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Cerebral Oxygen Saturation in Children with Congenital Heart Disease and Chronic Hypoxemia

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Abstract

Background—Increased Hb concentration accompanying hypoxemia is a compensatory response to maintain tissue oxygen delivery (DO₂). Near infrared spectroscopy (NIRS) is used clinically to detect abnormalities in the balance of cerebral DO₂ and consumption, including in children with congenital heart disease (CHD). Although NIRS-measured cerebral tissue O₂ saturation (ScO₂) correlates with SaO₂, jugular bulb O₂ saturation (SjvO₂), and Hb, little data exists on the interplay between these factors and cerebral O₂ extraction (COE). This study

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Conflicts of Interest

None.

Disclosures

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investigated the associations of ScO_2 and $\text{SaO}_2\text{--ScO}_2$ with SaO_2 and Hb and verified the normal range of ScO_2 in children with CHD.

Methods—Children undergoing cardiac catheterization for CHD were enrolled in a calibration and validation study of the FORE-SIGHT® NIRS monitor. Two pairs of simultaneous arterial and jugular bulb samples were drawn for co-oximetry, calculation of a reference ScO_2 (REF CX), and estimation of COE. Pearson correlation and linear regression were used to determine relationships between O_2 saturation parameters and Hb. Data were also analyzed according to diagnostic group defined as acyanotic ($\text{SaO}_2 \geq 90\%$) and cyanotic ($\text{SaO}_2 < 90\%$).

Results—Of 65 children studied, acceptable jugular bulb samples (SjbO_2 absolute difference between samples $\leq 10\%$) were obtained in 57 (88%). The $\text{SaO}_2\text{--SjbO}_2$, $\text{SaO}_2\text{--ScO}_2$, and $\text{SaO}_2\text{--REF CX}$ were positively correlated with SaO_2 and negatively correlated with Hb (all $P < 0.001$). Although by diagnostic group ScO_2 differed statistically ($P = 0.002$), values in the cyanotic patients were within the range considered normal ($69 \pm 6\%$). COE estimated by the difference between arterial and jugular bulb O_2 content ($\text{CaO}_2\text{--CjbO}_2$, mL O_2 /100 mL) was not different for cyanotic and acyanotic patients ($P = 0.10$), but estimates using $\text{SaO}_2\text{--SjbO}_2$, $\text{SaO}_2\text{--ScO}_2$, or $\text{SaO}_2\text{--ScO}_2/\text{SaO}_2$ were significantly different between the cyanotic and acyanotic children ($P < 0.001$).

Conclusions—Children with adequately compensated chronic hypoxemia appear to have ScO_2 values within the normal range. The $\text{SaO}_2\text{--ScO}_2$ is inversely related to Hb, with the implication that in the presence of reduced Hb, particularly if coupled with a decreased cardiac output, the ScO_2 can fall to values associated with brain injury in laboratory studies.

Introduction

With improved survival among children with congenital heart disease (CHD), neurodevelopmental impairment has become a primary focus in the evaluation of clinical outcomes. One factor of central importance in the neurodevelopmental pathophysiology is abnormal cerebral oxygen delivery (DO_2).^{1–3} Accordingly, a deeper understanding of the cerebral O_2 balance in these patients may help in the development of strategies and practices to mitigate the deleterious effects of cerebral hypoxia-ischemia. Many forms of CHD are characterized by cyanosis, with staged palliation or repair leaving children with a mixing circulation and hypoxemia for the first several years of life, and sometimes longer.⁴ The increased hemoglobin concentration (Hb) accompanying hypoxemia is an important compensatory response to increase arterial oxygen content (CaO_2) and maintain tissue DO_2 .⁵ Cerebral O_2 consumption (CMRO_2) regulates cerebral DO_2 , and the interplay between cerebral DO_2 and CMRO_2 determines the cerebral O_2 extraction (COE) defined as the amount (mL) or fraction (%) of O_2 removed from the arterial blood as it passes through the brain.⁶ Changes in cerebral venous O_2 saturation may provide useful information on the cerebral O_2 balance,^{7,8} but measurement is invasive or impractical.^{9–11}

