Regional low-flow perfusion provides comparable blood flow and oxygenation to both cerebral hemispheres during neonatal aortic arch reconstruction

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Objective: The aim of this study was to measure cerebral oxygenation, cerebral blood volume index, and cerebral blood flow velocity values in both cerebral hemispheres before, during, and after regional low-flow cerebral perfusion for neonatal aortic arch reconstruction and to test the hypothesis that cerebral blood volume index measured by near infrared spectroscopy correlates with cerebral blood flow velocity measured by transcranial Doppler ultrasonography.

Methods: Bilateral near infrared spectroscopy and transcranial Doppler ultrasonography sensors were placed, and values were recorded immediately before, during, and after regional low-flow cerebral perfusion at 18°C. Cerebral oxygen saturations, cerebral blood flow velocities, and cerebral blood volume index values were compared by Mann-Whitney U test. Correlations between values of cerebral blood volume index and cerebral blood flow velocity were tested with Spearman rank order correlation.

Results: Twenty patients were studied. Median cerebral oxygen saturations for the right and left sides were 95% and 95% before regional low-flow cerebral perfusion, 95% and 87% during regional low-flow cerebral perfusion (P = .054), and 93% and 94% after regional low-flow cerebral perfusion. Median cerebral blood flow velocity values did not change during regional low-flow cerebral perfusion. Cerebral blood volume index exhibited a poor correlation with cerebral blood flow velocity.

Conclusions: Regional low-flow cerebral perfusion provides comparable blood flows and oxygenation to both cerebral hemispheres. Transcranial Doppler ultrasonography is recommended as a corroborative method with near-infrared spectroscopy to guide flow during regional low-flow cerebral perfusion, because cerebral blood volume index does not correlate with cerebral blood flow velocity.

Regional low-flow cerebral perfusion (RLFP) has gained increasing use as a perfusion technique to avoid or limit deep hypothermic circulatory arrest (DHCA) for the Norwood operation for hypoplastic left heart syndrome and other aortic reconstruction operations in the newborn period.1-3 With this technique a 3- to 4-mm polytetrafluoroethylene (PTFE) graft is anastomosed to the right innominate artery and serves as aortic inflow during bypass. During aortic recon-
struction, the brain and right upper extremity only are perfused through the graft, with the brachiocephalic vessels and the descending thoracic aorta snared to achieve a bloodless field. Thus the brain receives direct unilateral perfusion through the right common carotid artery and right vertebral artery. Previous studies have used neurophysiologic monitoring of the right side of the brain (near-infrared spectroscopy [NIRS]) and transcranial Doppler ultrasonography (TCD) to demonstrate adequate cerebral blood flow velocity (CBFV), blood volume, and cerebral oxygenation during RLFP and to guide bypass flow rates. It has been assumed that the circle of Willis in the neonate is intact and that adequate blood flow is provided across it to the left side of the brain during RLFP. However, this assumption has been questioned recently, and there have been no reports of measurement of blood flow velocity and oxygenation in the left cerebral hemisphere during RLFP. Another assumption in previous work is that the cerebral blood volume index (CBVI) as measured by NIRS correlates with cerebral blood flow (CBF) and can be used to guide bypass flow during RLFP.

The purpose of this study was to measure regional cerebral oxygenation index (rSO_2,i), CBVI, and CBFV to both cerebral hemispheres before, during, and after RLFP. Our hypothesis was that RLFP would provide equal blood flows and oxygenation to both cerebral hemispheres. The secondary purpose of the study was to test the hypothesis that CBVI, as measured indirectly by NIRS, correlates with CBFV measured directly by TCD. The strength of association between CBVI and CBFV was tested to determine whether TCD monitoring was necessary or the same information could be derived from NIRS alone.

**Methods**

After institutional review board approval, infants undergoing aortic arch reconstruction were studied. Patients undergoing the Norwood operation for hypoplastic left heart syndrome and those undergoing aortic arch advancement for interrupted or hypoplastic aortic arch were studied if a period of RLFP was planned.

