Profiles of hemodynamics and oxygen transport derived by using continuous measured oxygen consumption after the Norwood procedure

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Supplemental material is available online.

Objectives: The lack of accurate measurement of hemodynamics and oxygen transport has limited our understanding of Norwood physiology and postoperative management. We used measured oxygen consumption to characterize hemodynamics and oxygen transport after the classic Norwood procedure.

Methods: Fourteen neonates had continuous respiratory mass spectrometry to measure oxygen consumption (VO_2). Arterial, superior vena caval, and pulmonary venous saturations were measured at 2- to 4-hour intervals for 72 hours postoperatively. Systemic (Q_s) and pulmonary (Q_p) blood flows, systemic vascular resistance (SVR) and pulmonary vascular resistance inclusive of the Blalock-Taussig shunt (BT-PVR), systemic oxygen delivery (DO_2), and the oxygen extraction ratio (ERO_2) were calculated.

Results: Q_s and DO_2 were low during the first 12 hours ($1.8 \pm 0.6 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ and $281 \pm 86 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ at the 12th hour, respectively) and increased over the study period ($P < .05$ for both). VO_2 decreased markedly during the first 24 hours (101 ± 26 to $86 \pm 16 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$, $P < .0001$). Consequently, ERO_2 decreased significantly over the study, most rapidly during the first 24 hours (0.44 ± 0.11 to 0.28 ± 0.09 , $P < .0001$). There was a close correlation of DO_2 to SVR and to Q_s ($P < .0001$ for both). There was no correlation of DO_2 to BT-PVR ($P = .14$) or to Q_p ($P = .67$). DO_2 was closely correlated with hemoglobin value ($P < .0001$), weakly correlated with Pao_2 ($P = .0002$), and not correlated with arterial oxygen saturation ($P = .32$).

Conclusions: There is wide variability of hemodynamics and oxygen transport after the Norwood procedure. The decrease in VO_2 during the first 24 hours is the main contributor to improving the balance of oxygen transport. DO_2 is most closely correlated to SVR and hemoglobin and weakly correlated to Pao_2 . It is not correlated to Q_p . Postoperative management strategies to decrease VO_2 and maintain a high hemoglobin level and a low SVR appear to be rational.

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The Norwood procedure for hypoplastic left heart syndrome and its similar anatomic variants continues to have significant morbidity and a mortality that ranges from 6% to 25%.^{1,2} Despite advances in surgical and postoperative management, these infants have little hemodynamic reserve. Instability after repair is inherent to the single ventricle supplying parallel pulmonary and systemic circulations and is compounded by the variable effects of cardiopulmonary bypass (CPB) and ischemia and reperfusion injury. As a result, the marginal systemic oxygen delivery (DO_2) is dependent on a balance between pulmonary blood flow (Q_p) and systemic blood flow (Q_s). A number of theoretic studies,^{3,4} clinical studies,⁵ and experimental models⁶ have been reported analyzing the effect of manipulation of Q_p or Q_s and its relationship to DO_2 . Previous human

Abbreviations and Acronyms

BT-PVR	= pulmonary vascular resistance inclusive of the Blalock-Taussig shunt
CO	= cardiac output
CPB	= cardiopulmonary bypass
DO ₂	= systemic oxygen delivery
ERO ₂	= oxygen extraction ratio
Hb	= hemoglobin
Qp	= pulmonary blood flow
Qs	= systemic blood flow
SVR	= systemic vascular resistance
VO ₂	= oxygen consumption

studies have used 2 key assumptions: constant pulmonary venous O₂ saturation and unchanged systemic oxygen consumption (VO₂).⁷⁻¹¹ There is little theoretic or clinical evidence for the validity of such assumptions, and therefore our understanding of postoperative hemodynamics in these patients is incomplete.

In human studies arterial and superior vena caval O₂ saturations and their derivations are most commonly used as surrogates of DO₂.^{5,7-11} In a study using measured VO₂ and pulmonary venous saturation, we reported that superior vena caval O₂ saturation, arteriovenous O₂ saturation difference, and Omega all very highly correlated with the oxygen extraction ratio (ERO₂) but at best moderately correlated with DO₂. This finding is due to the fact that a single measurement cannot discriminate between the relative contribution of the 2 variables DO₂ and VO₂.¹² Derived values of Qp, Qs, or Qp/Qs ratio have been made but are based on assuming a pulmonary venous O₂ saturation of greater than 95% and a fixed VO₂ value of 160 or 180 mL · min⁻¹ · m⁻².^{7,8,10} Significant pulmonary venous O₂ desaturation might occur after the Norwood procedure, thereby confounding Qp/Qs ratio assessments.¹³ We have previously shown that postoperative VO₂ has wide interpatient and inpatient variability in children.^{12,14,15} Thus significant errors might be introduced in the calculation of hemodynamic indices incorporating these variables.