Near infrared spectroscopy (NIRS) is a non-invasive optical technique that is increasingly being employed clinically to evaluate cerebral oxygenation.¹² In the pediatric population, NIRS has primarily been used to assess the cerebral O_2 supply-demand relationship in premature and term neonates^{13,14} and in children of all ages with CHD.^{15–18} Cerebral tissue

O₂ saturation (ScO₂) measured by NIRS is mostly (~63–84%) determined by the O₂ saturation of the venous compartment and likely reflects the cerebral venous O₂ saturation.^{19,20} It is important to appreciate that although the arterial/venous ratio is similar in normoxia, hypoxia, and hypocapnia, there is significant variability in this ratio between individuals²⁰ and under different clinical conditions.²¹ Although ScO₂ measured by NIRS correlates with SaO₂, SjbO₂, and Hb,^{15,20,22} little data exists on the interplay between these factors and COE. Based on the reliability of ScO₂ to represent SjbO₂, cerebral O₂ extraction has been estimated at the bedside by calculation of the arterial-cerebral O₂ saturation difference (SaO₂–ScO₂),¹⁵ or as the fractional O₂ extraction (FOE = [SaO₂–ScO₂]/SaO₂).¹⁴

The primary aim of this study was to evaluate the associations of ScO₂ and SaO₂–ScO₂ with SaO₂ and Hb in children with CHD. In cyanotic patients, we have observed that the ScO₂ tends to be higher than is expected from the SaO₂. We hypothesize that in patients with chronic hypoxemia the ScO₂ is within the range considered normal, and that the SaO₂–ScO₂ difference is decreased with lower SaO₂ as a result of an increase in Hb concentration. The answer to these questions is important to be able to correctly interpret and act upon NIRS measurements. Because jugular bulb sampling was performed, a secondary aim was to determine the COE by measurement of the difference in O₂ content between the arterial and jugular venous bulb blood (CaO₂–CjbO₂).

Methods

Patients

The study was approved by the Committee for Clinical Investigations, and written informed consent was obtained for all subjects from parents or legal guardians. Pediatric patients scheduled for elective cardiac catheterization at Boston Children's Hospital were prospectively recruited for a study to calibrate and validate the FORE-SIGHT[®] NIRS monitor (CAS Medical Systems, Inc., Branford, CT) with the medium sensor. The time period of the study was June 2008 to July 2009. Children with all cardiac diagnoses were eligible as long as they fell within the specified age (1 month to 18 years) and weight (3 and 50 kg) ranges and required both arterial and venous catheter placement. Patients with a known history of stroke, brain malformations, or craniofacial abnormalities were excluded. The first generation FORE-SIGHT[®] is a continuous-wave near-infrared spectroscopic instrument using laser-generated light of four wavelengths (690, 780, 805, and 850 nm).^{23,24} The optical sensor placed on the forehead has a fiber optic light source and two photodiode detectors 40 mm and 12 mm away from the light source.

Study Protocol

Patients underwent either general endotracheal anesthesia or nurse-administered sedation according to standard clinical practice. Once the patient was anesthetized (typically 1 to 5 mcg/kg of fentanyl and < 1 MAC isoflurane or sevoflurane) or sedated (midazolam and fentanyl per routine practice), medium-sized sensors (source-detector separation 12 and 40 mm) for the FORE-SIGHT[®] NIRS monitor were placed on the forehead bilaterally and adjusted as necessary to obtain consistent readings. Per usual practice, patients were