The anesthetic technique consisted of fentanyl (100-200 μg/kg), midazolam (0.3-1.0 mg/kg), and pancuronium or vecuronium. Isoflurane (<1%) was used to supplement the anesthetic before and during bypass. Arterial pressure monitoring consisted of an umbilical or femoral arterial catheter. In addition, a catheter was placed when possible in the left radial artery for patients undergoing the Norwood operation and the right radial artery for patients undergoing aortic arch advancement.

Cerebral physiologic monitoring included NIRS (INVOS 5100; Somanetics Corp., Troy, Mich) to measure rSO_2,i with bilateral sensors applied to the forehead just to the right and left of midline. This method uses near infrared light at 724- and 812-nm wavelengths to measure the absorption spectra of the total hemoglobin and deoxyhemoglobin in the frontal cerebral cortex. A shallow detector subtracts light absorbed by the skull and soft tissues, and a deep detector measures light absorbed by an area in the frontal cortex in the light path. A percentage rSO_2,i is displayed, which is derived as the ratio of oxyhemoglobin to total hemoglobin × 100%:

\[
\frac{\text{Total hemoglobin signal at 812 nm} - \text{Deoxyhemoglobin signal at 724 nm}}{\text{Total hemoglobin signal at 812 nm}} \times 100\% = rSO_2,i
\]

In addition, the INVOS 5100 displays an index of near-infrared signal strength at 812 nm, which is a dimensionless number from −50 to +50. The −50 value is set by internal calibration by the monitor at startup before patient measurement. This signal strength is proportional to the total hemoglobin in the light path. If the hemoglobin concentration is not changing, this signal strength should be proportional to the cerebral blood volume (CBV) in the light path, giving rise to the designation CBVI.

Bilateral transcranial Doppler pulsed-wave ultrasonography (EME Companion; Nicolet Biomedical Inc, Madison, Wis) of the right and left middle cerebral arteries was used to measure CBFV. A 2-MHz probe was placed over the right and left temporal areas, and depth of sample volume and angle of insonation were adjusted until a maximal bidirectional CBFV signal was obtained whenever possible, signifying sampling at the bifurcation of the middle and anterior cerebral arteries. When a bidirectional signal was not obtainable, the transducer was adjusted until the maximal signal above baseline (toward the transducer) was obtained in the middle cerebral artery. Mean sampling depth was 40 ± 6 mm. The depth of the sample volume was identical on both sides for all patients at all data points. In this manner we ascertained that the same area was being sampled on both sides of the brain. The mean CBFV and Doppler spectrum were displayed and recorded.

For patients undergoing the Norwood operation, bypass was initiated through an 8F or 10F aortic cannula inserted into the distal end of a 3- or 3.5-mm PTFE graft, with the proximal end anastomosed into the distal right innominate artery or proximal right subclavian artery. Monitoring of CBFV during innominate artery occlusion for graft placement ensured adequate right-sided cerebral flow during this period. Patients with interrupted aortic arch had a second arterial cannula placed in the patent ductus arteriosus to perfuse the lower body.

