Unrecognized Pulmonary Venous Desaturation Early After Norwood Palliation Confounds Qp:Qs Assessment and Compromises Oxygen Delivery

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Background—Hemodynamic stability after Norwood palliation often requires manipulation of pulmonary vascular resistance to alter the pulmonary-to-systemic blood flow ratio (Qp:Qs). Qp:Qs is often estimated from arterial saturation (SaO2), a practice based on 2 untested assumptions: constant systemic arteriovenous O2 difference and normal pulmonary venous saturation.

Methods and Results—In 12 patients early (≤3 days) after Norwood palliation, simultaneous arterial, superior vena caval (SvO2), and pulmonary venous (SpvO2) oximetry was used to test whether SaO2 accurately predicts Qp:Qs. Stepwise multiple regression assessed the contributions of SaO2, SvO2, and SpvO2 to Qp:Qs determination. SaO2 correlated weakly with Qp:Qs (R2 = 0.08, P < 0.05). Inclusion of SvO2 and SpvO2 improved Qp:Qs prediction accuracy. Pulmonary venous desaturation (SpvO2 < 95%) was observed frequently (30%), especially at FiO2 ≤ 0.21, but normalized with higher FiO2 or PEEP in all patients. In 6 patients, FiO2 was increased incrementally from 0.17 to 0.50 to determine whether this was an effective means to manipulate Qp:Qs. Qp:Qs failed to change predictably with increased FiO2. In 5 of 6 patients, however, higher SpvO2 and SaO2 enhanced systemic oxygen delivery, as demonstrated by improvement in oxygen extraction.

Conclusions—SaO2 correlated poorly with Qp:Qs because of variability in SvO2 and SpvO2. A novel observation was that pulmonary venous desaturation occurred frequently early after Norwood palliation but normalized with higher FiO2 or PEEP. Because unrecognized pulmonary venous desaturation confounds Qp:Qs assessment and compromises SaO2 and oxygen delivery, judicious use of inspired oxygen and PEEP may be beneficial in selected patients early after Norwood palliation. (Circulation. 2001;103:2699-2704.)

Key Words: heart defects, congenital • lung • surgery • hypoplastic left heart syndrome • Norwood operation

Hemodynamic stability in the early postoperative period after Norwood palliation for hypoplastic left heart syndrome is largely dependent on maintaining a balance between pulmonary blood flow (Qp) and systemic blood flow (Qs).1 Ventilation strategies that alter pulmonary vascular resistance are routinely used to manipulate the ratio of Qp to Qs (Qp:Qs).1,2 Estimation of the Qp:Qs ratio is thus vitally important for accurate assessment of an unstable hemodynamic state and to determine the effects of interventions designed to alter the Qp:Qs. It has long been accepted that arterial oxygen saturation (SaO2) is reflective of Qp:Qs after the Norwood operation.2

The assertion that Qp:Qs can be estimated from SaO2 alone in single-ventricle physiology is based on a simplification of the Fick equation that is not well founded. Because Qp is supplied by a systemic-to–pulmonary artery shunt, pulmonary and systemic arterial oxygen saturations are equivalent, so that Qp:Qs can be calculated as Qp:Qs = (SaO2 − SmvO2)/(SpvO2 − SaO2), where mv is mixed-venous and pv pulmonary venous. This equation has been further simplified on the basis of 2 untested assumptions: (1) that systemic arteriovenous oxygen saturation difference (ΔA-V O2) is constant (commonly assumed to be ~ 25), and (2) that the pulmonary venous (PV) blood is fully oxygen saturated (ie, SpvO2 = 95%).1 These assumptions yield the simplified equation: Qp:Qs = 25/(95 − SaO2). This equation has been used to estimate Qp:Qs from SaO2 alone.

The ability to determine Qp:Qs from SaO2 is highly desirable, given the ease with which SaO2 can be obtained in clinical practice. The assumptions that underlie this simplified Fick equation may be false, however, in the immediate postoperative Norwood period. ΔA-V O2 will be significantly greater than 25 if systemic blood flow is low, a common occurrence in the postoperative period. Rossi and colleagues3,4 reported the importance of monitoring superior vena cava (SVC) oxygen saturation (SvO2) after Norwood...
palliation as a means of assessing $Q_s$. The assumption that PV blood is fully saturated has never been tested in the postoperative Norwood circulation; however, it is a potentially dangerous assumption, given the routine use of minimal inspired oxygen (even subambient oxygen) and controlled hypercarbia in postoperative management of these infants. Failure to account for a decrease in $SpvO_2$ will result in an important underestimation of $Q_p:Q_s$ based on $SaO_2$ alone. If reduced levels of inspired oxygen result in PV desaturation without a significant decrease in $Q_p:Q_s$, the associated decrease in $SaO_2$ may be detrimental to overall systemic oxygen delivery.