In this study we used direct continuous measurement of VO₂ and intermittent measurement of arterial, pulmonary venous, and superior vena caval O₂ saturations to accurately profile hemodynamics and oxygen transport after the Norwood procedure.^{12,16} Changes and interrelationships of these variables were examined to determine factors that might contribute to hemodynamic instability in a group of neonates during the first 72 hours after the Norwood procedure. The patients studied in this report had a modified Blalock-Taussig shunt as the source of Qp.

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 14 neonates (11 boys and 3 girls; age range, 4-16 days; median, 7 days) undergoing the Norwood procedure between April 2004 and January 2006. Some of these patients were included in other reports.^{12,16} The clinical characteristics of the patients are shown in Table E1. Patients excluded from this study were those having an alternative strategy for palliation of hypoplastic left heart syndrome. During this time frame, 3 patients undergoing a conventional Norwood procedure were not offered the study because of reasons pertaining to equipment or technical support availability.

Operative Procedure

Patients were intubated with a cuffed endotracheal tube (Microcuff-Heidelberg-Pediatric; Microcuff GmbH, Weinheim, Germany). General anesthesia was maintained with inhaled isoflurane, intravenous fentanyl, and pancuronium bromide. A standard Norwood procedure with a preference for regional cerebral circulation was used.¹⁷ All patients had a 3.5-mm right modified Blalock-Taussig shunt, with the distal anastomosis placed centrally on the intrame-diastinal pulmonary artery. CPB was maintained for 66 to 172 minutes (median, 133 minutes), and an aortic crossclamp was maintained for 38 to 126 minutes (median, 62 minutes). Circulatory arrest was performed for 1 to 46 minutes (median, 12 minutes), and selected cerebral perfusion was performed in 13 of 14 patients for 20 to 70 minutes (median, 53 minutes) at 30 to 35 mL · min⁻¹ · kg⁻¹ (Table E1). Phenoxybenzamine, 0.25 mg/kg, was given in the heart-lung machine circuit after initiation of CPB. A bolus of 50,000 KIU of aprotinin was administered, followed by 100,000 KIU per 100 mL of prime. Before termination of CPB, milrinone (100 μg/kg) was administered, and dopamine (5 μg · kg⁻¹ · min⁻¹) was initiated. A pulmonary venous line was inserted into the orifice of the right upper pulmonary vein. A direct oximetric line (Abbott Critical Care Systems, Abbott Laboratories, Chicago, Ill) was inserted in the superior vena cava.

Critical Care

Infants received time-cycled volume ventilation with pressure support. Sedation was obtained with a continuous intravenous infusion of morphine (20-40 μg · h⁻¹ · kg⁻¹) and intermittent injections of a muscle relaxant (pancuronium, 0.1 mg/kg) and lorazepam (0.1 mg/kg). Pancuronium was discontinued when the patient achieved satisfactory hemodynamic stability.

The central temperature was maintained at 36°C to 37°C. Inotropic and vasoactive agents (milrinone, dopamine, phenoxybenzamine, and vasopressin) and ventilatory settings (the minute ventilation volume/rate) were adjusted according to our standard protocol, with an inspiratory oxygen fraction at or close to 0.21 (mean arterial blood pressure of 40-45 mm Hg with systolic pressure in the range of 55-65 mm Hg, arterial oxygen saturation of 70%-80%, and superior vena caval saturation of 44%-55%).¹⁸ Inspired oxygen was titrated upward for saturation of less than 70%. Volume infusions (5% albumin or blood) were given to maintain filling pressures of 7 to 10 mm Hg. Transfusions were

given for a hemoglobin (Hb) value of less than 14 mg/dL, and the Hb value was generally maintained between 14 and 16 mg/dL.

Methods of Measurement

Patient monitoring. All patients had continuous invasive monitoring of systemic, superior vena caval, and pulmonary venous pressures. Continuous monitoring of superior vena caval O₂ saturation was used, as was heart rate and central body temperature (esophageal).