maintained on 21% inspired oxygen if tolerated until baseline hemodynamic evaluation was completed. Vascular access was obtained by the interventional cardiologist. Before baseline hemodynamic and oximetric measurements, simultaneous blood samples were drawn from an arterial catheter in the aorta or femoral artery, and from an end-hole venous catheter in the internal jugular vein bulb. The tip of the venous catheter was advanced up the internal jugular vein under fluoroscopy until it was above the angle of the mandible (usually opposite C2) in the region of the jugular bulb. Blood gas analyses were performed on these samples and O₂ saturations were determined by co-oximetry (RAPIDPoint 405 System, Siemens Medical Solutions, Malvern, PA). After completion of baseline hemodynamic measurements a second set of study blood samples was obtained under the same physiologic conditions. Both sets of samples were collected near the beginning of the catheterization prior to any interventions. The first and second jugular bulb O₂ saturations (SjbO₂) were compared, and if the difference between the 2 samples was > 10% (absolute) without changes in clinical or blood gas measurements, extracerebral contamination or poor sampling technique was assumed and such patients were excluded from further analysis. Averages of the first and second sets of SaO₂ and SjbO₂ measurements were calculated and used for analysis; in occasional subjects (n=4) only one sample could be obtained, so that one measurement was used for the analysis. A reference tissue oxygen saturation to approximate the cerebral circulation (REF CX), based on the work of Ito¹⁹ and Benni,²⁵ was derived from measurements of SaO₂ and SjbO₂ according to the equation: REF CX = (0.3 × SaO₂) + (0.7 × SjbO₂). Systemic arterial oxygen content was calculated as CaO₂ (mL O₂/100 mL) = (Hb × 1.34 × SaO₂) + (0.0031 × PaO₂), and jugular venous oxygen content as CjbO₂ (mL O₂/100 mL) = (Hb × 1.34 × SjbO₂) + (0.0031 × PjbO₂). Cardiac index (L/min/m²) was calculated by the Fick method with assumption of O₂ consumption according to LaFarge and Miettinen.²⁶ Indexed systemic oxygen delivery was calculated as DO₂ (mL O₂/min/m²) = CaO₂ × Cardiac Index × 10. Estimates of cerebral O₂ extraction were determined by the SaO₂–SjbO₂ difference (SaO₂–SjbO₂), the SaO₂–ScO₂ difference (SaO₂–ScO₂), the ratio (SaO₂–ScO₂)/SaO₂ (fractional O₂ extraction, FOE), and the arterial-jugular bulb O₂ content difference (CaO₂–CjbO₂). Cerebral perfusion pressure (CPP) was calculated as mean arterial pressure minus central venous pressure (MAP–CVP), and systemic vascular resistance index (SVRI) was calculated as mean systemic arterial pressure–mean systemic venous pressure)/cardiac index. As there was no statistically significant difference between the ScO₂ measured from the left and right sensors (median (IQR) 1.8% (0.6–3.1%)), an average of the left and right ScO₂ was used for the analysis.

Statistical Analysis

The relationship between ScO₂ and REF CX was assessed using linear regression. Bland-Altman analysis was performed to determine the bias and precision of the FORE-SIGHT® monitor with the medium sensor, and was reported with 95% confidence intervals around the limits of agreement, calculated by the approximate method. Pearson correlation and linear regression were used to determine relationships between O₂ saturation parameters and Hb, and between these variables and demographic and diagnostic variables. Scatterplots are depicted with the linear regression equation, correlation coefficient (R) with 95% confidence intervals, coefficient of determination (R²), and standard error of the estimate (SE) values. Oximetric data was also analyzed according to diagnostic group, defined as acyanotic (SaO₂

90%) and cyanotic ($\text{SaO}_2 < 90\%$). Data were compared between cyanotic and acyanotic groups using Student's t-test. To detect a correlation coefficient of 0.6, with alpha set at 0.05 and 90% power, we would need 25 patients; for 80% power, we would need 19 patients. $P < 0.01$ was set conservatively as the significance criterion for all testing. Data are presented as mean $\pm$ SD, median (1st, 3rd quartiles) and/or [minimum-maximum], or frequency (%).

Results

Patients

Of the 65 children enrolled and studied, acceptable jugular bulb samples were obtained in 57 (88%). Data from these 57 subjects were used for the analysis. Demographic and clinical data are summarized in Table 1. The majority of patients underwent catheterization with general endotracheal anesthesia and mechanical ventilation, and nearly all subjects were breathing room air when samples were obtained. The median duration between the first and second set of blood samples was 8 (6, 12) minutes.

