

Noninvasive Cerebral Oximeter as a Surrogate for Mixed Venous Saturation in Children

Adnan T. Bhutta · Jesse W. Ford · James G. Parker · Parthak Prodhana ·
Eudice E. Fontenot · Paul M. Seib · Brittany I. Stroope · Elizabeth A. Frazier ·
Michael L. Schmitz · Jonathan J. Drummond-Webb · William R. Morrow

Received: 28 March 2006 / Accepted: 30 August 2006
© Springer Science+Business Media, Inc. 2007

Abstract We evaluated the relationship between regional cerebral oxygen saturation (rSO_2) measured by near-infrared spectroscopy (NIRS) cerebral oximeter with superior vena cava (SVC), inferior vena cava (IVC), right atrium (RA), and pulmonary artery (PA) saturation measured on room air and 100% inspired oxygen administered via a non-rebreather mask (NRB) in children. Twenty nine pediatric post-orthotopic heart transplant patients undergoing an annual myocardial biopsy were studied. We found a statistically significant correlation between rSO_2 and SVC saturations at room air and 100% inspired oxygen concentration via NRB ($r = 0.67$, $p = 0.0002$ on room air; $r = 0.44$, $p = 0.02$ on NRB), RA saturation ($r = 0.56$, $p = 0.002$; $r = 0.56$, $p = 0.002$), and PA saturation ($r = 0.67$, $p < 0.001$; $r = 0.4$, $p = 0.03$). A significant correlation also existed between rSO_2 and measured cardiac index ($r = 0.45$, $p = 0.01$) and hemoglobin levels ($r = 0.41$, $p = 0.02$). The concordance correlations were fair to moderate. Bias and precision of rSO_2 compared to

PA saturations on room air were -0.8 and 13.9% , and they were 2.1 and 15.6% on NRB. A stepwise linear regression analysis showed that rSO_2 saturations were the best predictor of PA saturations on both room air ($p = 0.0001$) and NRB ($p = 0.012$). In children with biventricular anatomy, rSO_2 readings do correlate with mixed venous saturation.

Keywords Pediatrics · Near-infrared spectroscopy · Cardiac catheterization · Mixed venous saturation · Central venous saturation · Oxygen consumption

Introduction

Jobsis [15] was the first to describe the use of near-infrared spectroscopy (NIRS) technology in humans when he detected transmission of photons through the brain tissue. Since then, the NIRS-based technology has found diverse applications in monitoring of deltoid muscle oxygen supply to guide resuscitation [30], monitoring of splanchnic circulation in neonates with acute abdomen [10, 43, 47], and in measuring regional blood supply in skeletal muscles to assess the effects of exercise [5, 8].

However, the most common application of this technology has been in assessing regional cerebral saturation. This application stems from multiple studies that have shown a positive correlation between cerebral oxygenation as measured by NIRS and jugular venous saturation ($SjVO_2$) [1, 2, 12, 19, 28, 29, 35, 36, 38]. Clinical studies in adults have suggested that a decline in regional cerebral oxygen saturation (rSO_2) values of $>20\%$ from baseline or absolute values of less than 50 are associated with decreased cognitive

A.T. Bhutta (✉) · J.W. Ford · J.G. Parker ·
P. Prodhana · E.E. Fontenot · P.M. Seib ·
B.I. Stroope · E.A. Frazier · W.R. Morrow
Department of Pediatrics, University of Arkansas for
Medical Sciences and Arkansas Children's Hospital,
Little Rock, AR 72202, USA
e-mail: bhuttaadnant@uams.edu

M.L. Schmitz
Department of Anesthesiology, University of Arkansas for
Medical Sciences and Arkansas Children's Hospital,
Little Rock, AR 72202, USA

J.J. Drummond-Webb
Department of Surgery, University of Arkansas for Medical
Sciences and Arkansas Children's Hospital, Little Rock, AR
72202, USA

function and prolonged intensive care unit (ICU) stay [6, 31]. Such a sharp decline from a baseline measurement or a low absolute value may affect long-term neurological outcome.

As many as 50% of neonatal patients undergoing cardiac surgery on cardiopulmonary bypass (CPB) are at risk for developing mild ischemic lesions, primarily in the form of Periventricular Leukomatacia (PVL), postoperatively [26]. Therefore, a monitor that allows clinicians to follow trends in cerebral oxygenation could identify critical periods associated with inadequate oxygenation [1, 2, 33], which in turn could lead to early interventions to minimize such periods. After initially being utilized in operating rooms [3], it is now increasingly being used as a non-invasive method to monitor regional oxygen saturation during the postoperative period after cardiac surgery [32, 46], and some authors have suggested that rSO_2 should be routinely used to guide therapy to minimize periods of low oxygen delivery [13].