VO₂. VO₂ was measured continuously by using an AMIS2000 mass spectrometer (Innovision A/S, Odense, Denmark). This is a sensitive and accurate method for continuous gas analysis that allows simultaneous measurements of multiple gas fractions.¹⁹

Calculations of hemodynamics and oxygen transport. Blood samples were taken from the arterial superior vena cava, and pulmonary venous lines for the measurements of blood gases. Qp and Qs were then calculated by using the direct Fick method. Total cardiac output (CO), DO₂, systemic vascular resistance (SVR), pulmonary vascular resistance inclusive of the Blalock-Taussig shunt (BT-PVR), and ERO₂ were calculated by using standard equations (Table E2).

Study Protocol

This study was performed during the first 72 hours after arrival in the intensive care unit (ICU). Values of hemodynamics, oxygen transport, and central body temperature were collected at 2-hour intervals during the first 24 hours and at 4-hour intervals from hours 25 through 72.

Data Analysis

Data are expressed as means $\pm$ standard deviation. Simple linear regression was used to determine correlations between preoperative (age, weight, and body surface area) and intraoperative demographics (duration of CPB, aortic crossclamp time, total circulatory arrest, or partial circulatory arrest with regional cerebral perfusion) and the first postoperative hemodynamic and oxygen transport measures. The comparison of intraindividual variations between 2 data sets was performed by using the Hartley F-max method. Mixed linear regression analysis for repeated measures was used to determine the nature of any time trend of the measures over the 72-hour study period. For some measures, various transformations of time (logarithmic and polynomial) were tested regarding the best fit for the time course. Interrelationships among the measures were sought by using mixed linear regression analysis for repeated measures without regard to time. Logarithmic transformation of both variables being compared was used when necessary to model nonlinear relationships. The extent of change and correlation was indicated by the intercept and parametric estimate. All data analysis was performed with SAS statistical software version 8 (SAS Institute, Inc, Cary, NC).

Results

Patients

There were no deaths and no episodes of circulatory collapse during the study period. One patient required extracorporeal membrane oxygenation support subsequent to the study period. Patients were extubated between 4 and 25

days (median, 10 days). All patients survived to hospital discharge. Milrinone ($0.33\text{--}0.99 \mu\text{g} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$) was used in all the patients throughout the study period. Dopamine ($5\text{--}10 \mu\text{g} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$) was initiated before the termination of CPB in all patients and subsequently stopped within the first 24 hours after arrival in the ICU in 13 patients; it was used for the entire study period in the remaining patient. Additional intravenous phenoxybenzamine ($0.5\text{--}2.0 \text{ mg} \cdot \text{day}^{-1} \cdot \text{kg}^{-1}$) was commenced within the first 10 hours and continued for the rest of the study period in 12 of 14 patients. Vasopressin ($0.0001\text{--}0.0005 \text{ U} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$) was administered to 10 patients at different times for 10 to 60 hours during the study period. Two patients had primary sternal closure. Delayed sternal closure was performed on the remainder on postoperative days 3 to 6, with 1 outlier occurring at day 17.

Profiles of Hemodynamics and Oxygen Transport

Table E3 shows the results for the trends of central body temperature, hemodynamics, oxygen transport, arterial oxygenation, and Hb value.

Baseline measures. On arrival to the ICU, central body temperature was $35.9^\circ\text{C} \pm 0.8^\circ\text{C}$. Total CO was $4.1 \pm 1.4 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$, with an SVR of 24.0 ± 13.8 , a BT-PVR of $17.6 \pm 5.5 \text{ Wood unit/m}^2$, and a Qp/Qs ratio of 1.4 ± 0.7 . Qp was $2.2 \pm 0.8 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$, and Qs was $1.9 \pm 1.0 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$. The Hb value was $14.3 \pm 42.7 \text{ g/dL}$, and DO₂ was $251 \pm 111 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$. VO₂ was $101 \pm 26 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$. ERO₂ was 0.44 ± 0.11 . The arterial blood lactate level was $5.5 \pm 2.2 \text{ mmol/L}$.

None of the initial oxygen transport and hemodynamic values were correlated with age, body weight, and body surface area ($P < .05$ for all). None of the operative variables (duration of CPB, aortic crossclamping, circulatory arrest, or regional cerebral perfusion time) correlated with the initial measured postoperative characteristics ($P > .05$ for all).

Oxygen transport changes during the study period. All the studied hemodynamic and oxygen transport measures showed substantial interindividual variations over the study period. The time course and the extent of changes in hemodynamic and oxygen transport measures also varied greatly (Table E3 and Figure 1).

