Cerebral near-infrared spectroscopy insensitively detects low cerebral venous oxygen saturations after stage 1 palliation

Erin Rescoe, MD,^{a,c} Xiaoqi Tang, MA,^a Dorothy Alison Perry, MBChB,^{a,c} Lynn A. Sleeper, ScD,^{a,c} James A. DiNardo, MD,^{b,d} Barry D. Kussman, MBBCh, FFA(SA),^{b,d} and John N. Kheir, MD^{a,c}

ABSTRACT

Background: Measurement of cerebral venous oxyhemoglobin saturation (ScvO₂) is considered a gold standard in assessing the adequacy of tissue oxygen delivery (DO₂) after the stage 1 palliation (S1P), with SvO₂ <30% often representing severely compromised DO₂. Regional oxygenation index (rSO₂) based on near-infrared resonance spectroscopy (NIRS) frequently is used to screen for compromised DO₂, although its sensitivity to detect severe abnormalities in SvO₂ is uncertain.

Methods: ScvO₂ was measured by co-oximetry from the internal jugular vein as clinically indicated in 73 neonates after S1P. These values were compared with cerebral rSO₂ (FORE-SIGHT; CASMED) via mixed effects model linear regression, Bland-Altman analysis, and sensitivity analysis. Because NIRS devices measure a composite of arterial and venous blood, we calculated an rSO₂-based ScvO₂ designed to remove arterial contamination from the rSO₂ signal: rSO₂-based ScvO₂ = (rSO₂ – arterial oxygen saturation × 0.3)/0.7.

Results: Among 520 time-matched pairs of ScvO₂ and cerebral rSO₂, the slope of the relationship between rSO₂ and ScvO₂ (after we adjusted for effects of hemoglobin) was 0.37 ± 0.04 with only modest correlation (r² = 0.39), and mean bias of +8.26. When ScvO₂ was <30%, cerebral rSO₂ was <30 in less than 1%, <40 less than 1%, and <50 in 45.7% of data points; specificity of rSO₂ in the same range is >99%. Correction of rSO₂ for arterial contamination significantly decreased mean bias (+3.03) and improved the sensitivity of rSO₂ to detect ScvO₂ <30 to 6.5% for rSO₂ <30, 29% for rSO₂ <40, and 77.4% for rSO₂ <50.

Conclusions: Cerebral rSO₂ in isolation should not be used to detect low ScvO₂, because its sensitivity is low, although correction of rSO₂ for arterial contamination may improve sensitivity. Cerebral rSO₂ of 50 or greater should not be considered reassuring, though values below 30 are specific for low ScvO₂. (J Thorac Cardiovasc Surg 2017;154:1056-62)

Sensitivity of near-infrared resonance spectroscopy for venous oxyhemoglobin saturation <30% is low after stage 1 palliation.

Central Message

Cerebral near-infrared resonance spectroscopy (regional oxygenation saturation [rSO₂]) insensitively detects cerebral venous oxyhemoglobin saturation less than 30% in the range of clinical interest (ie, rSO₂ 30-50), a problem improved by correcting for arterial contamination (rSO₂-based cerebral venous oxyhemoglobin saturation).

Perspective

Although cerebral near-infrared resonance spectroscopy (regional oxygenation saturation) is commonly used to detect low cardiac output, the sensitivity of cerebral near-infrared resonance spectroscopy to detect venous oxyhemoglobin saturation less than 30% is low in the range of clinical interest after stage 1 palliation. This problem is ameliorated by correction of the signal for arterial contamination by back-calculating venous oxyhemoglobin saturation from regional oxygenation saturation and arterial oxygen saturation.

See Editorial Commentary page 1063.

See Editorial page 1054.

From the Departments of ^aCardiology and ^bAnesthesiology, Perioperative, and Pain Medicine, Boston Children's Hospital, and the Departments of ^cPediatrics and ^dAnaesthesia, Harvard Medical School, Boston, Mass.

Supported by the Gerber Foundation, Hess Family Philanthropic Fund, and the Boston Children's Hospital Heart Center Strategic Investment Fund.

Received for publication Sept 2, 2016; revisions received Jan 20, 2017; accepted for publication March 16, 2017; available ahead of print June 7, 2017.

Address for reprints: John N. Kheir, MD, Department of Cardiology, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115 (E-mail: john.kheir@childrens.harvard.edu).