However, previously published studies show a correlation between rSO_2 and mixed venous saturation ($SmVO_2$) in patients with a variety of congenital heart diseases with different anatomy and physiology, surgical course, postoperative respiratory and hemodynamic support, and measurement sites for mixed venous saturations. Thus, the results from these studies cannot be generalized to other clinical settings.

In order to minimize some of this variability, we designed a prospective study to examine the relationship between rSO_2 and saturations measured in the superior vena cava (SVC) and right atrium (RA) (also known as central venous saturations or $ScVO_2$) and pulmonary artery (PA) ($SmVO_2$), both on room air and on 100% inspired oxygen administered via a non-rebreather mask. Our study population included patients with biventricular anatomy who were undergoing routine cardiac catheterization for annual biopsies after orthotopic heart transplant.

Materials and Methods

Study Population

Twenty-nine pediatric patients who had previously undergone an orthotopic heart transplant and were undergoing cardiac catheterization for a routine annual myocardial biopsy or for hemodynamic measurement were recruited for this study prospectively. The institutional review board of the University of Arkansas for Medical Sciences approved this study. The study was performed in the cardiac catheterization laboratory at

Arkansas Children's Hospital. Informed consent was obtained from the patients' legal guardians and patient assent from children older than 7 years.

Cerebral Oximeter

The continuous, non-invasive cerebral oximeter uses NIRS technology to measure regional changes in oxygenated and deoxygenated hemoglobin in the brain. It does this by emitting light of two different wavelengths (730 and 810 nm), which corresponds to the spectral absorption of oxygenated and deoxygenated hemoglobin. Light in the visible spectrum (400–700 nm) is highly absorbed and can penetrate only go a few millimeters into tissue [8]. Light in the near infrared spectrum (700–1100 nm) undergoes the least amount of absorption and scattering and can thus travel for long distances through biological materials [15]. Deoxygenated hemoglobin absorbs light in the range of 760 nm or lower, whereas both deoxygenated and oxygenated hemoglobin absorb light at 800 nm [27]. Thus, the passage of light of two different wavelengths can allow the opportunity to assess the quantitative changes in the concentrations of these molecules.

The INVOS 5100B cerebral oximeter (Somanetics, Troy, MI, USA) was purchased for use in this study through an intramural grant. The sensors were placed on each side of the patient's forehead, with the lower edge above the patient's eyebrows and the medial edge of the sensor in the midline as per the manufacturer's specifications. No data obtained by this device were used for making clinical decisions.

Data Collection

During these routine cardiac catheterizations, blood samples were collected in capillary tubes from the SVC, inferior vena cava (IVC), RA, and PA to measure oxygen saturations and hemoglobin while the patient was breathing room air using the GEM OPL oximeter (Instrumentation Laboratory, Lexington, MA, USA). In addition, thermodilution measurements to assess the cardiac index (CI) were performed. We also obtained the saturation measurements from sites previously mentioned on 100% fractional inspired oxygen (FiO_2) administered through a non-rebreather mask (NRB). Measurements were taken after patients had been on oxygen for 5 minutes. This was done to assess whether the NIRS monitor continues to have a good correlation under hyperoxic conditions. The blood samples for measurements of oxygen saturations were obtained from the same anatomical site in each of the patients when sampling the IVC, SVC, RA, and PA.

Data were collected by the primary investigator (PI) or a co-investigator. Data collected included baseline rSO_2 values and rSO_2 values every 2 minutes on room air and 100% FiO_2 via NRB mask. In addition, simultaneous rSO_2 values and oxygen saturation from the sites mentioned previously were collected. The CI was determined by thermodilution method. We collected other information, including patient age, sex, weight, height, medical diagnoses, baseline vital signs, and vital signs every 2 minutes during the procedure (heart rate, respiratory rate, blood pressure, and systemic oxygen saturations).

Data were entered in a Microsoft Excel spreadsheet designed for this study. This spreadsheet was only accessible to the PI or the co-investigators.

Statistical Analysis

Descriptive statistics were performed on the demographic data. We calculated the Pearson's correlation between the rSO_2 values and the measured saturations at the same time points. Statistical significance was set at p values of <0.05 . We also calculated Pearson's correlation, which tests whether the line of fit has a slope different from zero, and Lin's concordance correlation, which tests whether the line of fit has a slope different from identity (line of perfect agreement). Bland–Altman plots, which illustrate the difference versus the average of the two methods [4], were used to estimate the precision and bias of the study variables.

In addition, a linear regression analysis with stepwise variable selection was performed. Dependent variables included the SVC, IVC, RA, and PA saturations, whereas the independent variables included age, sex, systolic blood pressure percentile (adjusted for height), hemoglobin, pulse oximeter values, rSO_2 and cardiac index. A p value of 0.2 was used to enter the model, and a 0.1 cut off was used to be removed from the model.