LONGITUDINAL TRENDS OF SVR, Qs, CO, BT-PVR, AND QP. There were wide variations within individual patients with respect to SVR, Qs, CO, and Qp/Qs ratio. BT-PVR did not change significantly over time ($P > .05$), but Qp showed a small and significant increase over time ($P < .0001$). SVR, Qs, and CO were related to time in a complex polynomial function, with an early decrease in SVR ($P = .0006$) and an increase in Qs ($P < .0001$) and CO ($P = .001$) peaking around 28 to 32 hours, followed by a slow increase in SVR ($P = .001$) and a decrease in Qs and CO ($P < .0001$).

Figure 1. Individual and mean values of main variables of hemodynamics and oxygen transport, including total pulmonary vascular resistance inclusive of the resistance of the Blalock-Taussig shunt (*BT-PVR*) and systemic vascular resistance (*SVR*), pulmonary (*Qp*) and systemic (*Qs*) blood flows, hemoglobin value (*Hb*), oxygen delivery (*DO₂*), oxygen consumption (*VO₂*), oxygen extraction ratio (*ERO₂*), and arterial lactate levels during the first 72 hours after arrival in the ICU. *Data were entered after logarithmic transformation. **Data were entered after polynomial transformation, with *time* indicating the parametric estimate of the early trend and *time²* indicating the later trend.

for *Qs* and $P = .025$ for *CO*). *Qs* and *CO* were significantly lower during the first 24 hours compared with that seen during the subsequent 48 hours ($P < .0001$ for *Qs* and $P = .0004$ for *CO*). A comparison of the first 24 hours and subsequent 48 hours showed no change in *Qp*. There was no change over time for *Qp/Qs* ratio ($P > .05$).

LONGITUDINAL TRENDS IN TEMPERATURE OF *VO₂* AND *DO₂*. Central temperature did not change significantly during the study period ($P > .05$), except for the initial significant increase during the first 2 hours after arrival in the ICU ($P = .005$). *VO₂* was significantly related to time after logarithmic transformation and showed a rapid decrease in the first 24 hours ($P < .0001$). There were wide interindividual and intraindividual fluctuations. Total *VO₂* range was from 45 to 152 mL · min⁻¹ · m⁻². *DO₂* was significantly related to time in a complex polynomial function, with an early increase peaking around 28 to 36 hours ($P < .0001$), followed by a slow decrease ($P < .0001$). Wide variations

were noted within individuals.

ERO₂. *ERO₂* was significantly related to time in a complex polynomial function, with an initial rapid decrease in the first 24 hours, followed by a slow decrease ($P < .0001$) and a subsequent small but significant increase at 48 hours ($P < .0001$).

ARTERIAL SERUM LACTATE. Lactate levels were significantly related to time after logarithmic transformation and showed an initial rapid decrease in the first 6 hours, followed by a slower steady decrease ($P < .0001$).

LONGITUDINAL TRENDS IN CONTRIBUTORS TO ARTERIAL O₂ CONTENT. There was a small but significant increase in pulmonary venous O₂ saturation over time ($P < .0001$). Both *Pao₂* and arterial oxygen saturation (*Sao₂*) were significantly related to time after logarithmic transformation, with a fast increase in the first 24 hours, followed by a slow increase ($P < .0001$ for both). *Hb* value showed a small significant linear decrease over time ($P < .0001$). Arterial

Figure 2. Correlations between hemodynamic variables of pulmonary/systemic blood flow ratio (Q_p/Q_s), systemic vascular resistance (SVR), systemic blood flow (Q_s), total pulmonary vascular resistance inclusive of the Blalock-Taussig shunt (BT-PVR), pulmonary blood flow (Q_p), and systemic oxygen delivery (DO_2) in patients during the first 72 hours after arrival in the ICU. *Data were entered after logarithmic transformation.

O_2 content was related to time in a complex polynomial function, with an early increase in the first 10 hours ($P = .004$), followed by a slow decrease ($P = .0009$). Of note, pulmonary venous O_2 saturation was less than 95% in 40% of the total sample times (140/350).

Interrelationships Among the Variables

The statistical results of the interrelationships among the variables using mixed linear regressions are seen in Table E4 and Figure 2. The extent of the correlation is indicated by the intercept and coefficient values.

SVR. Over the entire study period, SVR was linearly and highly positively correlated with Q_p/Q_s ratio and nonlinearly negatively correlated with Q_s , CO, and DO_2 (after logarithmic transformation, $P < .0001$ for all).

BT-PVR. BT-PVR was significantly negatively and linearly correlated with Q_p/Q_s ratio ($P = .002$) and CO ($P < .0001$) and nonlinearly with Q_p (after logarithmic transformation, $P < .0001$). The influence of BT-PVR on Q_p/Q_s ratio, Q_s , and CO was not as strong as that seen with SVR,

as demonstrated by the difference in the intercept and parameter estimates in Table E4. There was a weak correlation of BT-PVR with Q_s ($P = .008$) but not DO_2 ($P = .14$).