0022-5223/\$36.00

Copyright © 2017 by The American Association for Thoracic Surgery
<http://dx.doi.org/10.1016/j.jtcvs.2017.03.154>

Abbreviations and Acronyms

DO ₂	= systemic oxygen delivery
NIRS	= near-infrared resonance spectroscopy
r ²	= correlation coefficient
rSO ₂	= regional oxygenation saturation
S1P	= stage 1 palliation
SaO ₂	= arterial oxygen saturation
ScvO ₂	= cerebral venous oxyhemoglobin saturation
SvO ₂	= venous oxyhemoglobin saturation

Scanning this QR code will take you to a supplemental video for the article.

Optimization of systemic oxygen delivery (DO₂) during the early postoperative period after stage 1 palliation (S1P) requires accurate assessment of venous oxyhemoglobin saturation (SvO₂). Although true mixed venous blood sampling is anatomically precluded in single-ventricle anatomy, sampling from the superior vena cava (ie, cerebral venous oxyhemoglobin saturation, ScvO₂) frequently is used as a representation of the adequacy of DO₂ after S1P.¹ When oxygen consumption exceeds DO₂, tissue hypoxia develops, which increases oxygen dissociation from hemoglobin and causes venous oxyhemoglobin desaturation. In the single-ventricle population, it has been suggested that ScvO₂ <30% represents the anaerobic threshold² and that maintaining ScvO₂ >50% in the early postoperative period is associated with improved survival.^{1,3,4} Thus, accurate assessment of ScvO₂ after S1P is vital to the postoperative management of these patients.

Some groups have used venous oximetric catheters to permit continuous monitoring.⁵ These catheters are somewhat larger in caliber than standard catheters, may be more challenging to insert, and exhibit significant drift in calibration during use, such that their use is not widespread. Thus, a mainstay of patient monitoring is the use of surface oximetry with near-infrared spectroscopy (NIRS) to measure tissue O₂ saturation. Cerebral oximetry is a noninvasive optical technology that relies on the relative transparency of biological tissues (eg, scalp and skull) to near-infrared light to measure brain oxygen saturation in an uncertain mixture of arterioles, capillaries, and venules. Commercial cerebral oximeters use continuous-wave, spatially resolved spectroscopy to measure the ratio of oxyhemoglobin to total hemoglobin, providing a cerebral hemoglobin oxygen saturation. The unit is percent (%) and is referred variably to as regional oxygen saturation (rSO₂), tissue oxygen

saturation, or tissue oxygenation index, depending on the manufacturer. The ratio of venous to arterial blood in the sampled volume is approximately 70% to 30%,⁶ although it can vary significantly (as much as 85%/15%).⁷ Although hemoglobin is distributed unevenly within arteries, arterioles, capillaries, venules, and veins, the venous to arterial ratio is estimated and fixed during the calibration and validation of the monitor (eg, 70%-75% venous/25%-30% arterial⁸⁻¹⁰). Because NIRS is used commonly as a noninvasive screening tool for inadequate DO₂ after S1P, we examined the sensitivity and specificity of NIRS to detect low ScvO₂ in the postoperative setting.

METHODS**Patients**

The following retrospective study was approved by the Institutional Review Board at Boston Children's Hospital. We retrospectively studied 84 consecutive patients undergoing single-ventricle palliation for hypoplastic left heart syndrome at our institution between January 2013 and May 2016. Cerebral rSO₂ (applied to the forehead without a preference or laterality) was measured as a part of routine clinical care during this period (FORE-SIGHT tissue oximeter; CASMED, Branford, Conn). Patients who did not have cerebral NIRS data recorded during the postoperative period (n = 3) were excluded from the study. During this period, placement of an internal jugular vein catheter with the tip in the proximal superior vena cava (at or above the junction with the right atrium) was also part of routine clinical practice. Blood sampled from the superior vena cava was analyzed routinely by co-oximetry in the hospital's core laboratory (Radiometer ABL 800; Radiometer America, Brea, Calif). Presence and position of the tip of the internal jugular catheter on the first chest radiograph after admission to the intensive care unit was assessed by 2 independent investigators (E.R. and J.K.). Data were excluded for patients in whom the tip of the catheter was deep within the right atrium (n = 8), leaving a total of 73 patients. Data also were excluded during the times that patients were on extracorporeal membrane oxygenation support. A total of 15,336 hours of patient monitoring were assessed.

Data Extraction and Processing

ScvO₂ and hemoglobin were extracted automatically (Boston Children's Hospital 360; MicroStrategy, Inc, Tysons Corner, Va) from the hospital database in time- and patient-stamped fashion. Similarly, rSO₂ was extracted from 1 of 2 sources. In a subset of patients (n = 20, 26.3%), the NIRS device was tethered to the bedside monitor and the data continuously (ie, every 5 seconds) stored in a database and subsequently exported (T3 Data Collection and Analytics Software System; Etiometry, Inc, Boston, Mass) and down-sampled to every 5-minute median values (MatLab, R2015b, 8.6; MathWorks Inc, Natick, Mass). In the remainder, NIRS data were entered manually by the bedside nurse at least twice per shift, and these data were extracted from the hospital database as described previously. All data were normalized to elapsed time after removal of the aortic crossclamp (the final was chosen if multiple) via a customized MatLab script.