Data were analyzed using SAS version 8.2.

Results

Of 29 patients, 13 (45%) were female and 16 (55%) were male. Twenty-two patients (76%) were Caucasian and 7 non-Caucasian. The mean age was 8 years, 7 months, with a range of 15 months to 17 years, 6 months. The mean weight was 28 kg (range, 8.2–70 kg).

Using Pearson's correlation, we found a statistically significant correlation between rSO_2 and the SVC saturation ($r = 0.65$, $p = 0.0003$ on room air; $r = 0.44$,

Table 1 Pearson's correlations and Lin's concordance correlations calculated between PA and IVC, rSO_2 SVC, and RA saturation on room air and NRB mask

PA	<i>n</i>	Pearson's correlation	Pearson's <i>p</i> value	Concordance
Room air				
IVC	23	0.50	0.0144	0.37
rSO_2	28	0.67	0.0001	0.53
SVC	26	0.85	<0.0001	0.73
RA	27	0.86	<0.0001	0.82
NRB mask				
IVC	22	0.35	0.1101	0.28
rSO_2	28	0.40	0.0330	0.35
SVC	26	0.69	<0.0001	0.66
RA	27	0.84	<0.0001	0.79

IVC, inferior vena cava; NRB, non-rebreather mask; PA, pulmonary artery; RA, right atrium; rSO_2 , regional cerebral oxygen saturation; SVC, superior vena cava

$p = 0.02$ on NRB mask), RA ($r = 0.56$, $p = 0.002$; RA $r = 0.57$, $p = 0.002$), and PA ($r = 0.67$, $p < 0.001$, $r = 0.4$, $p = 0.03$) at room air and NRB mask, respectively. A significant correlation also existed between rSO_2 and measured cardiac index (CI) ($r = 0.45$, $p = 0.01$) and hemoglobin ($r = 0.41$, $p = 0.02$). No statistically significant correlation was found between rSO_2 and IVC saturation ($r = 0.32$, $p = 0.13$ on room air; $r = -0.32$, $p = 0.14$ on NRB mask). The Pearson's and Lin's correlations between PA and SVC, RA, and IVC on room air and NRB are shown in Table 1.

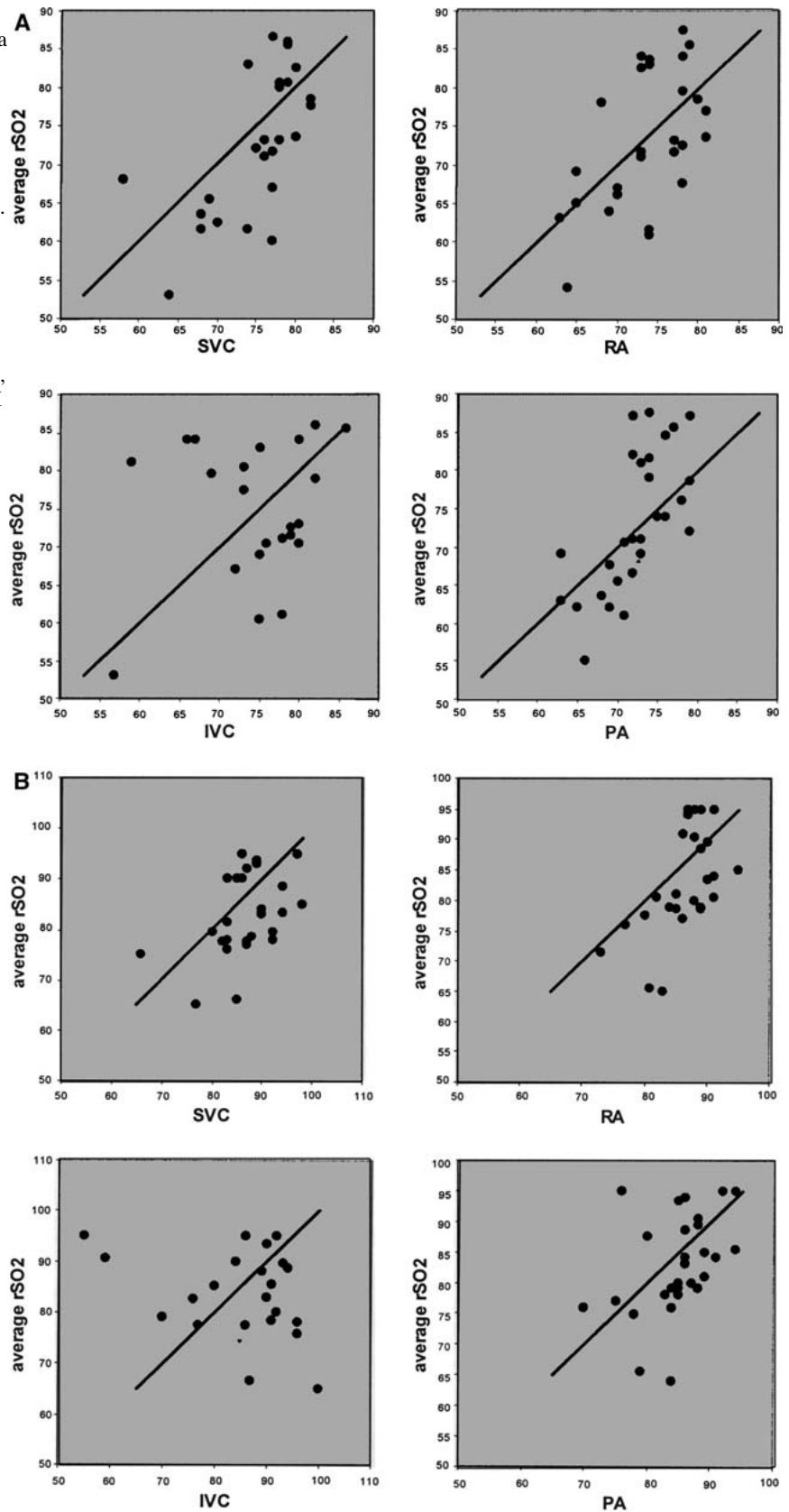
The Lin's concordance correlation coefficients for SVC, IVC, RA, and PA saturation measurements with rSO_2 on room air and oxygen are shown in Fig. 1. Using the scale proposed by Landis and Koch [24], the strength of agreement ranges between fair to moderate. The Bland–Altman plots showing the bias and precision are shown in Fig. 2.