Q_p/Q_s ratio. The Q_p/Q_s ratio was significantly ($P < .001$) affected by both Q_s and Q_p ; however, Q_s showed a stronger correlation, as seen by the difference in the intercept and coefficient in Table E4.

DO_2 . There was a close linear correlation of DO_2 with Q_s ($P < .0001$) but not with Q_p ($P = .67$). DO_2 was significantly and nonlinearly negatively correlated with Q_p/Q_s ratio (after logarithmic transformation, $P < .0001$).

Arterial O_2 content and DO_2 . Q_p had a weak positive correlation with SaO_2 and Pao_2 ($P < .0001$ for both). Pao_2 had a weak positive correlation with DO_2 ($P = .0002$). There was no correlation of SaO_2 with DO_2 ($P = .32$). Inclusion of SaO_2 , Pao_2 , Hb value, and Q_s showed that SaO_2 and Pao_2 were positively but weakly correlated with DO_2 ($P < .0001$ for SaO_2 and $P = .002$ for Pao_2). Hb value had a high positive correlation with DO_2 ($P < .0001$).

ERO₂. ERO₂ had a close positive correlation with VO₂ and a negative correlation with DO₂ ($P < .0001$ for both).

Discussion

This study examines detailed quantitative assessments of hemodynamics and oxygen transport after the Norwood procedure, where VO₂ and pulmonary venous O₂ saturations were not assumed. Measurement of VO₂; superior vena caval, arterial, and pulmonary venous pressures; and blood gases allows calculation of Qp and Qs. Total CO, Qp/Qs ratio, SVR, BT-PVR, DO₂, and ERO₂ can then be calculated. Previous studies used assumptions for VO₂ in the range of 160 to 180 mL · min⁻¹ · m⁻² to calculate hemodynamics.^{7,8,10} Those assumptions are much higher than what was observed in our patients (range, 45-152 mL · min⁻¹ · m⁻²; mean at arrival in the ICU, 101 mL · min⁻¹ · m⁻²). Overestimation of VO₂ leads to a direct proportional change in the estimation for the calculated variables. For example, an assumed VO₂ of 170 mL · min⁻¹ · m⁻² compared with the measured mean VO₂ on arrival to the ICU of 101 mL · min⁻¹ · m⁻² would lead to a 68% overestimation of total CO, Qp, and Qs and a 68% underestimation of PVR and SVR. Taeed and colleagues¹³ previously noted the occurrence of pulmonary venous O₂ desaturation after the Norwood procedure. We found pulmonary venous desaturation (defined as <95% saturation) in 40% of the pulmonary venous samples taken. The effect of a falsely high assumption of pulmonary venous saturation can be seen in the following example from one of our observed patients: measured pulmonary venous saturation was 90%, and an assumed pulmonary venous saturation of 96% would have led to an underestimation of Qp by 35% and therefore the Qp/Qs ratio by 35% as well. The data demonstrate that continuous VO₂ and measured pulmonary venous O₂ saturation have a significant effect on the calculated variables and therefore potential for having an effect on management strategy.

Cardiac Output and Characteristics of Qp and Qs

The single ventricle is subject to considerable demand for total CO. There is great variation both individually and within the cohort (total range, 1.9-8.3 L · min⁻¹ · m⁻²; mean range, 3.7-4.9 L · min⁻¹ · m⁻²). On an individual basis, the Qp/Qs ratio was highly variable (0.35-2.8) but on a mean basis, it was less varied for 0.9 to 1.5. On analysis, SVR was tightly correlated with the Qp/Qs ratio and negatively correlated with Qs, CO, and DO₂. BT-PVR was negatively correlated with the Qp/Qs ratio, CO, and Qp, but this was a weaker correlation than with SVR. In other words, SVR was far more important in determining the balance of the Qp/Qs ratio than was BT-PVR. SVR was also significantly more variable than BT-PVR, despite the use of α blockade and phosphodiesterase inhibitors. These find-