Validation, Oxygenation Parameters and Hemoglobin

Hemoglobin ranged from 7.6 to 17.5 g/dL (median 12.1 g/dL), SaO_2 from 70–99% (median 95%), SjbO_2 from 45–82% (median 64%), the REF CX from 54–87% (median 73%), and the ScO_2 from 56–82% (median 73%). There was good correlation between the ScO_2 and REF CX ($R = 0.72$ [0.58 to 0.91], $P < 0.001$) (Figure 1). By Bland-Altman analysis, bias was acceptable with a mean absolute bias of 1.2% (limits of agreement 9.9% to -7.7%) and a precision ($\pm 1\text{SD}$) of 4.6%, with confidence intervals of 11.0% and -9.6% around the limits of agreement (Figure 2). Oxygenation and Hb data for the cohort and each diagnostic group are summarized in Table 2. The association between ScO_2 and Hb was not significant ($P=0.58$), but smaller differences for $\text{SaO}_2\text{--SjbO}_2$, $\text{SaO}_2\text{--ScO}_2$, and $\text{SaO}_2\text{--REF CX}$ were all associated with higher Hb (all $P < 0.001$) (Figure 3). Fractional O_2 extraction was inversely related to Hb ($P < 0.001$).

The ScO_2 correlated with the SjbO_2 ($R = 0.68$ [0.49 to 0.88], $P < 0.001$) and with the SaO_2 ($R = 0.45$ [0.21 to 0.69], $P < 0.001$) (Figure 1). The median (1st, 3rd quartiles) difference between the ScO_2 and SjbO_2 was 7% (4, 10%). A higher SaO_2 was associated with greater differences for $\text{SaO}_2\text{--SjbO}_2$ ($R = 0.52$ [0.29 to 0.75], $P < 0.001$) and $\text{SaO}_2\text{--ScO}_2$ ($R = 0.61$ [0.39 to 0.82], $P < 0.001$) (Figure 4), and $\text{SaO}_2\text{--REF CX}$ ($R=0.52$ [0.29 to 0.75], $P < 0.001$). Although the linearity of the relationships between $\text{SaO}_2\text{--SjbO}_2$ and $\text{SaO}_2\text{--ScO}_2$ with SaO_2 was not assessed, visually the relationships appeared non-linear. As shown in Figure 5, the $\text{SaO}_2\text{--SjbO}_2$ strongly correlated with the $\text{SaO}_2\text{--ScO}_2$ difference ($R = 0.75$ [0.57 to 0.93], $P < 0.001$).

Oxygenation Parameters and Hemoglobin According to Diagnostic Group

As expected, there were significant differences between the acyanotic and cyanotic groups for SaO_2 ($P < 0.001$), Hb ($P < 0.001$), SjbO_2 ($P = 0.006$), ScO_2 ($P = 0.002$), and REF CX ($P < 0.001$), but no differences were found for CaO_2 , CjbO_2 , and DO_2 (Table 2). The

$\text{CaO}_2\text{--CjbO}_2$ was similar for both groups ($P=0.10$), but there were significant differences between the groups for the $\text{SaO}_2\text{--SjbO}_2$ ($P < 0.001$), $\text{SaO}_2\text{--ScO}_2$ ($P < 0.001$), $\text{SaO}_2\text{--REF}$

CX ($P=0.001$) and FOE ($P=0.002$) (Table 2). While the acyanotic group had a lower CVP and higher Qp:Qs, the cerebral perfusion pressures were similar.

Discussion

The findings from this study show that ScO₂ values in children with adequately compensated chronic hypoxemia are within the normal range and that COE, as measured by the difference between the arterial and jugular bulb O₂ content, does not differ between acyanotic (SaO₂ ≥ 90%) or cyanotic (SaO₂ < 90%) patients. The major implication of our findings is that a low ScO₂ value in the setting of chronic hypoxemia should not be interpreted as a 'normal' baseline for that patient.