The stepwise linear regression analysis was performed to examine the variables that best predict PA saturations. Age, sex, systolic blood pressure percentile (adjusted for height), hemoglobin, pulse oximeter values, rSO_2 , and cardiac index were used in the model. The best predictor of PA saturation was rSO_2 on both room air ($p = 0.001$) and NRB ($p = 0.012$). The only other statistically significant predictor of PA saturation on room air was pulse oximeter value ($p = 0.03$), whereas hemoglobin level was the only other significant predictor on NRB ($p = 0.04$).

Discussion

Our study shows that the NIRS cerebral oximeter readings do correlate with $SmVO_2$ both on room air

Fig. 1 (A) Lin's concordance correlation calculated on room air for superior vena cava (SVC) saturation compared to rSO₂ was 0.55 (95% CI 0.28–0.74); the concordance correlation for right atrium (RA) saturation was 0.49 (95% CI 0.2–0.7) that for interior vena cava (IVC) saturation was 0.31 (95% CI 0.09–0.63), and that for pulmonary artery (PA) saturation was 0.53 (95% CI 0.31–0.69). (B) Lin's concordance correlation calculated on 100% oxygen administered via a non-rebreather mask for SVC saturation compared to rSO₂ was 0.38 (95% CI 0.05–0.64); the concordance correlation RA saturation was 0.42 (95% CI 0.15–0.64); IVC saturation was -0.3 (95% CI -0.6–0.09), and that for PA saturation was 0.36 (95% CI 0.03–0.61)



and on 100% inspired oxygen administered via NRB mask. Although the absolute rSO_2 values are different from $SmVO_2$ because of the regional nature of monitoring, the mix of arterial and venous blood being monitored, and the physical properties of near infrared light, they trend in the same direction as the $ScVO_2$ and $SmVO_2$. We show a fair to moderate agreement of rSO_2 values with $ScVO_2$ and $SmVO_2$ on both room air and 100% inspired oxygen delivered via NRB mask in postcardiac transplant patients with no intracardiac shunting. However, the correlation between rSO_2 and $SmVO_2$ is better on room air than on NRB, and variance in mixed venous saturation accounted for the largest source of variance in rSO_2 . Furthermore, the bias and precision of rSO_2 values compared to $SmVO_2$ and $ScVO_2$ in our study (see Fig. 2) were similar to the measurements obtained in other studies [19, 46]. The bias between rSO_2 and $SmVO_2$ in our study is small, signifying that the difference between the averages of rSO_2 values and the measured values was small, whereas the large precision signifies the variability between the rSO_2 readings, which can result from changes in physiological states or changes in the measuring instrument.

The results of our study confirm findings of other published studies on postoperative patients. Tortoriello et al. [46] reported a Spearman's correlation of 0.67 between rSO_2 and $SmVO_2$ measured in the SVC or PA. They published a study of 20 patients with a variety of congenital cardiac lesions who underwent biventricular repair or single ventricle palliation. Nagdyman et al. [32] compared rSO_2 values with saturations measured in the RA in children who underwent repair of noncyanotic congenital heart lesions and found a significant correlation ($r = 0.52$) between rSO_2 and SvO_2 . However, these investigators did not measure saturations at any other site or under varying conditions of inspired oxygen.