Bypass was instituted at a flow of 150 to 200 mL/(kg · min). Phenoxybenzamine (0.25 mg/kg) was administered to all patients undergoing the Norwood operation on initiation of bypass. Phenoxybenzamine (0.25-1 mg/kg) or phentolamine hydrochloride (0.3-1 mg/kg) was administered to all other patients on bypass to achieve a mean arterial pressure of 30 to 40 mm Hg at a minimum flow of 150 mL/(kg · min) throughout the duration of bypass. Extracorporeal cooling to a nasopharyngeal temperature of 18°C was achieved through no less than 20 minutes. The target hematocrit was 25% to 30% during the period of hypothermia. The pH-stat blood gas strategy was used during all phases of the bypass period. For patients undergoing the Norwood operation, a brief period (<10 minutes) of circulatory arrest was used during atrial septectomy. Then RLFP was used for the aortic reconstruction as follows. Snares were placed around the base of the right innominate, left common carotid, and left subclavian arteries and around the descending thoracic aorta distal to the coarctation. Perfusion was then instituted through the PTFE graft to the right innominate artery only during the aortic reconstruction.
TABLE 1. Patient bypass data (n = 20)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before RLFP</th>
<th>During RLFP</th>
<th>After RLFP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right radial artery pressure (mm Hg, n = 11)</td>
<td>35 ± 7</td>
<td>33 ± 7</td>
<td>34 ± 4</td>
</tr>
<tr>
<td>Left radial artery pressure (mm Hg, n = 7)</td>
<td>31 ± 3</td>
<td>23 ± 9*</td>
<td>36 ± 6</td>
</tr>
<tr>
<td>Mean arterial pressure in umbilical or femoral artery (mm Hg)</td>
<td>31 ± 4</td>
<td>11 ± 3*</td>
<td>35 ± 5</td>
</tr>
<tr>
<td>Bypass flow (mL/[kg . min])</td>
<td>175 ± 45</td>
<td>64 ± 15*</td>
<td>170 ± 28</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>27 ± 2*</td>
<td>25 ± 2</td>
<td>25 ± 2</td>
</tr>
<tr>
<td>pH (temperature corrected)</td>
<td>7.36 ± 0.06</td>
<td>7.41 ± 0.07*</td>
<td>7.37 ± 0.04</td>
</tr>
<tr>
<td>Pco2 (mm Hg, temperature corrected)</td>
<td>40 ± 5</td>
<td>36 ± 6*</td>
<td>39 ± 4</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>1.9 ± 0.5</td>
<td>2.1 ± 0.5*</td>
<td>2.7 ± 0.8</td>
</tr>
<tr>
<td>Calculated base deficit</td>
<td>−1.2 ± 1.7</td>
<td>−0.2 ± 2.3</td>
<td>−0.7 ± 1.8</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD. Right radial artery pressure was measured only in patients with a right radial catheter, and left radial artery pressure was measured only in those with a left radial catheter.

*P < .05 for RLFP versus before or after RLFP by 1-way repeated measures analysis of variance.

†P < .03 versus right radial artery pressure during RLFP by t test.

‡P < .05 before RLFP versus during and after RLFP.

§P < .05 during RLFP versus after RLFP.

||P < .05 after RLFP versus before RLFP.

TABLE 2. Patient demographic data (n = 20)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (d, median and interquartile range)</td>
<td>6 (4-9)</td>
</tr>
<tr>
<td>Weight (kg, median and interquartile range)</td>
<td>3.4 (2.7-3.6)</td>
</tr>
<tr>
<td>Baseline hematocrit (% median and interquartile range)</td>
<td>39% (35%-46%)</td>
</tr>
<tr>
<td>Norwood operation (No.)</td>
<td>11</td>
</tr>
<tr>
<td>Aortic arch advancement (No.)</td>
<td>9</td>
</tr>
<tr>
<td>Bypass time (min, median and interquartile range)</td>
<td>154 (124-186)</td>
</tr>
<tr>
<td>Myocardial ischemic time (min, median and interquartile range)</td>
<td>83 (52-98)</td>
</tr>
<tr>
<td>DHCA time (min, median and interquartile range)</td>
<td>11 (0-14)</td>
</tr>
<tr>
<td>RLFP time (min, median and interquartile range)</td>
<td>36 (30-70)</td>
</tr>
<tr>
<td>30-d in-hospital deaths (No.)</td>
<td>0</td>
</tr>
<tr>
<td>New neurologic deficits (No.)</td>
<td>0</td>
</tr>
</tbody>
</table>

Bypass flow was adjusted as described later. At the completion of the aortic reconstruction, the aortic cannula was placed in the neoaorta during a brief (1-2 minute) period of DHCA. DHCA was not otherwise used for the patients undergoing the Norwood operation.

