlated with Qp ($r = 0.18, P = .03$ and $r = 0.08, P < .01$, respectively), and Ω showed no correlation with Qp ($r = 0.01, P = .36$).

Discussion

After the introduction of the Norwood procedure, the strategy for postoperative management was primarily directed at

TABLE 3. Statistical analysis results using the generalized linear model for repeated measures of the correlations between SvO₂, Sa-vo₂, and Ω and the direct measures of hemodynamics and oxygen transport in 13 patients during the 72 hours after the Norwood procedure

Independent variables	Dependent variable	Intercept	Coefficient	r	P value
ERo ₂	SvO ₂	78.1530	-84.0414	-0.92	<.0001
	Sa-vo ₂	2.2918	67.2630	0.96	<.0001
	Ω^*	-2.0088	-3.7520	-0.97	<.0001
Qs	SvO ₂ *	43.2140	13.9958	0.39	<.0001
	Sa-vo ₂ *	33.4813	-16.2394	-0.65	<.0001
	Ω	-0.1597	1.3541	0.66	<.0001
Do ₂	SvO ₂ *	-61.2285	19.9879	0.57	<.0001
	Sa-vo ₂ *	123.44	-17.6873	-0.70	<.0001
	Ω	-16.2926	3.3264	0.78	<.0001
vo ₂	SvO ₂	69.2978	-0.1949	-0.40	<.0001
	Sa-vo ₂	13.5039	0.1091	0.24	<.0001
	Ω^*	9.9743	-1.6618	-0.25	<.0001
Qp	SvO ₂	46.0825	3.0292	0.18	.03
	Sa-vo ₂	18.5011	2.2865	0.08	<.01
	Ω	2.7847	-0.1027	-0.01	.36
Qp/Qs	SvO ₂	60.2282	-7.3649	-0.21	<.0001
	Sa-vo ₂	8.8763	12.9871	0.34	<.0001
	Ω	4.6510	-1.8934	-0.35	<.0001

SvO₂, superior vena caval oxygen saturation; Sa-vo₂, difference between arterial and superior vena caval oxygen saturations; Ω , oxygen excess factor; ERo₂, oxygen extraction ratio; Qs, systemic blood flow; Do₂, systemic oxygen delivery; vo₂, systemic oxygen consumption; Qp, pulmonary blood flow. *Data were entered after logarithmic transformation.

balancing Qp/Qs through manipulation of pulmonary vascular resistance. More recent strategy has focused on the importance of Qs and systemic vascular resistance.⁹⁻¹² As such, measures thought to reflect systemic cardiac output have become increasingly used. Low SvO₂ has been shown to correlate with a base deficit.⁵ Sa-vo₂ reflects the adequacy of Do₂,^{4,11,12} and Ω is a ratio of available oxygen to extracted oxygen (Sao₂/Sa-vo₂). Each of these is thought to be a surrogate measure reflecting Do₂. Present management strategies have focused on maintaining physiologic conditions whereby these surrogate measures have appropriate values. By using respiratory mass spectrometry to measure vo₂, we now have the ability to directly calculate Do₂, Qp, and Qs using the Fick equation and to test the validity of the surrogate measures using correlations to the measured and calculated parameters.

Correlation of Surrogate Measures and ERo₂

There was a significant and close correlation of ERo₂ to SvO₂, Sa-vo₂, and Ω ($r = 0.92, 0.96$, and 0.97 , respectively). ERo₂ is an oxygen transport measure that provides a ratio that incorporates the 3 major components of oxygen transport: oxygen content, Do₂, and vo₂. This study demonstrates

Figure 3. An example of increasing superior vena caval oxygen saturation (SvO_2) in the presence of a decreasing systemic oxygen delivery (DO_2). In this patient the finding in the first 12 hours after arrival in the intensive care unit (ICU) can be explained by the disproportionate decrease in systemic oxygen consumption (VO_2). Because SvO_2 is a single measure of the balance of DO_2 and VO_2 , the source of a changing SvO_2 might be DO_2 , VO_2 , or both.

that each of the surrogate measures used is most accurately a reflector of ER_{O_2} . The very close reciprocal correlation curve seen with Ω ($SaO_2/Sa-vO_2$) is explained by the fact that it is intrinsically the ratio of DO_2 to VO_2 and thus the reciprocal of ER_{O_2} .