$SmVO_2$ reflects a global balance between oxygen delivery and tissue oxygen demands. A decrease in $SmVO_2$ reflects either a decrease in oxygen delivery or an increase in tissue oxygen demands. Current continuous $SmVO_2$ monitors use infrared oximetry to detect oxygenated hemoglobin. However, these monitors are placed invasively in the pulmonary artery, which limits their clinical application in children. As an alternative, central venous oxygen saturation measured via catheters placed in the SVC or RA is often used. This technique, although invasive, is more easily achieved due to routine placement of central venous catheters in ICU patients. Rivers et al. [40] have summarized the numerous studies done to evaluate the correlation between $ScVO_2$ and $SmVO_2$ and concluded that

$ScVO_2$ is a satisfactory substitute for $SmVO_2$. Although the absolute values of $ScVO_2$ and $SmVO_2$ may differ, they track each other closely under both physiologic and pathologic conditions [25, 39]. When $SmVO_2$ remains persistently low, tissue hypoxia and lactic acidosis develop [17, 40]. $SmVO_2$ monitoring is used extensively in a multitude of clinical scenarios in both adults and children to monitor the relationship between oxygen delivery and tissue oxygen demand [7, 14, 18, 20–22, 34, 37, 41, 42].

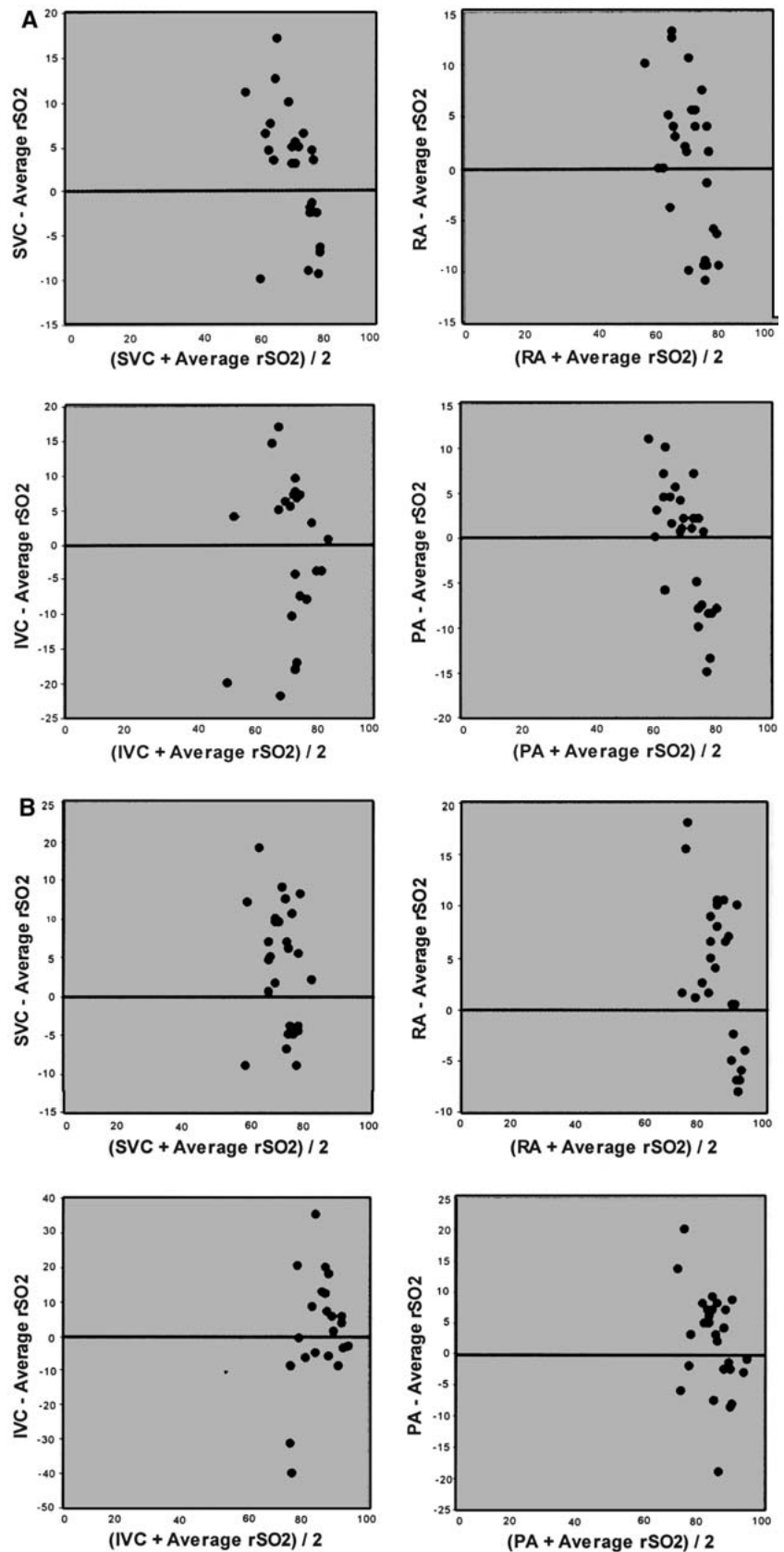
Multiple studies have shown that $SmVO_2$ values do not correlate well with IVC saturations in children [9, 44, 45]. Our study results also confirm the findings from these prior investigations.