For patients undergoing aortic arch advancement, RLFP was instituted through a PTFE graft (placed solely for the purposes of RLFP) to the innominate artery with the brachiocephalic vessels snared. Intracardiac defects were repaired after aortic reconstruction during hypothermic full-flow cardiopulmonary bypass at a minimum flow of 150 mL/kg · min.

The following patient data were collected: age; weight; diagnosis; operation; times for bypass, aortic crossclamp, DHCA, and RLFP; and baseline precission steady-state values for rS O 2 i, CBVI, mean CBFV, and hematocrit. In addition, data collected on bypass were compared at three times: (1) during full-flow whole-body bypass at deep hypothermic temperatures (18°C) immediately preceding RLFP; (2) during RLFP at 18°C after adjustment of bypass flow rate to achieve mean CBFV values within 10% of baseline (measured at full-flow hypothermic bypass during period 1 just preceding) values for both, and (3) within 5 minutes after aortic reconstruction during full-flow bypass to the whole body at 18°C after steady-state rS O 2 i and CBFV values were achieved before rewarming. Data collected at the three bypass times included bypass flow rate; bilateral rS O 2 i, CBVI, and CBFV values; mean pressure in the radial and umbilical or femoral arteries; temperature-corrected blood gas values; hematocrit; calculated base excess; and plasma lactate. Normally distributed data are expressed as mean ± SD, and nonnormally distributed data are expressed as median with 25% to 75% interquartile ranges. Bypass data in Table 1 were normally distributed and were compared by t test and 1-way repeated measures analysis of variance. Other data were not normally distributed, so the Mann-Whitney U test was used to compare right- and left-sided values of rS O 2 i, CBVI, and CBFV. Kruskal-Wallis 1-way analysis of variance on ranks was used to compare values among the three times for each cerebral hemisphere. Spearman rank order correlation was used to correlate CBFV values with their corresponding CBVI values at identical times for each cerebral hemisphere (SPSS Inc, Chicago, Ill).

Outcome follow-up consisted of a medical record review for the following: 30-day postoperative or in-hospital mortality, late mortality after 30 days, and neurologic deficits recorded by each patient’s primary cardiologist during postoperative outpatient clinic visits.

Results

Twenty patients were studied. Eleven patients underwent the Norwood operation for hypoplastic left heart syndrome, and 9 underwent aortic arch advancement with other intracardiac procedures for severely hypoplastic or interrupted aortic arch. Patient bypass data are displayed in Table 1, and
patient demographic data are displayed in Table 2. During RLFP, pressure in the radial artery was significantly lower in those patients with a left radial catheter than in those with a right radial catheter. Neurologic monitoring data are reported in Table 3.

Paired values for CBFV were the same before, during, and after RLFP. The median rSO₂i values were 8% lower on the left side during RLFP (P = .054, Mann-Whitney U test). Five of 20 patients had a difference of at least 10% in rSO₂i during RLFP, always with the left side lower than the right. The largest single discrepancy was in a patient with 92% on the right and 68% on the left; this was the only patient with rSO₂i less than 70%. Eight of 20 patients had a difference of at least 25% in CBFV during RLFP, with the right side greater than the left in 4 and the left greater than the right in 4. Right-sided CBFV during RLFP did not correlate with RLFP flow rate (P > .05 by Spearman Rank Order Correlation; Figure 1). Poor correlation between individual CBVI and CBFV values is shown in Figure 2 (P > .05, Spearman rank order correlation). All paired values were studied together, because hematocrit demonstrated little change during the study period (27% before vs 25% during and after RLFP), and separate analysis revealed no differences.

There were no in-hospital deaths within 30 days of the operation and no new neurologic deficits in this group of patients. One patient was discharged to home at the age of 28 days. Another patient who underwent the Norwood operation died of multiorgan system failure related to bacterial sepsis. A brain magnetic resonance imaging study done 2 weeks before was unremarkable.