Cerebral O₂ saturation values in the cyanotic group were $69 \pm 6\%$ and thus within the range considered normal ($68 \pm 10\%$).^{15,27} This can be explained in part by the compensatory erythrocytosis associated with chronic hypoxemia resulting in a normal CaO₂. Our findings are supported by a study evaluating cerebral oxygenation at high altitude. Furian and colleagues found no difference in cerebral O₂ saturation values between subjects living at high altitude (> 8200 ft.) or low altitude (< 2625 ft.), despite chronic hypoxemia (SaO₂ < 90%) in the residents at high altitude.²⁸ While a decreasing difference between SaO₂ and SjbO₂ has also been shown during acute hypoxemia,²¹ it is important to be aware that different factors are operational.^{5,29} Specifically, the increased expression of hypoxia inducible factors with chronic hypoxemia results in up regulation of genes controlling angiogenesis, erythropoiesis, energy utilization, nitric oxide metabolism, and carotid body chemosensitivity,³⁰ in addition to increased plasma volume and cardiac output.³¹ Unlike the frequent assumption of a fixed difference (~ 25%) between SaO₂ and mixed venous oxygen saturation as an indication of adequate systemic O₂ delivery compared with demand, it would be incorrect to assume that a low ScO₂ in a patient with chronic hypoxemia is just due to a lower SaO₂ and a "normal" difference between SaO₂ and SjbO₂.

This study also shows that estimation of COE at the bedside is dependent on the parameters used for the calculation. The study protocol allowed for measurement of arterial and jugular venous bulb O₂ content. Cerebral O₂ extraction, when estimated by the difference between the CaO₂ and CjbO₂, did not differ for patients with SaO₂ above or below 90%. This is consistent with the regulation of cerebral DO₂ by CMRO₂.^{6,32} With a similar CI for each group and assuming that CBF (which was not directly measured) is equivalent, the CMRO₂ is likely similar for patients with SaO₂ above or below 90%. However, as shown in Table 2, estimation of COE using cerebral oximetry (SaO₂-ScO₂ or FOE) found significant differences in COE between the groups. Significant group differences were also found for SaO₂-SjbO₂. One likely factor accounting for these findings is the exclusion of Hb when only using O₂ saturation parameters for the estimation of COE. As shown by our findings, when CMRO₂ is presumably constant, the brain extracts the same amount (mL) of O₂, but the fraction (%) extracted can be variable.

The SaO₂-SjbO₂ and SaO₂-ScO₂ increased significantly with decreasing Hb. The implication of this finding is that an increased or increasing difference between the SaO₂ and ScO₂ in a cyanotic patient who is anemic (or relatively anemic) or bleeding could lead to

ScO₂ levels associated with brain injury in laboratory studies.^{33,34} As there was no difference in the relationship between the cardiac index and DO₂ for the cyanotic and acyanotic groups, Hb assumes an increasing importance in maintaining DO₂ if the cardiac output is also decreased.

We found that ScO₂ had a stronger correlation with SjbO₂ than with SaO₂, which is not surprising considering the much larger volume of the venous compartment²⁰ and the method in which cerebral oximeters are calibrated.³⁵ Similar to the observations of Kurth et al., the predictive value of SaO₂ for ScO₂ was low.¹⁵ The correlation between the ScO₂ and the SjbO₂ is consistent with prior studies.³⁶ By Bland-Altman analysis (Figure 2) the mean bias and precision ($\pm 1SD$) was 1.2% and 4.6%, respectively, with confidence intervals around the limits of agreement of 11.0% and -9.6%. Our findings are similar to that reported by Kreeger et al.³⁷, and despite the wide confidence intervals around the limits of agreement, the precision still allows for discrimination between normal ScO₂ levels and those associated with cerebral hypoxia-ischemia.³³