ings are important because, historically, the postoperative management strategy of patients undergoing the Norwood procedure was directed at diminishing Qp by increasing PVR.^{5,20,21} More recently, some, including us, have advocated aggressive reduction of SVR as a primary management strategy. This has resulted in improved outcomes for those who have reported the strategy.^{10,18,22} In the presence of aggressive afterload reduction, it has been thought that PVR was relatively fixed.^{10,11} The findings of this study indicate that both the systemic and pulmonary vascular compartments have variable resistance, but the systemic circulation has a more profound effect on the balance of the Qp/Qs ratio. SVR also has an effect on Qs and total CO. Although the study does not address the ability of ventilation and oxygenation strategy to alter BT-PVR, a rational clinical approach would appear to be a combined approach of ventilation strategies to increase BT-PVR (additional inspired CO₂) plus effective afterload reduction. Both would promote an improved Qp/Qs ratio and increased Qs and therefore improved DO₂. Interestingly, increasing Pao₂ had only a weak positive correlation with Qp, implying that relative hypoxia yields little benefit to the balance of the Qp/Qs ratio.

Contribution of VO₂ to the Balance of Oxygen Transport

Matching DO₂ to VO₂ is one of the tenets of care in critically ill patients.^{15,19,23,24} The first 24-hour improvement seen in this group of patients in ERO₂ and arterial lactate levels occurred when CO, Qs, and DO₂ were most decreased. The data demonstrate that the main early contributor to the improved ERO₂ was decreasing VO₂.

VO₂ can be increased after CPB as a consequence of rewarming^{15,19,25} and the systemic inflammatory response.^{15,26} After arrival in the ICU, there was a continuous but biphasic decrease in VO₂ in the presence of normothermia. A more rapid decrease occurred for 24 hours, followed by a slower decrease for the following 48 hours. After 24 hours, DO₂ became the primary contributor to the balance of DO₂ and VO₂.

Another important issue with respect to VO₂ is the potential effect of vasoactive and inotropic agents. In a neonatal lamb model the use of β -sympathomimetic drugs was associated with a rapid and substantial increase in VO₂, offsetting the benefits of increased DO₂.²⁴ Our routine is to terminate CPB on 5 μ g · min⁻¹ · kg⁻¹ dopamine but to subsequently discontinue its use in the ICU to try to decrease myocardial oxygen demand. Cessation of dopamine might have contributed to the decrease in VO₂ in the first 24 hours in the ICU.¹⁶ The introduction of α blockade might also be important in this regard. Animal data suggest that inhibition of α stimulation in brown fat tissue might reduce the metabolic rate.²⁷ Further studies might be warranted to directly quantitatively assess the effects of inotropes and

vasoactive drugs on VO_2 and DO_2 in these patients, while controlling for other variables that might affect VO_2 .

Optimizing Oxygen Delivery

Systemic DO_2 mean values were $281 \pm 86 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ at the 12th hour after the Norwood procedure. Although there were significant interindividual and intraindividual variations throughout the study, these values are low in comparison with our studies of complete repair for congenital heart defects in older children (281 ± 86 vs $368 \pm 94 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$).¹⁵ DO_2 is limited by the effects of common mixing and low Qs ($1.8 \pm 0.6 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$).^{28,29} The variables for potentially improving DO_2 include increasing Sao_2 , Pao_2 , and Hb value; altering the Qp/Qs ratio; and absolutely increasing total CO. Our analysis demonstrated that within the ranges of Sao_2 and Pao_2 observed, there was only weak correlation with DO_2 . There was, however, a tight correlation between DO_2 and Hb value. Our data therefore support the common practice of maintaining the postoperative hematocrit value at greater than 40%.

With respect to the Qp/Qs ratio, Barnea and associates⁴ theorized that maximal DO_2 occurs at a Qp/Qs ratio of less than 1 over a wide range of COs. Our data show that DO_2 was closely, negatively, and logarithmically correlated with the Qp/Qs ratio within the wide range (0.35-2.8) for our patients. Mean DO_2 (for a similar Hb value) was highest ($460 \pm 152 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$) when the Qp/Qs ratio was less than 0.7 and lower ($260 \pm 69 \text{ mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$) when the Qp/Qs ratio was 1.0 or greater. The data suggest that a direct increase in Qs would result in a lower Qp/Qs ratio and therefore a higher DO_2 . Therefore maintaining a high Hb value and decreasing the SVR to most effectively optimize the Qp/Qs ratio would be most effective in improving DO_2 .

Limitations

Superior vena caval blood was used as an estimate of the mixed venous saturation for the calculations of Qs and DO_2 . The relative oxygen contents of the superior and inferior venae cavae might differ.^{30,31} Pulmonary venous saturations were obtained from only 1 pulmonary vein. This would not account for regional lung perfusion and ventilation differences in pulmonary vein saturation.