The purpose of this study was to use simultaneous oximetry of arterial, SVC, and PV blood to test the hypothesis that $SaO_2$ alone is an accurate predictor of $Q_p:Q_s$ in the early postoperative Norwood circulation. We thus hoped to evaluate the validity of common assumptions regarding $\Delta A-V O_2$ and $SpvO_2$ in postoperative Norwood patients. A second aim was to determine whether changes in fraction inspired oxygen ($F_iO_2$) are an effective means to alter $Q_p:Q_s$.

**Methods**

**Patient Enrollment**

Infants with single-ventricle anatomy and aortic arch obstruction undergoing stage I Norwood palliation with functional SVC and PV catheters were eligible for inclusion. These catheters are routinely placed intraoperatively during the Norwood procedure at our institution. Exclusion criteria included weight <2 kg, clinical or radiographic evidence of pulmonary disease, or the inability to draw samples from SVC or PV catheters. The study was approved by the Institutional Review Board of Children’s Hospital Medical Center, and informed consent was obtained from a parent or legal guardian before the study.

**Intraoperative Procedure**

A narcotic anesthetic was used for optimal myocardial function. After sternotomy and bypass initiation, dissection was completed during cooling. An atrial septectomy was performed via atriotomy, the aortic arch was reconstructed with a homograft patch, and the pulmonary artery bifurcation was closed primarily. Retrograde cardioplegia was administered during circulatory arrest. A Gore-tex shunt was placed during rewarming. Intracardiac catheters were inserted by the transfemoral approach and the tips directed into the SVC and left lower pulmonary vein under direct visualization.

**Postoperative Management**

Patients were returned to the Cardiac Intensive Care Unit with open sternotomy on a fentanyl infusion and neuromuscular blockade. Postoperative monitoring included atrial and systemic arterial pressures, ECG, pulse oximetry, and end-tidal CO2. Patients were ventilated with volume control ventilation at a tidal volume of 20 mL/kg and positive end-expiratory pressure (PEEP) of 4 cm H2O. Ventilator settings, ECG, pulse oximetry, and end-tidal CO2 were systematically altered during changes in $FiO_2$. After administration of fentanyl (10 $\mu$g/kg) and vecuronium (0.1 mg/kg) and endotracheal tube suctioning, baseline oximetric data ($SaO_2$, $SsvcO_2$, and $SpvO_2$) were obtained at an $FiO_2$ of 0.21. Hemodynamic and oximetric data were subsequently collected as $FiO_2$ was adjusted incrementally to 0.17, 0.21, 0.30, and 0.50. Hemoglobin was measured for each oximetric data set. After each change in $FiO_2$, patients were allowed 10 minutes for equilibration before oximetric data were collected.

Oximetric data were analyzed to determine the effects of changes in $FiO_2$ on $Q_p:Q_s$. As surrogates of systemic oxygen delivery, alterations in $\Delta A-V O_2$ and the oxygen extraction ratio were examined.

**Data Analysis and Statistical Methods**

Data were analyzed with Statview software (Abacus Concepts). For the purpose of correlating $SaO_2$ with true $Q_p:Q_s$, all measurements were assumed to be independent, and stepwise linear multiple regression was used to determine the contributions of $SaO_2$, $SsvcO_2$, and $SpvO_2$ to the determination of $Q_p:Q_s$. Data are presented as mean±SD. Statistical significance was defined as a value of $P<0.05$.

**Results**

From April 1997 to December 1998, 20 patients underwent Norwood palliation at Children’s Hospital Medical Center. Twelve patients were included in this study. Of the remaining 8 patients, there was 1 intraoperative death, 1 patient weighed <2 kg, and another patient developed Gram-negative sepsis/pneumonia. In 5 patients, the PV or SVC catheter was not placed successfully or could not be used for sampling, including 1 patient who was excluded because of atrial contamination of PV blood, as evidenced by $SpvO_2$ data that closely approximated the $SaO_2$. Oximetric data from the 12 study patients were used to test the assumptions underlying the simplified Fick equation, and in 6 of these patients, $FiO_2$ was systematically altered to determine the effect of $FiO_2$ on $Q_p:Q_s$. One patient was not studied at subambient oxygen ($FiO_2=0.17$) because of significant PV desaturation during baseline room air ventilation.