The limitations of NIRS technology include absorption of 10–15% of the emitted light by extracranial tissue and skull [11, 15, 27]. However, the degree of absorption of emitted light by the extracranial tissue and skull may vary with patient age. In infants and younger children, this light absorption may be smaller because the light can penetrate into deeper tissues compared to older children. Photons get absorbed in larger blood vessels, whereas light passing through small vessels is absorbed to a very small degree. Therefore, NIRS predominantly detects changes in tissue oxygenation at the level of capillaries, venules, arterioles, and the intracellular compartment [27]. The biologic variations in transcranial optical path length and cerebral hemoglobin concentration between subjects may also introduce potential sources of error and variability [23].

The validity of comparing rSO_2 and $SjVO_2$ has been questioned by some investigators [38] because $SjVO_2$ measures saturation in the venous compartment, whereas rSO_2 measures saturation in arteries, capillaries, and veins. The rSO_2 values displayed are based on the assumption that cerebral tissue contains arterial and venous blood distributed in a 1:3 ratio. Watzman et al. [48] have shown that the contribution of arterial and venous blood may vary between 40:60 and 0:100, respectively. However, blood in the venous compartment does account for the majority of the hemoglobin measured by NIRS technology. rSO_2 values do change appropriately with changes in inspired oxygen concentration. A decrease in arterial and venous saturations was seen in studies on healthy volunteers who were administered a hypoxic gas mixture [28, 35].

Our investigation is limited to studying only two different clinical conditions (room air and NRB mask). We did not perform our study over a range of varying FiO_2 concentrations. We found that the correlation and agreement between rSO_2 and PA were higher on room air and worsened on NRB mask. This was true

Fig. 2 (A) The bias and precision (twice the standard deviation of the error) of rSO_2 when compared on room air with superior vena cava (SVC) saturation were 1.9 and 14.4%; the bias and precision in comparison with right atrium (RA) saturation were 0.48 and 14.7% those in comparison with interior vena cava (IVC) saturation -0.9 and 22%, and those in comparison with pulmonary artery (PA) saturation were -0.8 and 13.9%. (B) The bias and precision (twice the standard deviation of the error) of rSO_2 when compared on 100% oxygen administered via a non-rebreather mask with SVC saturation were 3.9 and 15.7%; the bias and precision in comparison with RA saturation were 3.5 and 13.9%, those in comparison with IVC saturation were 1.6 and 32%, and those in comparison with PA saturation were 2.1 and 15.6%



for the relationship between the PA and ScVO₂ as well. Hemoglobin concentration becomes more significant as a predictor of rSO₂ when breathing inspired oxygen. It is possible that the increased FiO₂ delivered via NRB mask may have altered the distribution ratio of blood between the venous and arterial compartments in the cerebral circulation. This may have led to a decrease in correlation and agreement between rSO₂ and SmVO₂ in our study [48]. Another limitation of our study is that we did not measure PaCO₂ levels, which can significantly alter cerebral blood flow [16, 36], or investigate the effects of hyper or hypo ventilation on rSO₂ and the effects on correlation with various measured saturation values in our study subjects. We assumed that for the duration of the procedure, the PaCO₂ values would remain unchanged. Our study population did not include neonates and infants.

Conclusions

In children with no intracardiac shunts, who have no obvious cerebral injury or evidence of inadequate systemic oxygen delivery, continuous rSO₂ measured using the noninvasive NIRS monitor shows correlation and agreement with mixed venous saturations. This agreement is stronger on room air than on 100% inspired oxygen. Therefore, rSO₂ measurements can be used as a monitor for trends in mixed venous saturations. However, this should be used keeping in mind the limitations of this technique.

Acknowledgment This work was supported by the University of Arkansas for Medical Sciences College of Medicine Dean's CUMG/Research Development Fund Grant Program.