PVR in this study is actually a measure of resistance across the Blalock-Taussig shunt and the pulmonary vasculature. An indwelling pulmonary arterial catheter would be required to directly measure pulmonary arterial pressure to differentiate actual PVR from that including the Blalock-Taussig shunt.

Finally, the hemodynamic and oxygen transport measurements were derived by using the common variables of VO_2 , blood gases, and pressures. Some were calculated from one another; for example, DO_2 and SVR were calculated from Qs . This might induce mathematic coupling and therefore

affect correlation analysis.³² This study does not address oxygen transport for hypoplastic left heart syndrome palliation by using the Sano modification (right ventricle-pulmonary artery conduit).

Inferences and Conclusions

Measurement of hemodynamics and oxygen transport allowed detailed observation and analysis of the physiology of neonates after the Norwood procedure. There were wide, unstable, interindividual and intraindividual variations. The balance of VO_2 and DO_2 (ERO_2) improved significantly in the first 24 hours, primarily as a result of a decreasing VO_2 . Thereafter, DO_2 became the main contributor to the balance of oxygen transport. Within the limits of the parameters measured, DO_2 was most affected by SVR, to a lesser extent by Hb value, and very minimally by Pao_2 . DO_2 was not affected by the pulmonary circuit resistance or Qp . The finding of minimal variability of contribution in the pulmonary circuit to DO_2 indicates that manipulation of the systemic side of the parallel circulation is of greater importance than the pulmonary side. Future strategies should be designed to improve DO_2 and its balance with VO_2 . Specifically, management strategies to maintain a high Hb value, a low VO_2 , and a controlled SVR appear to be rational.

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TABLE E1. Clinical data for the 14 patients

Patient no.	Age (d)	Weight (kg)	BSA (m ²)	CPB (min)	ACC (min)	Circulatory arrest (min)	Cerebral perfusion (min)	Diagnosis
1	7	3.5	0.23	108	47	12	35	HLHS, AS, MS
2	4	3.7	0.25	151	100	35	53	HLHS, AS, MS
3	7	4	0.26	105	47	3	44	HLHS, AS, MS,
4	16	3.5	0.24	133	39	34	0	HLHS, endocardial fibroelastosis of LV, AS, MS
5	7	4.2	0.27	122	62	3	60	HLHS, AS, MS
6	12	3.5	0.23	165	75	13	59	DILV, TGA
7	6	3.5	0.23	172	82	9	70	HLHS, AA, MA,
8	16	3.9	0.25	170	60	1	60	HLHS, AS, MS
9	7	4	0.25	167	64	17	44	HLHS, AA, MA
10	6	2.9	0.20	142	62	1	62	HLHS, AA, MA
11	7	2.8	0.19	66	59	17	20	HLHS, AA MA
12	5	2.5	0.18	170	126	46	60	HLHS, AA, MA
13	4	4.2	0.27	124	99	44	49	HLHS, AS, MS, TAPVC
14	5	3.9	0.26	98	50	12	37	HLHS, AA, MA

BSA, Body surface area; CPB, cardiopulmonary bypass; ACC, aortic crossclamp; HLHS, hypoplastic left heart syndrome; AS, aortic stenosis; MS, mitral stenosis; LV, left ventricle; DILV, double-inlet left ventricle; TGA, transposition of the great arteries; AA, aortic atresia; MA, mitral atresia; TAPVC, total abnormal pulmonary venous connection.

TABLE E2. Equations using oxygen consumption to calculate hemodynamics and oxygen transport parameters

Parameters	Equations
Q_p (L · min ⁻¹ · m ⁻²)	$VO_2/(Cpvo_2 - CaO_2)$
Q_s (L · min ⁻¹ · m ⁻²)	$VO_2/(CaO_2 - Cvo_2)$
CO (L · min ⁻¹ · m ⁻²)	$Q_s + Q_p$
SVR (Wood unit × m ²)	$(MAP - MVP)/Q_s$
$BT-PVR$ (Wood unit × m ²)	$(MAP - MPVP)/Q_p$
DO_2 (mL · min ⁻¹ · m ⁻²)	$Q_s \times CaO_2$
ERO_2	VO_2/DO_2

Q_p , Pulmonary blood flow; VO_2 , systemic oxygen consumption; $Cpvo_2$, pulmonary venous O₂ content; CaO_2 , arterial (equals to pulmonary arterial) O₂ content; Q_s , systemic blood flow; Cvo_2 , superior vena caval O₂ content; CO , total cardiac output; SVR , systemic vascular resistance; MAP , mean arterial pressure; MVP , mean superior vena caval pressure; $MPVP$, mean pulmonary venous mean pressure; $BT-PVR$, total pulmonary vascular resistance inclusive of the Blalock-Taussig shunt; DO_2 , systemic oxygen delivery; ERO_2 , oxygen extraction ratio.