The findings of this study are constrained by certain limitations. Direct measurement of cerebral oxygen consumption was not performed and CMRO₂ was assumed to be constant over the measurement period. With respect to methodology, there was a constant level of oxygenation within each subject with a range of SaO₂ across subjects. For this reason, we believe that our findings are valid and not affected by the cerebral oximeter bias associated with acute hypoxia.^{21,38} Furthermore, this bias is reduced when it is plotted against the difference in arterial and jugular bulb O₂ saturation.²¹ The unknown variability of the arterial to venous blood volume ratio in the interrogated tissue is a source of error for cerebral oximetry,²¹ as is the use of an assumed O₂ consumption to calculate cardiac output.³⁹ Finally, analyses of differences between groups in oxygen deltas (e.g., SaO₂-ScO₂, SaO₂-REF CX, and SaO₂-SjbO₂) were not adjusted for baseline variables. We would expect the findings of this study to be similar with other NIRS devices.

In conclusion, children with adequately compensated chronic hypoxemia should have ScO₂ values within the normal range. A low ScO₂ baseline in the setting of chronic hypoxemia should not be interpreted as a 'normal' baseline for that patient, and a cause(s) for the low ScO₂ value should be sought. Hemoglobin assumes increasing importance for cerebral DO₂ in the cyanotic child, and in the presence of bleeding, particularly if coupled with a decreased cardiac output, the ScO₂ can fall to values associated with brain injury in laboratory studies.

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Figure 1.

Scatterplot of relationships between ScO₂ and the following: REF CX (purple triangles; $y=0.75x + 19.05$, $R=0.72$ [0.57 to 0.91], $R^2=0.52$, $SE=4.45$, $p<0.001$), SjbO₂ (solid blue circles; $y=0.86x + 3.52$, $R=0.68$ [0.49 to 0.88], $R^2=0.47$, $SE=5.71$, $p<0.001$), and SaO₂ (open red diamonds; $y=0.51x + 55.3$, $R=0.45$ [0.21 to 0.69], $R^2=0.20$, $SE=6.28$, $p<0.001$) by linear regression and Pearson correlation.

Figure 2.

Bland-Altman plot demonstrating the bias and limits of agreement for ScO₂ relative to the gold-standard REF CX.³⁵ Mean absolute bias was 1.2% (limits of agreement 9.9% to -7.7%) with confidence intervals of 11.0% and -9.6% around the limits of agreement.

Figure 3. Scatterplot demonstrating relationships between Hb concentration and the $\text{SaO}_2\text{--ScO}_2$ (open red diamonds; $y = -2.53x + 48.04$, $R = -0.63$ [-0.84 to -0.42], $R^2 = 0.39$, $SE = 5.45$, $p < 0.001$), and the $\text{SaO}_2\text{--SjbO}_2$ (solid blue circles; $y = -2.48x + 56.19$, $R = -0.53$ [-0.76 to -0.30], $R^2 = 0.28$, $SE = 7.37$, $p < 0.001$) by linear regression and Pearson correlation.

Figure 4.

Scatterplot demonstrating relationships between SaO₂ and the $\Delta\text{SaO}_2 - \text{SjbO}_2$ (solid blue circles; $y=0.65x - 32.77$, $R=0.52$ [0.29 to 0.75], $R^2=0.27$, $\text{SE}=7.41$, $p<0.001$), and $\Delta\text{SaO}_2 - \text{ScO}_2$ (open red diamonds; $y=0.60x - 35.55$, $R=0.61$ [0.39 to 0.82], $R^2=0.37$, $\text{SE}=5.56$, $p<0.001$) by linear regression and Pearson correlation.

Figure 5. Scatterplot demonstrating the relationship between the $\text{SaO}_2\text{-SjbO}_2$ and the $\text{SaO}_2\text{-ScO}_2$. ($y=0.60x + 3.85$, $R=0.75$ [0.57 to 0.93], $R^2=0.56$, $\text{SE}=4.63$, $p<0.001$) by linear regression and Pearson correlation.