However, ER_{O_2} might not fully account for the adequacy of DO_2 because of the potential for changes induced by the phenomenon of DO_2 -dependent oxygen extraction. Paradoxically, in the presence of poor or worsening DO_2 , a disproportionate decrease in VO_2 might yield an adequate or improving SvO_2 (a close surrogate for ER_{O_2}), as shown in a specific example of a patient (Figure 3) who had a normalizing lactate level and normal base deficit despite a decreasing DO_2 .

Correlation of Surrogate Measures to Qs and DO_2

Correlation of SvO_2 , $Sa-vO_2$, and Ω to Qs was significant but variable. There was correlation to a moderate degree ($r = 0.39, 0.65$, and 0.66 , respectively). Correlation to DO_2 is moderate to close for the same 3 variables ($r = 0.57, 0.70$, and 0.78 , respectively). The variability and failure to achieve a uniformly close correlation can be explained by the fact that each of the surrogate measures is a single measure or ratio that is dependent on changes in oxygen content, DO_2 , and VO_2 (ie, all the components of oxygen transport). As seen in Figure 2, Qs and DO_2 are marginal in the first 24 hours and subsequently gradually increase, a profile that has been seen in other studies after CPB.^{21,26,27} The improvements in SvO_2 , $Sa-vO_2$, and Ω in the first 12 to

24 hours occurred during the period when Qs and DO_2 were most decreased. This finding is explained by the improvement in VO_2 , as discussed below. In previous analysis, based on an estimated and fixed VO_2 , the improvement was attributed to favorable changes in Qs and DO_2 .^{3,4,19}

Correlation of Surrogate Measures to VO_2

There was significant but moderate-to-poor correlation of VO_2 to SvO_2 , $Sa-vO_2$, and Ω ($r = 0.40, 0.24$, and 0.25 , respectively). The most rapid improvement in all the indirect indicators was seen in the first 12 hours after the Norwood procedure and can be explained by the slope of the decrease in VO_2 during the first 12 hours. The VO_2 profile is similar to previously reported findings for other cardiac procedures.²¹ The addition of VO_2 to the regression analysis increases the correlation of all 3 variables, SvO_2 , $Sa-vO_2$, and Ω , to r values of 0.66 to 0.92 , all of which are significant. Qs and DO_2 are contributors to the changes in SvO_2 , $Sa-vO_2$, and Ω , particularly over the later time frame, when there are less changes in VO_2 .

Present strategy to treat postoperative Norwood patients has been to compartmentalize Qp (a contributor to oxygen content) and Qs (the major contributor to DO_2). Because there have been little clinical data on VO_2 , manipulation of VO_2 has not gone beyond theoretic concerns. Major contributors to VO_2 are temperature,²⁰ inflammatory mediators,^{21,24} and inotropic agents.²⁸ The addition of VO_2 as a third compartment for a targeted treatment strategy, particularly in the first 12 hours, when there is a significant increase, remains to be explored both for the ability to manipulate VO_2 and for its effect on hemodynamic stability.

Correlation of Surrogate Measures and Qp

There was little correlation of Qp to SvO_2 and $Sa-vO_2$ ($r = 0.18$ and 0.08 , respectively) and no correlation to Ω ($r = 0.01$). These findings suggest that Qp estimates require standard measurement of Qp/Qs or Fick equation calculations. Surrogate measures of DO_2 might reflect the adequacy of oxygenation for the ranges of systemic arterial saturation seen in this study (55% to 86%).

Limitations

SvO_2 was used as an estimate of the mixed venous saturation for the calculations of Qs and DO_2 . This measure does not account for potential differences in the inferior vena caval saturation.^{29,30} Further investigations analyzing both superior and inferior vena caval oxygen saturation are warranted.

Conclusions

Clinical measures of adequate systemic DO_2 , SvO_2 , $Sa-vO_2$, and Ω do not completely reflect the changes in Qs and DO_2 because of the variability of VO_2 . SvO_2 , $Sa-vO_2$, and Ω are

measures of both Do_2 and vo_2 , as demonstrated by their close correlation to ERo_2 . Measured oxygen transport and hemodynamics might improve the optimization of a postoperative management strategy for individual patients.