TABLE E3. Statistical analysis results of the changes of hemodynamics and oxygen transport in the 14 patients during the study period with mixed linear regression

Variables	Intercept	Parameter estimate	P values
SVR (Wood unit $\times$ m ²)*	23.2	Time -0.22 Time ² 0.003	.0006 .001
BT-PVR (Wood unit $\times$ m ²)	18.1	-0.0026	.76
CO (L $\cdot$ min ⁻¹ $\cdot$ m ⁻²)*	3.8	Time 0.025 Time ² 0.002	.001 .025
Qs (L $\cdot$ min ⁻¹ $\cdot$ m ⁻²)*	1.7	Time 0.026 Time ² -0.0003	<.0001 <.0001
Qp (L $\cdot$ min ⁻¹ $\cdot$ m ⁻²)	2.0	0.0057	<.0001
Qp/Qs	1.2	0.0008	.45
Pao ₂ (mm Hg)†	32.3	2.6	<.0001
Sao ₂ (%)†	69.2	1.9	<.0001
Hb (g/dL)	15.2	-0.021	<.0001
CaO ₂ (mL/L)*	149.7	Time 0.47 Time ² 0.007	.004 .0009
DO ₂ (mL $\cdot$ min ⁻¹ $\cdot$ m ⁻²)*	242	Time 5.1 Time ² -0.07	<.0001 <.0001
Temperature (°C)	36.5	0.001	.27
VO ₂ (mL $\cdot$ min ⁻¹ $\cdot$ m ⁻²)†	99.3	-4.4	<.0001
ERO ₂ *	0.41	Time -0.007 Time ² 0.00009	<.0001 <.0001
Lactate (mmol/L)†	3.3	-0.49	<.0001
SpvO ₂ (%)	94.5	0.03	<.0001

SVR, Systemic vascular resistance; BT-PVR, total pulmonary vascular resistance including Blalock-Taussig shunt; CO, total cardiac output; Qs, systemic blood flow; Qp, pulmonary blood flow; Sao₂, arterial oxygen saturation; Hb, hemoglobin; CaO₂, arterial oxygen content; DO₂, systemic oxygen delivery; VO₂, systemic oxygen consumption; ERO₂, oxygen extraction ratio; SpvO₂, pulmonary venous oxygen saturation. *Data were entered after polynomial transformation, with *time* indicating the coefficient of the early trend and *time*² indicating the later trend. †Data were entered after logarithmic transformation.

TABLE E4. Statistical analysis results of the interrelationships among the variables of hemodynamics and oxygen transport and the determinants of systemic oxygen delivery and oxygen extraction ratio in the 14 patients during the study period with mixed linear regression

Independent variables	Dependent variable	Intercept	Parameter estimate	P values
SVR	Qp/Qs ratio	0.13	0.051	<.0001
SVR*	Qs	7.2	−1.7	<.0001
SVR*	CO	8.7	−1.5	<.0001
SVR*	DO ₂	989	−233	<.0001
BT-PVR	Qp/Qs ratio	1.54	−0.020	.002
BT-PVR*	Qp	5.1	−1.0	<.0001
BT-PVR	Qs	2.5	−0.026	.008
BT-PVR	CO	5.7	−0.08	<.0001
BT-PVR	DO ₂	341	−2.2	.14
Qs*	Qp/Qs ratio	1.9	−1.1	<.0001
Qp	Qp/Qs ratio	0.04	0.52	<.0001
Qp/Qs ratio*	DO ₂	321	−193	<.0001
Qs	DO ₂	22.9	139	<.0001
Qp	DO ₂	293	4.0	.67
Qp	PaO ₂	34.6	2.6	<.0001
Qp	SaO ₂	66.1	4.2	<.0001
PaO ₂	DO ₂	117	4.6	.0002
SaO ₂	DO ₂	222	1.1	.32
Hb	DO ₂	112	13.1	.0008
Qs + SaO ₂ + PaO ₂ + Hb	DO ₂	−592.42	Qs 149	<.0001
			SaO ₂ 3.4	<.0001
			PaO ₂ 1.1	.002
			Hb 21.2	<.0001
VO ₂	ERO ₂	0.10	0.002	<.0001
DO ₂ *	ERO ₂	1.78	−0.26	<.0001

Abbreviations are as indicated in Table E3. *Data were entered after logarithmic transformation for both variables being compared.