Data Analyses

Time-matched rSO₂ measurements were compared with ScvO₂ measurements with the use of several techniques. First, the partial correlation coefficient and slope of the relationship were measured with mixed-effects model linear regression to account for repeated measures and to control for hemoglobin with ScvO₂ as the outcome. Second, the mean bias and standard deviation (limits of agreement) between the 2 measurements were compared by Bland-Altman analysis corrected for replicate

TABLE 1. Preoperative and operative characteristics of patients included in the study

Variables	Mean $\pm$ SD
Preoperative variables	
Age at surgery, d	7.9 $\pm$ 15.2
Birth weight, kg	3.15 $\pm$ 0.48
Shunt type	
Sano conduit	57 (78%)
Modified Blalock-Taussig shunt	16 (22%)
Bypass times, min	
Cardiopulmonary bypass time	173 $\pm$ 46
Aortic crossclamp time	98 $\pm$ 37
RLFP time	71 $\pm$ 23
Circulatory arrest time	21 $\pm$ 19

SD, Standard deviation; RLFP, regional low flow perfusion.

measurements.¹¹ Third, the sensitivity and specificity of NIRS to detect ScvO₂ critical thresholds were assessed with receiver operating characteristic analysis by defining the presence of deficient oxygen delivery (ie, disease present) as ScvO₂ <30%, <40%, or <50%. Sensitivity and specificity curves were then created to describe the rSO₂ values at which NIRS is sufficiently sensitive to detect ScvO₂ <30%.

Calculation of rSO₂-based ScvO₂

Because the FORE-SIGHT device is calibrated based on a 30% arterial to 70% venous ratio,^{7,8} we calculated an rSO₂-based ScvO₂ using rSO₂ and arterial oxygen saturation (SaO₂; exported in similar fashion to SvO₂ as described previously) according to the following equation¹²: rSO₂-based ScvO₂ = (rSO₂ - SaO₂*0.3)/0.7. Completion of this calculation requires simultaneous estimation of SaO₂, ScvO₂, and rSO₂. To permit this exploratory evaluation, we interpolated all values for these 3 variables over time to provide a “best guess” for each value at 5-minute intervals. This process assumed that the rate of change between each intermittently measured value was linear. For example, if ScvO₂ at hour 1 was 50% and at hour 2 was 60%, ScvO₂ at 90 minutes was assumed to have been 55%. rSO₂-based ScvO₂ was then compared with ScvO₂ via the same techniques as described previously for rSO₂ and ScvO₂.

Evaluation of rSO₂ as a Trend Monitor

Because NIRS frequently is considered an effective trend monitor, we examined changes in rSO₂ with changes in ScvO₂ using the interpolated dataset described previously. Change in rSO₂ and change in ScvO₂ were calculated at hourly intervals and compared with one another. Data points in which there was a less than $\pm 5\%$ change in both ScvO₂ and rSO₂ were excluded. The proportion of data points in which both rSO₂ and ScvO₂ changed in the same or opposite directions by more than 5% (empirically chosen as a potentially significant change) were described, as was the proportion in which rSO₂ or ScvO₂ changed without a corresponding change in the other test. Data were described as percentages of total data points.

RESULTS

Demographic and Surgical Variables

The demographic and surgical information regarding shunt types and operative times is described in Table 1. The majority of shunt types during the study period were Sano conduits.

Relationship Between rSO₂ and ScvO₂

Among 3539 ScvO₂ measurements, a time-matched rSO₂ was found in 520 instances. Notably, in all results in which

FIGURE 1. A, Raw data for rSO₂ and ScvO₂ with crude linear regression line. Among all ScvO₂ <30, there were no rSO₂ values <30. B, Bland-Altman analysis of rSO₂ relative to ScvO₂ demonstrated a mean bias of +8.3 (limits of agreement +34.3 to -17.9). rSO₂, Regional oxygenation index; ScvO₂, cerebral venous oxyhemoglobin saturation.

ScvO₂ was <30%, rSO₂ was >30 (Figure 1, A). Even with adjustment for effects of time and hemoglobin concentration, we found rSO₂ to be an independent predictor of ScvO₂ (partial $r^2 = 0.39$, $P < .0001$); for every 1-unit increase in rSO₂ there is on average a 0.37 ± 0.04 unit (% point) increase in ScvO₂. The mean bias of rSO₂ compared with ScvO₂ was +8.26 with a standard deviation of 13.1 (Figure 1, B).