References

- Abdul-Khaliq H, Schubert S, Troitzsch D, et al. (2001) Dynamic changes in cerebral oxygenation related to deep hypothermia and circulatory arrest evaluated by near-infrared spectroscopy. *Acta Anaesth Scand* 45:696–701
- Abdul-Khaliq H, Troitzsch D, Schubert S, et al. (2002) Cerebral oxygen monitoring during neonatal cardiopulmonary bypass and deep hypothermic circulatory arrest. *Thorac Cardiovasc Surg* 50:77–81
- Andropoulos DB, Stayer SA, Diaz LK, Ramamoorthy C (2004) Neurological monitoring for congenital heart surgery. *Anesth Analg* 99:1365–1375
- Bland JM, Altman DG (1999) Measuring agreement in method comparison studies. *Stat Methods Med Res* 8:135–160
- Boushel R, Langberg H, Olesen J, et al. (2000) Regional blood flow during exercise in humans measured by near-infrared spectroscopy and indocyanine green. *J Appl Physiol* 89:1869–1878
- Casati A, Fenelli G, Pietropaoli P, Proietto R (2004) Paper presented at the American Society of Anesthesiologists annual meeting, Las Vegas, NV
- de la Rocha AG, Edmonds JF, Williams WG, Poirier C, Trusler RN (1978) Importance of mixed venous oxygen saturation in the care of critically ill patients. *Can J Surg* 21:227–229
- Edwards AD, Richardson C, Van der Zee P, et al. (1993) Measurement of hemoglobin flow and blood flow by near-infrared spectroscopy. *J Appl Physiol* 75:1884–1889
- Fernandez EG, Green TP, Sweeney M (2004) Low inferior vena caval catheters for hemodynamic and pulmonary function monitoring in pediatric critical care patients. *Pediatr Crit Care Med* 5:14–18
- Fortune PM, Wagstaff M, Petros AJ (2004) Cerebro-splanchnic oxygenation ratio (CSOR) using near infrared spectroscopy may be able to predict splanchnic ischaemia in neonates. *Intensive Care Med* 27:1401–1407
- Hampson NB, Piantadosi CA (1998) Near infrared monitoring of human skeletal muscle oxygenation during forearm ischemia. *J Appl Physiol* 64:2449–2457
- Henson LC, Calalang C, Temp JA, Ward DS (1998) Accuracy of a cerebral oximeter in healthy volunteers under conditions of isocapnic hypoxia. *Anesthesiology* 88:58–65
- Hoffman GM, Mussatto KA, Brosig CL, et al. (2005) Systemic venous oxygen saturation after the Norwood procedure and childhood neurodevelopmental outcome. *J Thorac Cardiovasc Surg* 130:1094–1100
- Inomata S, Nishikawa T, Taguchi M (1994) Continuous monitoring of mixed venous oxygen saturation for detecting alterations in cardiac output after discontinuation of cardiopulmonary bypass. *Br J Anaesth* 72:11–16
- Jobsis FF (1977) Non-invasive, infra-red monitoring of cerebral O₂ sufficiency, blood volume HbO₂-Hb shifts and blood flow. *Acta Neurol Scand Suppl* 64:452–453
- Kaiser JR, Gauss CH, Williams DK (2004) Surfactant administration acutely affects cerebral and systemic hemodynamics and gas exchange in very-low-birth-weight infants. *J Pediatr* 144:809–814
- Kasnitz P, Druger GL, Yorra F, Simmons DH (1976) Mixed venous oxygen tension and hyperlactatemia. Survival in severe cardiopulmonary disease. *J Am Med Assoc* 236:570–574
- Kazarian KK, Del Guercio LR (1980) The use of mixed venous blood gas determinations in traumatic shock. *Ann Emerg Med* 9:179–182
- Kim MB, Ward DS, Cartwright CR, et al. (2000) Estimation of jugular venous O₂ saturation from cerebral oximetry or arterial O₂ saturation during isocapnic hypoxia. *J Clin Monit Comput* 16:191–199
- Krauss XH, Verdouw PD, Hughenholtz PG, Nauta J (1975) Online monitoring of mixed venous oxygen saturation after cardiopulmonary surgery. *Thorax* 30:636–643
- Kremzar B, Spéac-Marn A, Kompan L, Cerovic O (1997) Normal values of SvO₂ as therapeutic goal in patients with multiple injuries. *Intensive Care Med* 23:65–70
- Krivec B, Vogá G, Podbregar M (2004) Monitoring mixed venous oxygen saturation in patients with obstructive stock after massive pulmonary embolism. *Wiener Klin Wochenschrift* 116:326–331
- Kurth CD, Steven JL, Montenegro LM, et al. (2001) Cerebral oxygen saturation before congenital heart surgery. *Ann Thorac Surg* 72:187–192
- Landis JR, Koch GG (1977) The measurement of observer agreement for categorical data. *Biometrics* 33:159–174