References

- Ashburn DA, McCrindle BW, Tchervakov CI, Jacobs ML, Lofland GK, Bove EL, et al. Outcomes after the Norwood operation in neonates with critical aortic stenosis or aortic valve atresia. *J Thorac Cardiovasc Surg.* 2003;125:1070-82.
- Mahle WT, Spray TL, Wernovsky G, Gaynor JW, Clark BJ III. Survival after reconstructive surgery for hypoplastic left heart syndrome: a 15-year experience from a single institution. *Circulation.* 2000;102(suppl 3):III136-41.
- Charpie JR, Dekeon MK, Goldberg CS, Mosca RS, Bove EL, Kulik TJ. Postoperative hemodynamics after Norwood palliation for hypoplastic left heart syndrome. *Am J Cardiol.* 2001;87:198-202.
- Tweddell JS, Hoffman GM, Fedderly RT, Ghanayem NS, Kampine JM, Berger S, et al. Patients at risk for low systemic oxygen delivery after the Norwood procedure. *Ann Thorac Surg.* 2000;69:1893-9.
- Hoffman GM, Ghanayem NS, Kampine JM, Berger S, Mussatto KA, Litwin SB, et al. Venous saturation and the anaerobic threshold in neonates after the Norwood procedure for hypoplastic left heart syndrome. *Ann Thorac Surg.* 2000;70:1515-20.
- Bradley SM, Simsic JM, Atz AM. Hemodynamic effects of inspired carbon dioxide after the Norwood procedure. *Ann Thorac Surg.* 2001;72:2088-93.
- Bradley SM, Atz AM, Simsic JM. Redefining the impact of oxygen and hyperventilation after the Norwood procedure. *J Thorac Cardiovasc Surg.* 2004;127:473-80.
- Taeed R, Schwartz SM, Pearl JM, Raake JL, Beekman RH III, Manning PB, et al. Unrecognized pulmonary venous desaturation early after Norwood palliation confounds Gp:Gs assessment and compromises oxygen delivery. *Circulation.* 2001;103:2699-704.
- De Oliveira NC, Ashburn DA, Khalid F, Burkhart HM, Adatia IT, Holtby HM, et al. Prevention of early sudden circulatory collapse after the Norwood operation. *Circulation.* 2004;110(suppl 1):II133-8.
- De Oliveira NC, Van Arsdel GS. Practical use of alpha blockade strategy in the management of hypoplastic left heart syndrome following stage one palliation with a Blalock-Taussig shunt. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* 2004;7:11-5.
- Tweddell JS, Hoffman GM, Fedderly RT, Berger S, Thomas JP Jr, Ghanayem NS, et al. Phenoxybenzamine improves systemic oxygen delivery after the Norwood procedure. *Ann Thorac Surg.* 1999;67:161-7.
- Hoffman GM, Tweddell JS, Ghanayem NS, Mussatto KA, Stuth EA, Jaquis RD, et al. Alteration of the critical arteriovenous oxygen saturation relationship by sustained afterload reduction after the Norwood procedure. *J Thorac Cardiovasc Surg.* 2004;127:738-45.
- Kitaichi T, Chikugo F, Kawahito T, Hori T, Masuda Y, Kitagawa T. Suitable shunt size for regulation of pulmonary blood flow in a canine model of univentricular parallel circulations. *J Thorac Cardiovasc Surg.* 2003;125:71-8.
- Riordan CJ, Randsbeck F, Storey JH, Montgomery WD, Santamore WP, Austin EH III. Effects of oxygen, positive end-expiratory pressure, and carbon dioxide on oxygen delivery in an animal model of the univentricular heart. *J Thorac Cardiovasc Surg.* 1996;112:644-54.
- Barnea O, Austin EH, Richman B, Santamore WP. Balancing the circulation: theoretic optimization of pulmonary/systemic flow ratio in hypoplastic left heart syndrome. *J Am Coll Cardiol.* 1994;24:1376-81.
- Barnea O, Santamore WP, Rossi A, Salloum E, Chien S, Austin EH, et al. Estimation of oxygen delivery in newborns with a univentricular circulation. *Circulation.* 1998;98:1407-13.
- Migliavacca F, Pennati G, Dubini G, Fumero R, Pietrabissa R, Urcelay G, et al. Modeling of the Norwood circulation: effects of shunt size, vascular resistances, and heart rate. *Am J Physiol Heart Circ Physiol.* 2001;280:H2076-86.
- Maher KO, Pizarro C, Gidding SS, Januszewska K, Malec E, Norwood WI Jr, et al. Hemodynamic profile after the Norwood procedure with right ventricle to pulmonary artery conduit. *Circulation.* 2003;108:782-4.
- Rossi AF, Sommer RJ, Lotvin A, Gross RP, Steinberg LG, Kipel G, et al. Usefulness of intermittent monitoring of mixed venous oxygen saturation after stage I palliation for hypoplastic left heart syndrome. *Am J Cardiol.* 1994;73:1118-23.
- Li J, Schulze-Neick I, Lincoln C, Shore D, Scallan M, Bush A, et al. Oxygen consumption after cardiopulmonary bypass surgery in children: determinants and implications. *J Thorac Cardiovasc Surg.* 2000;119:525-33.
- Li J, Hoschtitzky A, Allen ML, Elliott MJ, Redington AN. Improved balance between oxygen consumption and oxygen delivery in eutermic infants after cardiopulmonary bypass with modified ultrafiltration. *Ann Thorac Surg.* 2004;78:1389-96.
- Li J, Hoskote A, Hickey C, VanArsdel G, Redington A, Adatia I. Hypercapnia improves systemic oxygenation and decreases oxygen consumption and blood lactate levels in children after bidirectional cavopulmonary shunt operation. *Crit Care Med.* 2005;33:984-9.
- Li J, Bush A, Schulze-Neick I, Penny DJ, Redington AN, Shekerdemian LS. Measured versus estimated oxygen consumption in ventilated patients with congenital heart disease: the validity of predictive equations. *Crit Care Med.* 2003;31:1235-40.
- Oudemans-van Straaten HM, Jansen PG, te VH, Beenackers IC, Stoutenbeek CP, van Deventer SJ, et al. Increased oxygen consumption after cardiac surgery is associated with the inflammatory response to endotoxemia. *Intensive Care Med.* 1996;22:294-300.
- Azake T, Merklinger SL, McCrindle BW, Van Arsdel GS, Lee KJ, Benson LN, et al. Evolving strategies and improving outcomes of the modified Norwood procedure: a 10-year single-institution experience. *Ann Thorac Surg.* 2001;72:1349-53.
- Wernovsky G, Wypij D, Jonas RA, Mayer JE Jr, Hanley FL, Hickey PR, et al. Postoperative course and hemodynamic profile after the arterial switch operation in neonates and infants. A comparison of low-flow cardiopulmonary bypass and circulatory arrest. *Circulation.* 1995;92:2226-35.
- Gessler P, Pfenninger J, Pfammatter JP, Carrel T, Baenziger O, Dahinden C. Plasma levels of interleukin-8 and expression of interleukin-8 receptors on circulating neutrophils and monocytes after cardiopulmonary bypass in children. *J Thorac Cardiovasc Surg.* 2003;126:718-25.
- Penny DJ, Sano T, Smolich JJ. Increased systemic oxygen consumption offsets improved oxygen delivery during dobutamine infusion in newborn lambs. *Intensive Care Med.* 2001;27:1518-25.
- Kety SS, Schmidt CF. The effects of altered arterial tensions of carbon dioxide and oxygen on cerebral blood flow and cerebral oxygen consumption of normal young man. *J Clin Invest.* 1948;27:484-92.
- Landow L, Phillips DA, Heard SO, Prevost D, Vandersalm TJ, Fink MP. Gastric tonometry and venous oximetry in cardiac surgery patients. *Crit Care Med.* 1991;19:1226-33.