Sensitivity and Specificity of rSO₂ for ScvO₂ <30%

Using the same time-matched pairs of rSO₂ and ScvO₂, we found that the area under receiver operating characteristics curves for rSO₂ as a diagnostic test to detect ScvO₂ <30%, <40%, and <50% were 0.82, 0.84, and 0.87, respectively (Figure 2, A). However, the sensitivity of rSO₂ in the range of clinical interest in detecting ScvO₂ <30% is extremely low. As shown in Figure 2, B, rSO₂ is <30 less than 1% of the time that ScvO₂ is <30%, rSO₂ <40 less than 1% of the time, and <50 only 45.7% of the time that ScvO₂ is <30%. Conversely, the specificity of rSO₂ is favorable; rSO₂ <30 indicates that ScvO₂ will be <30% more than 99% of the time. As is

FIGURE 2. A, Receiver operating characteristics curve analysis of rSO₂ to detect ScvO₂ <30% (red line, AUC 0.82, optimal cutoff point rSO₂ 58.3), ScvO₂ <40% (blue line, AUC 0.84, optimal cutoff point rSO₂ 58.8), and ScvO₂ <50% (green line, AUC 0.87, optimal cutoff point rSO₂ 59.5). B, Defining ScvO₂ <30% as the presence of disease, rSO₂ (black line) was <30 in <1% of data points, <40 in <1% of data points, and <50 in 45.7% of data points. Subtracting arterial contamination (ie, rSO₂-based ScvO₂, gray dotted line) improved sensitivity significantly: when ScvO₂ <30, rSO₂-based ScvO₂ was <30 in 6.5% of data points, <40 in 29% of data points, and <50 in 77.4% of data points. The specificity of rSO₂ (solid red line) for ScvO₂ <30% decreased from 97% at rSO₂ of 40 to 88% at rSO₂ of 50. Subtracting arterial contamination (ie, rSO₂-based ScvO₂, red dotted line) decreased the specificity to 81% at rSO₂ of 40 and 46% at rSO₂ of 50. ScvO₂, Cerebral venous oxyhemoglobin saturation; rSO₂, regional oxygenation index.

the case with many diagnostic tests, the choice of threshold values represents a compromise between sensitivity and specificity. Some authors have suggested addressing this problem through a “gray zone” approach in which 2 (in this case, rSO₂) cutoffs are set: the first cutoff is chosen to exclude the diagnosis (here, ScvO₂ <30%) with near-certainty (ie, privilege specificity) and the second cutoff is chosen to include the diagnosis with near-certainty (ie, privilege sensitivity).¹³ In this case, the gray zone would be between an rSO₂ value of 49 (affording a privilege specificity of 90%) and 58 (affording a privilege sensitivity of 90%), which overlaps the expected range of rSO₂ completely.

rSO₂-based ScvO₂ Calculations

We identified 3539 ScvO₂ values, 3084 SaO₂ values, and 28,836 rSO₂ values among the 73 patients examined. Interpolation of these data over time permitted the comparison of 94,739 time-matched data points of rSO₂ and ScvO₂ (every 5 minutes). As expected, correcting rSO₂ for arterial contamination (by back-calculating ScvO₂ based on rSO₂) increased the slope of the rSO₂-based ScvO₂ estimate relative to time-matched ScvO₂ (from 0.38 to 0.41). The mean bias of rSO₂-based ScvO₂ relative to ScvO₂ was 3.03. Correction for arterial contamination improved the sensitivity of rSO₂ to detect ScvO₂ <30 to 6.5% for rSO₂ <30, 29.0% for rSO₂ <40, and 77.4% for rSO₂ <50 (Figure 2, B, gray dotted line). Even with adjustment for effects of time and hemoglobin concentration, we found rSO₂-based ScvO₂ to be an independent predictor of ScvO₂ (partial $r^2 = 0.42$, $P < .0001$); for every 1-unit increase in rSO₂-based ScvO₂ there is on average a 0.58 ± 0.08 unit (% point) increase in ScvO₂.

Use of rSO₂ to Trend ScvO₂

We calculated 7834 time-matched hourly changes in rSO₂ and ScvO₂. Of these, there were 7242 (92.4%) changes in which both the rSO₂ and ScvO₂ changed <5%. Excluding these “minimal change values,” ~70% of data points were characterized by a >5% change in rSO₂ with a minimal change in ScvO₂ and ~25% by a significant (>5%) change in ScvO₂ with minimal (<5%) change in rSO₂ (Figure 3). A minority (5%) of data points exhibited significant changes in rSO₂ and ScvO₂ in the same direction.