25. Lee J, Wright F, Barber R, Stanley L (1972) Central venous oxygen saturation shock: a study in man. *Anesthesiology* 36:472–478
26. Mahle WT, Tavani F, Zimmerman RA, et al. (2002) An MRI study of neurological injury before and after congenital heart surgery. *Circulation* 106:I109–I114
27. Mancini DM, Bolinger L, Li H, et al. (1994) Validation of near-infrared spectroscopy in humans. *J Appl Physiol* 77:2740–2747
28. McCormick PW, Stewart M, Goetting MG, Balakrishnan G (1991) Regional cerebrovascular oxygen saturation measured by optical spectroscopy in humans. *Stroke* 22:596–602
29. McCormick PW, Stewart M, Goetting MG, et al. (1991) Noninvasive cerebral optical spectroscopy for monitoring cerebral oxygen delivery and hemodynamics. *Crit Care Med* 19:89–97
30. McKinley BA, Marvin RG, Cocanour CS, Moore FA (2000) Tissue hemoglobin O₂ saturation during resuscitation of traumatic shock monitored using near infrared spectrometry. *J Trauma-Injury Infect Crit Care* 48:637–642
31. Monk T, Weldon J, Van der Aa M (2002) Paper presented at the American Society of Anesthesiologists annual meeting, Orlando, FL
32. Nagdyman N, Fleck T, Barth S, et al. (2004) Relation of cerebral tissue oxygenation index to central venous oxygen saturation in children. *Intensive Care Med* 30:468–471
33. Nollert G, Jonas RA, Reichart B (2000) Optimizing cerebral oxygenation during cardiac surgery: a review of experimental and clinical investigations with near infrared spectrophotometry. *Thorac Cardiovasc Sur* 48:247–253
34. O'Connor TA, Hall RT (1994) Mixed venous oxygenation in critically ill neonates. *Crit Care Med* 22:343–346
35. Pollard V, Prough DS, DeMelo AE, et al. (1996) Validation in volunteers of a near-infrared spectroscope for monitoring brain oxygenation in vivo. *Anesth Analg* 82:269–277
36. Pollard V, Prough DS, DeMelo AE, et al. (1996) The influence of carbon dioxide and body position on near infrared spectroscopic assessment of cerebral hemoglobin oxygen saturation. *Anesth Analg* 82:278–287
37. Powelson J, Maini BS, Bishop RL, Sottile FD (1992) Continuous monitoring of mixed venous oxygen saturation during aortic operations. *Crit Care Med* 20:332–336
38. Prough DS, Pollard V (1995) Cerebral near-infrared spectroscopy: ready for prime time? *Crit Care Med* 23:1624–1626
39. Reinhart K, Rudolph T, Bredle DL, Hannemann L, Cain SM (1989) Comparison of central-Venous to mixed-venous oxygen saturation during changes in oxygen supply/demand. *Chest* 95:1216–1221
40. Rivers EP, Ander DS, Powell D (2001) Central venous oxygen saturation monitoring in the critically ill patient. *Curr Opin Crit Care* 7:204–211
41. Schranz D, Schmitt S, Oelert H, et al. (1989) Continuous monitoring of mixed venous oxygen saturation in infants after cardiac surgery. *Intensive Care Med* 15:228:232
42. Sumimoto T, Takayama Y, Iwasaka T, et al. (1991) Mixed venous oxygen saturation as a guide to tissue oxygenation and prognosis in patients with acute myocardial infarction. *Am Heart J* 122:27–33
43. Teller J, Wolf M, Keel M, et al. (2000) Can near infrared spectroscopy of the liver monitor tissue oxygenation? *Eur J Pediatr* 159:549
44. Thayssen P, Klarholt E (1980) Relation between caval and pulmonary artery oxygen saturation in children. *Br Heart J* 43:574–578
45. Thomsen A (1978) Calculation of oxygen saturation of mixed venous blood in infants. *Scand J Clin Lab Invest* 38:389–392
46. Tortoriello T, Stayer SA, Mott AR, et al. (2005) A noninvasive estimation of mixed venous oxygen saturation using near-infrared spectroscopy by cerebral oximetry in pediatric cardiac surgery patients. *Pediatr Anaesth* 15:495–503
47. Varela JE, Cohn SM, Giannotti GD, et al. (2001) Near-infrared spectroscopy reflects changes in mesenteric and systemic perfusion during abdominal compartment syndrome. *Sur* 129:363–370
48. Watzmam HM, Kurth CD, Montenegro LM (2000) Arterial and venous contributions to near-infrared cerebral oximetry. *Anesthesiology* 93:947–953