Table 1**Demographic and Clinical Data (n=57)**

Age (years)	4.8 ± 4.0
Weight (kg)	17.4 ± 11.8
Head circumference (cm)	47.8 ± 4.8
Race/ethnicity	
Caucasian	44 (77%)
Asian	4 (7%)
African American	4 (7%)
Hispanic	5 (9%)
Gender	
Male	30 (53%)
Female	27 (47%)
Type of CHD	
Acyanotic	36 (63%)
Cyanotic	21 (37%)
Type of catheterization	
Diagnostic	11 (19%)
Interventional	46 (81%)
Method of anesthesia	
General endotracheal anesthesia	36 (63%)
Monitored sedation	21 (37%)
Ventilatory parameters	
Fraction of inspired oxygen	0.21 ± 0.0
Peak inspiratory pressure (cm H ₂ O)	16.4 ± 3.4
End-expiratory pressure (cm H ₂ O)	1.4 ± 1.9

Data presented as mean ± standard deviation or frequency (%).

Table 2

Oxygenation and Physiologic Data

	All Patients (n=57)	Acyanotic (n=36)	Cyanotic (n=21)	P Value
Age (years)	4.8 ± 4.0	4.6 ± 3.5	4.9 ± 4.7	0.80
Hb (g/dL)	12.0 ± 1.9	11.2 ± 1.3	13.4 ± 1.9	< 0.001
SaO ₂ (%)	92 ± 7	96 ± 2	84 ± 5	< 0.001
SpO ₂ (%)	92 ± 7	96 ± 3	84 ± 4	< 0.001
CaO ₂ (mL O ₂ /100 mL)	14.9 ± 1.6	14.8 ± 1.6	15.2 ± 1.7	0.38
DO ₂ (mL/min/m ²)	564 ± 154	537 ± 136	612 ± 174	0.08
SjbO ₂ (%)	65 ± 8	67 ± 8	62 ± 6	0.006
CjbO ₂ (mL O ₂ /100 mL)	10.5 ± 2.0	10.0 ± 1.8	11.4 ± 1.9	0.06
ScO ₂ (%)	72 ± 6	74 ± 6	69 ± 6	0.002
REF CX (%)	73 ± 6	76 ± 6	68 ± 5	< 0.001
SaO ₂ – SjbO ₂ (%)	26 ± 9	29 ± 9	22 ± 6	< 0.001
CaO ₂ – CjbO ₂ (mL O ₂ /100 mL)	4.2 ± 1.2	4.3 ± 1.3	3.8 ± 2.0	0.10
SaO ₂ – ScO ₂ (%)	20 ± 7	23 ± 6	15 ± 6	< 0.001
ScO ₂ – SjbO ₂ (%)	6.7 ± 5.7	6.8 ± 6.0	6.3 ± 5.3	0.81
SaO ₂ – REF CX (%)	19 ± 6	20 ± 6	15 ± 4	0.001
FOE	0.21 ± 0.07	0.23 ± 0.06	0.18 ± 0.07	0.002
Cardiac index (L/min/m ²)	3.8 ± 1.0	3.7 ± 0.9	4.0 ± 1.0	0.17
Qp:Qs	1.01 ± 0.39	1.12 ± 0.40	0.80 ± 0.27	0.003
CVP (mm Hg)	10 ± 4	8 ± 3	12 ± 4	0.001
Heart rate (beats per minute)	98 ± 24	93 ± 28	106 ± 15	0.056
Mean systemic arterial BP (mm Hg)	53 ± 8	52 ± 7	54 ± 8	0.38
Cerebral perfusion pressure (mm Hg)	43 ± 9	44 ± 8	42 ± 10	0.48
SVRi (mm Hg/L/min/m ²)	15.6 ± 4.6	16.0 ± 4.2	14.8 ± 5.2	0.41

Data presented as mean ± standard deviation.

P-values are from between-group comparison using Student's t-test

Qp:Qs, pulmonary-to-systemic blood flow ratio; CVP, central venous pressure; BP, blood pressure; SVRi, systemic vascular resistance index. See text for other abbreviations.