DISCUSSION

Although the primary purpose of NIRS monitoring is to permit the early detection of venous desaturation, we found that cerebral rSO₂ in isolation is highly insensitive but very specific for venous hypoxia in newborns after S1P. The area under the curve for cerebral rSO₂ was high for a diagnostic test, although this finding did not reflect the extremely poor utility of the test as a screening tool for ScvO₂ <30%. In our cohort, patients with ScvO₂ <30% exhibited a cerebral rSO₂ <30 less than 1% of the time (ie, sensitivity), and rSO₂ <50 only 46% of the time. Correction of the rSO₂ signal for the 30% SaO₂ component decreased the mean bias relative to ScvO₂, but the sensitivity remained extremely poor in the range of clinical interest. Regarding ScvO₂, a “reassuring” cerebral NIRS (eg, rSO₂ >50) should not be considered reassuring in isolation, and an rSO₂ <40% should be concerning.

There is compelling evidence that NIRS values in the operating room correlate with clinical outcomes. Operative monitoring during cardiopulmonary bypass is now a routine part of monitoring, and with good reason. Low cerebral NIRS values have been correlated with an increased

FIGURE 3. Among the 7834 hourly matched rSO_2 - $ScvO_2$ pairs, the majority (7242; 92.4%) of pairs were characterized by $<5\%$ change in both rSO_2 and $ScvO_2$. Excluding these “minimal change values,” there were more values characterized by a significant change in rSO_2 with a minimal change ($<5\%$) in $ScvO_2$ (404; 68.2%) than were characterized by a significant change in $ScvO_2$ with minimal change in rSO_2 (156; 26.3%, $P < .0001$, McNemar test). A minority of data points exhibited significant changes in both rSO_2 and $ScvO_2$ in the same direction (shaded red, 5%) or in opposite directions (shaded black, 1.1%). $ScvO_2$, Cerebral venous oxyhemoglobin saturation; rSO_2 , regional oxygenation index.

prevalence of radiographically apparent neurologic injury,¹⁴ increased biochemical markers of brain injury,¹⁵ and developmental maturity at 1-year follow-up.¹⁶ It also has been suggested that preoperative cerebral NIRS values may correlate with neurodevelopmental outcome.¹⁷

In addition to its use in the operating room, however, NIRS frequently is used in the intensive care environment as a screening tool to identify deficient DO_2 among biochemically and otherwise-reassuring patients. Thus, a clear understanding of its correlation with $ScvO_2$ is paramount to its proper interpretation. Specifically, because it is clear that $ScvO_2 < 30\%$ is associated with poor outcomes,^{2,18} the sensitivity and specificity of NIRS to detect this extreme physiologic state is important to quantify. The strength of correlation between cerebral rSO_2 and $ScvO_2$ has been described several times, often in the catheterization laboratory setting, and is highly variable, ranging from ~ 0.3 ¹⁹ to (less commonly) ~ 0.9 .²⁰ The slope of the relationship between rSO_2 and $ScvO_2$ has been reported repeatedly to be less than 0.5, indicating that rSO_2 reproducibly overestimates $ScvO_2$ with a mean bias in the $+5\%$ to 10% (ie, cerebral $rSO_2 > ScvO_2$) range.^{19,21-23} We found results similar to these and were surprised by the extremely low sensitivity of cerebral NIRS to detect even the most severe aberrations in DO_2 (ie, $ScvO_2 < 30\%$). We also noted that cerebral rSO_2 frequently changes in the absence of corresponding $ScvO_2$ changes and conversely may not reflect measured $ScvO_2$ changes. This phenomenon was also described in 70

infants after congenital heart surgery, in which cerebral rSO_2 and $ScvO_2$ changed in opposite directions $\sim 40\%$ of the time.²⁴ These findings raise concerns regarding the utility of cerebral NIRS even as a trend monitor, as shown in Video 1.