Patient characteristics are summarized in the Table. The median age at the time of surgery was 7 days (range 3 to 45 days). The median weight was 3.23 kg (range 2.2 to 4.1 kg). During the study period, 14 of 20 neonates (70%) were discharged home and subsequently returned for successful bidirectional Glenn anastomosis. Of the 12 infants included in the...
Study, 2 infants died in the early postoperative period and 1 died 2 months after the Norwood procedure of persistent hepatic failure. All nonsurviving infants demonstrated marked pulmonary overcirculation, demonstrating the highest maximum Qp:Qs measurements recorded. Excessive pulmonary blood flow in these patients was associated with clinically important PV desaturation. PV desaturation (SpvO₂<95%) was observed in 11 of 12 patients but normalized with higher FiO₂ or PEEP in all patients.

### Prediction of Qp:Qs From SaO₂

A total of 115 complete, simultaneous sets of oximetric data (SaO₂, SsvCO₂, and SpvO₂) were available for analysis. True Qp:Qs calculated from simultaneous oximetry data ranged from 0.45 to 5.43 and correlated poorly with SaO₂ (R²=0.08, P<0.05). There was a particularly poor correlation between true Qp:Qs and SaO₂ at arterial saturations of 65% to 85%, where one might expect a “balanced” circulation on the basis of the usual clinical assumptions (Figure 1).

Stepwise linear regression using SaO₂, SsvCO₂, and SpvO₂ to predict Qp:Qs showed significant improvement in ability to estimate Qp:Qs with inclusion of each additional variable. SaO₂ alone accounted for only 8% of the variation in Qp:Qs (R²=0.08), a remarkably low finding. Addition of SsvCO₂ increased this to 56%, and the PV component accounted for the remaining variability in Qp:Qs.

### Systemic ΔA-V O₂

The mean ΔA-V O₂ in the 115 samples was 30±11% (95% CI 8% to 52%). There was wide intrapatient and interpatient variability, with a range of 9% to 50%. Variation in SsvCO₂ contributed most significantly to alterations in systemic ΔA-V O₂. Consistent with the observations of previous investigators,³ our data indicate that variability in the systemic ΔA-V O₂ confounds bedside assessment of Qp:Qs from SaO₂ alone.

### PV Desaturation Is Common in the Early Postoperative Period After Norwood Palliation

Measured SpvO₂ ranged from 76% to 100%, and PV desaturation (defined as SpvO₂ <95%) was observed in 35 of the 115 samples (30%). SpvO₂ was <90% in 17 of the 115 samples (15%). All but 1 patient had ≥1 desaturated PV sample, and 8 of 9 samples taken during administration of subambient oxygen were <95%. Although PV desaturation was observed more frequently at lower FiO₂, it was also observed in 5 samples at FiO₂ of ≥0.30 (Figure 2). Desaturation of PV blood occurred without evidence of pulmonary edema, atelectasis, or infiltrates or catheter migration on repeated chest radiographs.

To verify that these were true PV samples and not samples contaminated with atrial blood, an effort was made to normalize SpvO₂ in all patients who exhibited PV desaturation. By use of a combination of increased FiO₂ and PEEP, SpvO₂ was raised to ≥95% in all patients, and PpO₂ was >200 mm Hg in all patients studied at an FiO₂ of 0.50. The minimum and maximum SpvO₂ values for each individual patient are displayed in the Table, and the interventions used to normalize SpvO₂ are noted.

### FiO₂ and Qp:Qs

As FiO₂ was increased, SaO₂ increased in all patients (Figure 3, top). The corresponding PV blood, which was desaturated...
in 5 of 6 patients at 0.17 FiO₂, became fully saturated as FiO₂ was increased (Figure 3, second panel). Somewhat surprisingly, no significant relationship between FiO₂ and Q˙p:Q˙s was observed with systematic manipulation of FiO₂ (Figure 3, middle panel). As FiO₂ was increased from 0.17 to 0.50, only 1 patient (▲ symbols) demonstrated a clinically important increase in Q˙p:Q˙s with apparent reduction in systemic O₂ delivery (increased ΔA-V O₂, decreased O₂ extraction ratio).