**Discussion**

This study demonstrates that RLFP, when flow rate is guided by TCD, results in adequate blood flow and oxygenation to both cerebral hemispheres. We believe that the median difference in rSO₂i between right and left hemispheres of 8% during RLFP is not clinically significant. Discrepancies between hemispheres in individual patients suggest that bilateral monitoring, especially of rSO₂i, may be useful. An alternative to bilateral monitors would be to place the NIRS sensor on the left side of the forehead, because this side appears to have a lower rSO₂i in some patients. The TCD probe could be placed on the right temporal window; thus both hemispheres could be monitored with a single set of sensors. The lowest left hemisphere rSO₂i of 68% was still significantly higher than the baseline preoperative rSO₂i for that patient. Thus the usual “luxury cerebral perfusion” with rSO₂i greater than 90% seen at deep hypothermia may not always be consistent during RLFP; however, the lower rSO₂i on the left side would not appear to put the patients at risk for cerebral hypoxemia if RLFP is performed according to this protocol.

There are several possible explanations for the decreased rSO₂i in the left cerebral hemisphere during RLFP. Although the circle of Willis is expected to be intact without stenoses in newborn patients, variations from the classic anatomic description are frequent, occurring in as many as 40% of adult autopsy specimens.9,10 In a study of color Doppler flow patterns in 53 patients, 10% of healthy term neonates showed deviations from normal flow patterns.11 In our patients, preferential flow to the right side or a nonintact circle of Willis can be argued against because CBFV on the left side was unchanged or slightly increased in all 5 patients with decreased rSO₂i relative to the pre-RLFP period. In addition, we performed a test occlusion of the right innominate artery just before the anastomosis of the proximal end on the PTFE graft and demonstrated adequate CBFV and rSO₂i to both cerebral hemispheres before proceeding with RLFP. Another possibility would be monitoring artifacts or failures; however, the NIRS system signal was adequate during all of the measurements, and the left side was always the side affected when there was a significant discrepancy in rSO₂i. The baseline rSO₂i on the left was at least 10% less than the right before RLFP in 4 of the 5 patients who had a discrepancy during RLFP. Baseline rSO₂i before incision in these patients was within 7% in 3 of these 4 patients, suggesting that in most cases the issues with unequal oxygenation began with the institution of full bypass, not RLFP itself. Only 1 of the 5 patients had unequal cerebral oxygenation exclusively during the period of RLFP. One explanation for both the lower rSO₂i values on the left side for individual patients is that our practice in this institution is to retract the left innominate vein during bypass in newborns with a silicone elastomer vessel loop. This

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**TABLE 3. Bilateral neurologic monitoring data (n = 20)**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Before RLFP</th>
<th>During RLFP</th>
<th>After RLFP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>rSO₂i (%)</td>
<td>55 (43-63)</td>
<td>51 (46-59)</td>
<td>95 (91-95)</td>
<td>95 (83-95)</td>
</tr>
<tr>
<td>CBFV (cm/s)</td>
<td>18 (14-23)</td>
<td>18 (13-24)</td>
<td>19 (15-23)</td>
<td>19 (14-23)</td>
</tr>
<tr>
<td>CBVI</td>
<td>15 (9-17)</td>
<td>18 (12-30)</td>
<td>7 (6-16)</td>
<td>8 (6-16)</td>
</tr>
</tbody>
</table>

Results are expressed as median with 25% to 75% interquartile range deviation.

*P = .054 for right versus left side during RLFP, Mann-Whitney U test.
A maneuver could partially obstruct this vessel and decrease cerebral venous drainage. In addition, the patient’s head is always turned 45° to 60° to the left. These maneuvers could result in accumulation of a volume of slowly desaturating venous blood in the left cerebral hemisphere. Because the venous/arterial blood ratio ranges from 75:25 to 85:15, this would explain the lower saturations seen in the left cerebral hemisphere in some patients.