There are several possible explanations for the poor sensitivity, or systematic overestimation, of rSO_2 relative to $ScvO_2$ in our study. One of the important limitations of current NIRS technology is the use of a fixed ratio of venous to arterial blood volume distribution (eg, 30:70), an estimate that has not been validated for the cerebral circulation in vivo and may in fact be closer to 15:85.⁷ This is consistent with the substantially improved sensitivity of cerebral rSO_2 in our study after correction of rSO_2 for arterial contamination. Furthermore, it is likely that this ratio is dynamic in the perioperative period, given the variability in cardiac output, arterial, and venous pressures and capacitance, temperature, carbon dioxide and oxygen tensions, and vasoactive agent administration that is common after SIP. It is possible that the emergence of frequency domain NIRS will obviate the need to estimate the venous-arterial ratio and permit more sensitive identification of cerebral venous desaturation.²⁵

Another explanation may be contamination of the region of interest with myoglobin, which shares similar optical properties to hemoglobin. Because of myoglobin's profound affinity for oxygen (oxygen tension at which hemoglobin is 50% saturated ~ 3.5 mm Hg), myoglobin

VIDEO 1. Cerebral oxygen delivery in the single-ventricle circulation can be compromised by diminished cardiac output, diminished systemic blood flow, arterial hypoxemia, anemia, and other causes. Accurate assessment of the adequacy of cerebral oxygen delivery is vital to the treatment of these patients. Because measurement of gold standards such as tissue oxygen tension and mixed venous saturation are precluded in infants with univentricular heart disease, adequacy of DO_2 frequently is performed through oxyhemoglobin saturation of blood from the superior vena cava (ScvO_2). Because of the risks of repeated phlebotomy, cerebral NIRS is used commonly as a surrogate metric to screen patients for deficient DO_2 . In this study, we found that cerebral NIRS values are insensitive in detecting $\text{ScvO}_2 < 30\%$ until the rSO_2 exceeds 50, which is near the normal range. Mathematically subtracting the arterial component from rSO_2 improved sensitivity for $\text{ScvO}_2 < 30\%$ significantly. In the intensive care unit, a cerebral rSO_2 in the normal range should not be considered reassuring, at least in isolation. Video produced by Alexanimation, LLC. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)30900-5/addons](http://www.jtcvsonline.org/article/S0022-5223(17)30900-5/addons).

remains in the oxygenated state in nearly all clinically relevant circumstances and may lead to a systematic overestimation of oxyhemoglobin concentration if the signal is not distinguished properly. However, this would not be expected to be a major contributor to transcranial readings in a newborn, given the diminutive muscle mass of the fronto-temporal region.²⁶ Furthermore, different iterations of devices from a variety of manufacturers may perform differently based on internal algorithms.^{27,28}

It is important to note that rSO_2 has been shown to be useful as a screening tool when somatic and cerebral rSO_2 are used in combination. Specifically, the difference between somatic and cerebral rSO_2 in healthy infants is known to be $\sim 10\%$ (ie, renal-somatic rSO_2 is ~ 8 - 10 greater than cerebral rSO_2 ²⁹), putatively reflecting the high ratio of oxygen delivery to oxygen demand of the kidneys (given their function as a blood filter) relative to that of the brain. Under conditions of redistribution (eg, shock states), however, the somatic-cerebral rSO_2 difference is abolished or even reversed, reflecting the redistribution of limited blood flow toward the brain and away from the abdomen. It has even been suggested that a lower somatic-cerebral rSO_2 difference correlates with length of stay, biochemical markers of malperfusion, and mortality after SIP.³⁰ Thus, it is likely that use of cerebral and somatic NIRS in combination would improve sensitivity for low ScvO_2 ; cerebral rSO_2 in isolation performs poorly.

Limitations

There are several limitations to our study that merit discussion. Given that this was intended to be a study of the utility of NIRS as a reflection of clinically followed ScvO_2 , the ScvO_2 was drawn from internal jugular catheters placed at the superior vena cava-right atrial junction, rather than within the jugular bulb. It is possible that the sensitivity of rSO_2 would have improved if we had compared it with SvO_2 from the jugular bulb. We were careful to only use ScvO_2 from catheters terminating outside the bounds of the common atrium, although it is possible for venous samples to become arterialized by rapid sampling or by bubble contamination. However, these sources of error would raise ScvO_2 measurements and diminish the biases we found. Second, we used a data interpolation scheme to accomplish data matching between SaO_2 , ScvO_2 , and rSO_2 to remove arterial contamination from the rSO_2 signal and to examine changes over time. This technique makes major assumptions regarding linear rates of change over time that may not be true. In the future, a prospective study with matched arterial and venous blood sampling may obviate the need for this technique.

CONCLUSIONS

Cerebral rSO_2 in isolation should not be used to detect low ScvO_2 , because its sensitivity is low, although correction of rSO_2 for arterial contamination significantly improves sensitivity. Cerebral rSO_2 of 50 or greater should not be considered reassuring with regard to ScvO_2 , although values < 30 are specific for low ScvO_2 .