Although the systemic-pulmonary shunt in this patient (patient 1, Table) was not excessively large, it is relevant that this patient had the highest Q˙p:Q˙s on subambient oxygen of all patients studied, suggesting excessive baseline pulmonary blood flow. In the remaining 5 patients, systematic increases in FiO₂ failed to cause a corresponding change in Q˙p:Q˙s. In these patients, changes in Q˙p:Q˙s and ΔA-V O₂ with FiO₂ were minimal, but a reduced O₂ extraction ratio in these patients suggested more luxuriant systemic O₂ delivery (Figure 3, lower 3 panels). Improvement in SpvO₂ at higher FiO₂ helped to enhance oxygen delivery, demonstrating the importance of fully saturated PV blood to help optimize SaO₂ and systemic oxygen delivery. These data support the supposition that decreases in pulmonary vascular resistance may have minimal effect on Q˙p:Q˙s in patients in whom the aortopulmonary shunt limits pulmonary blood flow mechanically.

Discussion

The fragile early postoperative course after Norwood palliation is exquisitely sensitive to the balance of systemic and pulmonary blood flow.¹⁻²⁻⁶⁻⁷ Bedside estimation of Q˙p:Q˙s from SaO₂ alone has been advocated on the basis of 2 untested assumptions: constant systemic ΔA-V O₂ and normal SpvO₂ (≥95%). This study demonstrates that SaO₂ is a poor predictor of Q˙p:Q˙s after Norwood palliation; SaO₂ alone predicted only 8% of the variability in Q˙p:Q˙s. Inaccuracy in Q˙p:Q˙s estimation was caused by variability in both SmvO₂ and SpvO₂, thus challenging the dual assumptions used by clinicians for rapid bedside assessment of Q˙p:Q˙s.

Although others have demonstrated variability in SmvO₂ after Norwood palliation,¹⁻⁸ this is the first study to demonstrate that PV desaturation is also common. PV desaturation was observed in 30% of PV samples even though there was no evidence of pulmonary edema, atelectasis, or infiltrates on chest radiograph. The data thus suggest that postoperative Norwood patients may have pulmonary gas exchange abnormalities resulting from cardiopulmonary bypass, circulatory arrest, and the extensive surgical procedure. Furthermore, ventilatory maneuvers used to manipulate pulmonary vascular resistance in these patients (ie, controlled hypoventilation, low FiO₂) may predispose patients to microatelectasis and ventilation-perfusion mismatch.

The presence of unrecognized PV desaturation may contribute to substantial errors in Q˙p:Q˙s estimated from SaO₂ alone. The data indicate that Q˙p:Q˙s is underestimated at higher levels of true Q˙p:Q˙s, when it is most clinically relevant (Figure 4A). Our observations (Figure 4B) provide clinical evidence to substantiate the computer modeling predictions.
The conclusions of this study are contingent on accurate sampling of PV blood. To verify that atrial contamination of PV samples was minimal, an effort was made to normalize SpvO2 in all patients exhibiting PV desaturation. With a combination of increased FiO2 and PEEP, SpvO2 was raised to ≥96% in all patients, and the PV Po2 was >200 mm Hg in all patients studied at an FiO2 of 0.50 (Table). The substantial improvements in PV Po2 with increases in FiO2 and/or PEEP indicate minimal atrial contamination of PV samples. Another limitation of the study is the assumption that SVC and PV samples reflect SmVO2 and mixed SpvO2, respectively. Although these assumptions are commonly used during catheterization of single-ventricle patients, they may be inaccurate. Finally, we would caution that the findings should not be generalized too broadly. These data represent only a small sample of postoperative Norwood patients, and the observations reported are specifically relevant to the early postoperative period. The data should be interpreted carefully and should not be applied broadly to all single-ventricle patients. Low-level or subambient inspired oxygen is presumably not detrimental for patients with preoperative single-ventricle physiology and healthy lungs in whom pulmonary blood flow is limited by pulmonary vascular resistance alone. We do not advocate use of high FiO2 in single-ventricle patients with obvious pulmonary overcirculation, especially those with preoperative single-ventricle physiology. Similarly, unnecessarily high PEEP in single-ventricle patients may reduce venous return and thus be detrimental to overall cardiac output.

In summary, this study demonstrates that systemic SaO2 alone is a poor predictor of Qp:Qs in the early postoperative period after Norwood palliation. Because inaccuracy in Qp:Qs estimation resulted from variability in both SvO2 and SpvO2, the data challenge the dual assumptions used by clinicians for rapid bedside assessment of Qp:Qs. The novel observation that PV desaturation is common in the early postoperative period after Norwood palliation raises the possibility that undetected pulmonary gas exchange defects may adversely affect systemic oxygen delivery in some patients after Norwood palliation. Because unrecognized PV desaturation confounds Qp:Qs...
assessment and compromises $\text{Sao}_2$ and oxygen delivery, judicious use of inspired oxygen and PEEP in the early postoperative period after Norwood palliation may be beneficial in selected patients.

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