Discussion

Dr Scott M. Bradley (Charleston, SC). This study is important because it is the first to measure vo_2 in postoperative Norwood patients. The findings confirm one of our management beliefs but challenge another.

One of our beliefs is that a mixed venous oxygen saturation that is higher and an arteriovenous oxygen saturation difference that is lower are desirable. This is because they correlate with higher Qs and Do_2 . Your study confirms this belief. Although some of the correlations were rated as moderate, the directly measured values of vo_2 actually improved the correlation. These findings therefore affirm postoperative management aimed at maximizing mixed venous oxygen saturation.

In contrast, this report challenges our understanding of the physiology of the first 48 hours. Immediately after surgical intervention, mixed venous saturation is low, and arteriovenous saturation difference is high. They then improve over the next 48 hours. As you noted, this has been observed in previous studies

and interpreted to indicate low systemic cardiac output. However, your study shows that low cardiac output plays only a minor role. The major reason that mixed venous saturation is low is that vo_2 is high immediately after surgical intervention and then decreases markedly over the next 48 hours. Like many interesting findings, this one is somewhat counterintuitive because this is exactly the time vo_2 might be expected to be low because many of the patients are sedated, paralyzed, and mechanically ventilated at this time.

The first question then is this: Why is vo_2 high early after surgical intervention? Is it a generalized inflammatory response to bypass, or is it due to the particular CPB technique used in these patients? Your article indicates that your patients underwent CPB with phenoxylbenzamine with low-flow rather than high-flow bypass, as recommended by Roger Mee. Does this create a whole-body oxygen debt in the operating room that must then be repaid in the intensive care unit? Could you give us your group's thoughts on the explanation for this very interesting finding.