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

References

- Tweddell JS, Ghanayem NS, Mussatto KA, Mitchell ME, Lamers LJ, Musa NL, et al. Mixed venous oxygen saturation monitoring after stage 1 palliation for hypoplastic left heart syndrome. *Ann Thorac Surg*. 2007;84:1301-11.
- Hoffman GM, Ghanayem NS, Kampine JM, Berger S, Mussatto KA, Tweddell JS. Venous saturation and the anaerobic threshold in neonates after the Norwood procedure for hypoplastic left heart syndrome. *Ann Thorac Surg*. 2000;70:1515-20; discussion 1521.
- Tweddell JS, Hoffman GM, Mussatto KA, Fedderly RT, Berger S, Jaquiss RD, et al. Improved survival of patients undergoing palliation of hypoplastic left heart syndrome: lessons learned from 115 consecutive patients. *Circulation*. 2002;106(12 suppl 1):I82-9.
- 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.
- 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; discussion 167-8.
- Ito H, Kanno I, Iida H, Hatazawa J, Shimosegawa E, Tamura H, et al. Arterial fraction of cerebral blood volume in humans measured by positron emission tomography. *Ann Nucl Med*. 2001;15:111-6.

7. Watzman HM, Kurth CD, Montenegro LM, Rome J, Steven JM, Nicolson SC. Arterial and venous contributions to near-infrared cerebral oximetry. *Anesthesiology*. 2000;93:947-53.
8. Benni PB, Chen B, Dykes FD, Wagoner SF, Heard M, Tanner AJ, et al. Validation of the CAS neonatal NIRS system by monitoring vv-ECMO patients: preliminary results. *Adv Exp Med Biol*. 2005;566:195-201.
9. Pollard V, Prough DS, Demelo AE, Deyo DJ, Uchida T, Stoddart HF. Validation in volunteers of a near-infrared spectroscope for monitoring brain oxygenation in vivo. *Anesth Analg*. 1996;82:269-77.
10. McCormick PW, Stewart M, Goetting MG, Balakrishnan G. Regional cerebrovascular oxygen saturation measured by optical spectroscopy in humans. *Stroke*. 1991;22:596-602.
11. Carstensen B, Simpson J, Gurrin LC. Statistical models for assessing agreement in method comparison studies with replicate measurements. *Int J Biostatist*. 2008;4:1-28.
12. Ikeda K, MacLeod DB, Grocott HP, Moretti EW, Ames W, Vacchiano C. The accuracy of a near-infrared spectroscopy cerebral oximetry device and its potential value for estimating jugular venous oxygen saturation. *Anesth Analg*. 2014;119:1381-92.
13. Cannesson M, Le-Manach Y, Hofer CK, Goarin JP, Lehot JJ, Vallet B, et al. Assessing the diagnostic accuracy of pulse pressure variations for the prediction of fluid responsiveness: a "gray zone" approach. *Anesthesiology*. 2011;115:231-41.
14. Dent CL, Spaeth JP, Jones BV, Schwartz SM, Glauser TA, Hallinan B, et al. Brain magnetic resonance imaging abnormalities after the Norwood procedure using regional cerebral perfusion. *J Thorac Cardiovasc Surg*. 2006;131:190-7.
15. Abu-Sultaneh S, Hehir DA, Murkowski K, Ghanayem NS, Liedel J, Hoffmann RG, et al. Changes in cerebral oxygen saturation correlate with S100B in infants undergoing cardiac surgery with cardiopulmonary bypass. *Pediatr Crit Care Med*. 2014;15:219-28.
16. Kussman BD, Wypij D, Laussen PC, Soul JS, Bellinger DC, DiNardo JA, et al. Relationship of intraoperative cerebral oxygen saturation to neurodevelopmental outcome and brain magnetic resonance imaging at 1 year of age in infants undergoing biventricular repair. *Circulation*. 2010;122:245-54.
17. Hansen JH, Rotermann I, Logoteta J, Jung O, Dütschke P, Scheewe J, et al. Neurodevelopmental outcome in hypoplastic left heart syndrome: impact of perioperative cerebral tissue oxygenation of the Norwood procedure. *J Thorac Cardiovasc Surg*. 2016;151:1358-66.
18. Ronco JJ, Ronco JJ, Fenwick JC, Wiggs BR, Phang PT, Cooper DJ, et al. Identification of the critical oxygen delivery for anaerobic metabolism in critically ill septic and nonseptic humans. *JAMA*. 1993;270:1724-30.
19. Ricci Z, Garisto C, Favia I, Schloderer U, Giorni C, Fragasso T, et al. Cerebral NIRS as a marker of superior vena cava oxygen saturation in neonates with congenital heart disease. *Paediatr Anaesth*. 2010;20:1040-5.
20. Abdul-Khaliq H, Troitzsch D, Berger F, Lange PE. Regional transcranial oximetry with near infrared spectroscopy (NIRS) in comparison with measuring oxygen saturation in the jugular bulb in infants and children for monitoring cerebral oxygenation [in German]. *Biomed Tech (Berl)*. 2000;45:328-32.
21. Nagdyman N, Ewert P, Peters B, MIERA O, Fleck T, Berger F. Comparison of different near-infrared spectroscopic cerebral oxygenation indices with central venous and jugular venous oxygenation saturation in children. *Paediatr Anaesth*. 2008;18:160-6.
22. Li J, Van Arsdell GS, Zhang G, Cai S, Humpl T, Caldarone CA, et al. Assessment of the relationship between cerebral and splanchnic oxygen saturations measured by near-infrared spectroscopy and direct measurements of systemic haemodynamic variables and oxygen transport after the Norwood procedure. *Heart*. 2006;92:1678-85.
23. Tortoriello TA, Stayer SA, Mott AR, McKenzie ED, Fraser CD, Andropoulos DB, et al. A noninvasive estimation of mixed venous oxygen saturation using near-infrared spectroscopy by cerebral oximetry in pediatric cardiac surgery patients. *Paediatr Anaesth*. 2005;15:495-503.
24. McQuillen PS, Nishimoto MS, Bottrell CL, Fineman LD, Hamrick SE, Glidden DV, et al. Regional and central venous oxygen saturation monitoring following pediatric cardiac surgery: Concordance and association with clinical variables. *Pediatr Crit Care Med*. 2007;8:154-60.
25. Dehaes M, Aggarwal A, Lin P-Y, Rosa Fortunato C, Fenoglio A, Roche-Labarbe N, et al. Cerebral oxygen metabolism in neonatal hypoxic ischemic encephalopathy during and after therapeutic hypothermia. *J Cereb Blood Flow Metab*. 2014;34:87-94.
26. Scheeren TWL, Schober P, Schwarte LA. Monitoring tissue oxygenation by near infrared spectroscopy (NIRS): background and current applications. *J Clin Monit Comput*. 2012;26:279-87.
27. Naguib AN, Winch PD, Sebastian R, Gomez D, Guzman L, Rice J, et al. The correlation of two cerebral saturation monitors with jugular bulb oxygen saturation in children undergoing cardiopulmonary bypass for congenital heart surgery. *J Intensive Care Med*. August 15, 2016 [Epub ahead of print].
28. Bickler PE, Feiner JR, Rollins MD. Factors affecting the performance of 5 cerebral oximeters during hypoxia in healthy volunteers. *Anesth Analg*. 2013;117:813-23.
29. Bernal NP, Hoffman GM, Ghanayem NS, Arca MJ. Cerebral and somatic near-infrared spectroscopy in normal newborns. *J Pediatr Surg*. 2010;45:1306-10.
30. Hoffman GM, Ghanayem NS, Mussatto KA, Berens RJ, Tweddell JS. Postoperative two-site NIRS predicts complications and mortality after stage 1 palliation of HLHS. *Anesthesiology*. 2007;107:A234.