Bilateral monitoring could theoretically detect decreased cerebral oxygenation related to anatomic problems and allow for planning alternative surgical or bypass techniques. Bilateral monitoring of adult patients during aortic arch surgery has been described as potentially averting neurologic disaster when significant desaturation on one side was detected, allowing rapid alteration of surgical approach to normalize rSO2 on both sides.

In a previous report, we described the use of TCD as the primary determinant of necessary bypass flow during RLFP. The added value of TCD relative to NIRS alone is avoidance of cerebral hyperperfusion. In that study, more than a third of patients had rSO2 values of 95% during deep hypothermia, which is the maximum reading by the monitor, leaving them potentially vulnerable to cerebral hyperperfusion when flow is adjusted to achieve this saturation. Radial artery pressure and a predetermined flow rate (25% of normal full-bypass flow) have been used to guide RLFP flow, but both have poor correlation with CBFV. Another reason to add TCD is that the frontal lobe and the territory of the anterior and middle cerebral arteries can be monitored so that as much as 70% of one hemisphere can potentially be assessed. CBVI was described by Pigula and coworkers as an important guide to adequate but not excessive RLFP flow. In this study we have demonstrated that individual CBVI values correlate poorly with CBFV values, and therefore an independent method of measuring CBF is desirable to guide RLFP flow. CBVI is actually an index of signal strength detected by the infrared light detectors. The signal strength for NIRS may be affected by factors other than blood volume, such as ambient light, interference with signal detection by darkly pigmented skin or hair, and improper application of the sensor. Thus the designation CBVI may be misleading and in fact is not a measurement approved by the US Food and Drug Administration. On the other hand, CBFV in the middle cerebral artery has demonstrated strong correlations with CBF measured by thermodilution in adults and children (r = 0.83, P < .0001), and with bypass pump flow (a surrogate for CBF) in children (r = 0.73, P < .001).

There are several limitations to this study. First, the significance of “low” rSO2 values and of a 10% or greater difference between cerebral hemispheres in neonates undergoing cardiac surgery is unknown. Austin and colleagues found that an rSO2 decrease of more than 20% (from a baseline established just before aortic cannulation) sustained for 3 minutes or longer in infants and children undergoing con genital heart surgery with cardiopulmonary bypass resulted in an incidence of acute postoperative neurologic morbidity (seizure, cerebral infarct, or choreoathetosis) of 26%, versus an incidence of 7% if cerebral desaturation did not occur. Kurth and coworkers, in a study of 26 infants and children undergoing DHCA for cardiac surgery, found acute neurologic morbidity in the 3 patients (coma in 2 and seizures in 1) whose cerebral oxygen saturation failed to increase during cooling on bypass, as is the norm. The patients whose cerebral oxygen saturation did increase (mean 30% above baseline) had no detectable neurologic morbidity. To date, this is the only evidence that low rSO2 values lead to adverse outcomes in congenital heart surgery. Although encouraging, the brief neurologic follow-up with
standard clinical examination in our patients does not prove the adequacy of RLFP to preserve long-term central nervous system function.

We made the following assumptions in hypothesizing that the CBVI would correlate with the CBFV about the relationships between CBV, CBVI, CBF, and CBFV during RLFP: CBVI \( \approx \) CBV \( \approx \) CBF \( \approx \) CBFV. CBVI should correlate with CBV if the total hemoglobin and the near infrared light path are not changing. Correlation between CBFV on the same side. Indeed, our measurements demonstrated in those patients who had a lower rSO\(_2\) on the left even though we measured the same or even increased CBFV on the same side. Indeed, our measurements demonstrated no correlation between RLFP flow rate and CBFV during RLFP.

In conclusion, RLFP provides comparable delivery of oxygenated blood to both cerebral hemispheres during neonatal aortic arch reconstruction. CBVI, as measured by NIRS, has poor correlation with CBFV measured by TCD, suggesting that TCD is useful in addition to NIRS as a guide to RLFP flow rates.

We thank Debora East, RN, for assistance with data collection, and E. O’Brian Smith, PhD, for statistical consultation.

References