Dr Li. Thank you for your comments. It is well documented that vo_2 increases after CPB. The increase in vo_2 has been attributed to several factors, including rewarming from hypothermic CPB, repayment of oxygen debt, and, most importantly, systemic inflammatory response. As shown in our previous study in a group of older children after complete repair of congenital heart disease, the initial postoperative vo_2 was also high, and similarly to our current study, it decreased significantly over the first 12 hours. The decrease in vo_2 coincided with the decrease in circulating cytokine levels.

Dr Bradley. Is there any relationship, for example, between the level of vo_2 coming out of the operating room and the length of CPB?

Dr Li. In this particular group of patients, the longer CPB time was associated with a higher vo_2 .

Dr Bradley. The second question is this: Can this phenomenon be avoided? Specifically, were anti-inflammatory strategies, such as modified ultrafiltration, preoperative steroids, or aprotinin, used in your patients? Alternatively, should we be keeping our patients deliberately cool for the first 48 hours after surgical intervention? That might be an unfair question to ask you.

Dr Li. I will try.

Dr Bradley. Do you know whether your patients had modified ultrafiltration?

Dr Li. Yes, they all had modified ultrafiltration. Modified ultrafiltration has been reported to filter out some cytokines. Again, in our previous study in the older group of children with the use of modified ultrafiltration, the postoperative cytokine levels were generally lower compared with data in the literature in children without the use of modified ultrafiltration. This might reduce the systemic inflammatory response, potentially resulting in a decrease in vo_2 .

All children received at least intraoperative steroids. Steroids have been reported to reduce the systemic inflammatory response and thus might reduce vo_2 . In fact, we are proposing a research project to investigate the effect of steroids on vo_2 in children during and after CPB. All children received aprotinin. The central body temperature was maintained at euthermia for the first 48

hours. In our previous studies we have demonstrated that the increase in vo_2 during the early post-CPB period is mainly attributed to the increase in central body temperature: for a 1°C increase in central body temperature, vo_2 increases by 11%, and simply maintaining body temperature at euthermia results in a continuous decrease in vo_2 .

Indeed, manipulating vo_2 is increasingly realized to be an important alternative component to optimize the balance of oxygen transport in children with limited reserve of cardiac function early after CPB.

Dr Bradley. Perioperative steroids or aprotinin use?

Dr Li. Yes, we all used steroids. I think it might contribute, too. It might indeed reduce vo_2 . In fact, we are thinking of proposing a study to compare—to investigate this effect on vo_2 .

Dr Bradley. Thank you. I think it is a very interesting and important study.

Dr Antonio Corno (Liverpool, United Kingdom). Surgeons are generally very simple-minded. Do you have a practical suggestion for the surgeon in the postoperative care of this patient? If we want to improve the oxygen saturation, that means the balance between Do_2 and vo_2 . What we can do as surgeons is to provide a higher total Qp. Should we modify our surgical technique to increase the total Qp knowing that this will cause an increase of the total vo_2 because of increased myocardial consumption? How can you maintain a positive balance to provide a better Do_2 ?

Dr Li. In this group of patients, we have also analyzed the relationships between pulmonary vascular resistance, systemic vascular resistance, and Do_2 . Our data showed that varying Qp had little contribution to systemic Do_2 , largely because of the mechanical limitation from the Blalock-Taussig shunt. The best way to improve systemic Do_2 is to maintain a relatively low and stable systemic vascular resistance and, additionally, to maintain a relatively high level of hemoglobin.

Dr Carl L. Backer (Chicago, Ill). Was there any difference in the management strategy as far as the ventilator that you use in the operating room compared with the one that you use in the intensive care unit?

One of the problems we have with our patients is that we have a completely different ventilator system in the operating room than we have in the intensive care unit. There is always a transition phase after transport, with hand ventilation to the intensive care unit ventilator, and I just wondered whether you thought that played any role in the vo_2 in the immediate time period when the patient arrives in the intensive care unit?

Dr Li. The ventilator systems are different in the operating room and intensive care unit, but our ventilation management protocols are the same for these patients in the 2 settings. Yes, there is a transition phase after transport, with hand ventilation to the intensive care unit ventilator, and certain adjustment of ventilation was often required to achieve adequate levels of arterial carbon dioxide and oxygen because they might have profound effects on both Do_2 and vo_2 . Yet we have found the hemodynamic variability to ventilation issues to be minimized by aggressive afterload reduction with phenoxylbenzamine.