Key Words: Norwood procedure, near-infrared spectroscopy, oxygen delivery, hypoxemia, postoperative monitoring

Readers who found these articles interesting may also like to read the following papers found in recent and future issues of our sister publications, *Seminars in Thoracic and Cardiovascular Surgery* and *Operative Techniques in Thoracic and Cardiovascular Surgery*!

Acquired: Perioperative Management

ORIGINAL SUBMISSION: The Effects of Steroids on Coagulation Dysfunction Induced by Cardiopulmonary Bypass: A Steroids in Cardiac Surgery (SIRS) Trial Substudy. Domenico Paparella. *Semin Thoracic Surg* 2017: In press.

Editorial Commentary: Steroids and Cardiopulmonary Bypass: a Never-ending Story. Thierry Carrel. *Semin Thoracic Surg* 2017: In press.

ORIGINAL SUBMISSION: Controlled Exponentially Weighted Moving Average Chart in Cardiac Surgery: A Simulation Study Across 9 Italian Cardiac Centers. Marco Moscarelli. *Semin Thoracic Surg* 2016:253-258.

Editorial Commentary: Statistical Process Control in Cardiac Surgery? Ask Your Doctor. Paul Kurlansky. *Semin Thoracic Surg* 2016:259-260.

ORIGINAL SUBMISSION: Early Extubation: A Proposed New Metric. Todd C. Crawford. *Semin Thoracic Surg* 2016:290-299.

Editorial Commentary: Early Extubation: A Proposed New Metric or What Was First: The Egg or the Chicken? Thierry Carrel. *Semin Thoracic Surg* 2016:300-301.