Change in regional (somatic) near-infrared spectroscopy is not a useful indicator of clinically detectable low cardiac output in children after surgery for congenital heart defects

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Objective: Near-infrared spectroscopy correlation with low cardiac output has not been validated. Our objective was to determine the role of splanchnic and/or renal oxygenation monitoring using near-infrared spectroscopy for detection of low cardiac output in children after surgery for congenital heart defects.

Design: Prospective observational study.

Setting: Pediatric intensive care unit of a tertiary care teaching hospital.

Patients: Children admitted to the pediatric intensive care unit after surgery for congenital heart defects.

Interventions: None.

Measurements and Main Results: We hypothesized that splanchnic and/or renal hypoxemia detected by near-infrared spectroscopy is a marker of low cardiac output after pediatric cardiac surgery. Patients admitted after cardiac surgery to the pediatric intensive care unit over a 10-month period underwent serial splanchnic and renal near-infrared spectroscopy measurements until extubation. Baseline near-infrared spectroscopy values were recorded in the first postoperative hour. A near-infrared spectroscopy event was a priori defined as ≥20% drop in splanchnic and/or renal oxygen saturation from baseline during any hour of the study. Low cardiac output was defined as metabolic acidosis (pH <7.25, lactate >2 mmol/L, or base excess ≤−5), oliguria (urine output <1 mL/kg/hr), or escalation of inotropic support. Receiver operating characteristic analysis was performed using near-infrared spectroscopy event as a diagnostic test for low cardiac output. Twenty children were enrolled: median age was 5 months; median Risk Adjustment for Congenital Heart Surgery category was 3 (1–6); median bypass and cross-clamp times were 120 mins (45–300 mins) and 88 mins (17–157 mins), respectively. Thirty-one episodes of low cardiac output and 273 near-infrared spectroscopy events were observed in 17 patients. The sensitivity and specificity of a near-infrared spectroscopy event as an indicator of low cardiac output were 48% (30%–66%) and 67% (64%–70%), respectively. On receiver operating characteristic analysis, neither splanchnic nor renal near-infrared spectroscopy event had a significant area under the curve for prediction of low cardiac output (area under the curve: splanchnic 0.45 [95% confidence interval 0.30–0.60], renal 0.51 [95% confidence interval 0.37–0.65]).

Conclusions: Splanchnic and/or renal hypoxemia as detected by near-infrared spectroscopy may not be an accurate indicator of low cardiac output after surgery for congenital heart defects. (Pediatr Crit Care Med 2012; 13:529–534)

Key Words: cardiac surgery; cardiopulmonary bypass; congenital heart defect; low cardiac output syndrome; near-infrared spectroscopy; renal; splanchnic.
as the heart and brain (9). In animal experiments, it has been demonstrated that increasing degrees of cardiogenic shock induced by cardiac tamponade raise inferior mesenteric resistance up to four times more than total vascular resistance (10). In healthy adult human volunteers, a 15% reduction in circulating blood volume resulted in a 40% reduction in splanchic blood volume while heart rate, blood pressure, and CO remained unchanged (11).

Near-infrared spectroscopy (NIRS) is a technique that has been used in various clinical settings to evaluate regional tissue oxygenation in a noninvasive manner (12–19). NIRS renal and splanchic regional oxygenation monitoring has been shown to positively correlate with metabolic acidosis (pH <7.25, lactate >2 mmol/L, base excess ≤-5), oliguria (urine output <1 mL/kg/hr), and/or escalation in inotropic support. In all the patients, point-of-care arterial blood gases and lactate levels were measured using iSTAT, a portable clinical analyzer device (i-stat, East Windsor, NJ), every hour and as needed in the postoperative period until extubation. Also, urine output was recorded every hour until extubation.

Outcome

This study’s primary outcome was the occurrence of LCO. Previous studies in children after cardiac surgery have used surrogate markers like oliguria, tachycardia, cool extremities, arterio-venous oxygen difference, occurrence of metabolic acidosis, initiation of a new inotropic agent, escalation of existing pharmacologic support, and initiation of extracorporeal membrane oxygenation to define LCO syndrome (7, 8). Similar to these pediatric studies, we defined LCO as one or more of the following surrogate markers: need for fluid bolus, occurrence of metabolic acidosis (pH <7.25, lactate >2 mmol/L, base excess ≤-5), oliguria (urine output <1 mL/kg/hr), and/or escalation in inotropic support.

Measurement of Somatic Regional Oxygen Saturation Using NIRS

Somatic regional oxygen saturation (sRsO₂) was monitored until extubation using a multichannel NIRS device (Somanetics, Troy, MI). Regional oxygen saturation at splanchic and renal regions were measured by applying age- and weight-appropriate NIRS probes over the anterior abdominal wall above the umbilicus and over the flank at the renal angle, respectively. The NIRS device measured splanchic and renal oxygen saturations every 6 to 30 secs. Probes, cables, and monitors were placed and maintained by study personnel and nursing staff.

The bedside medical team was not responsible for NIRS setup and maintenance, and clinical management was not altered based on the display. The NIRS values recorded in the first postoperative hour were used to define each subject’s baseline.

Statistical Analysis

All data were analyzed in hourly epochs during the postoperative phase until extubation. A NIRS event (NE) was a priori defined as a relative drop in splanchic and/or renal oxygen saturation (SrSO₂ and RrSO₂, respectively) by ≥20% from baseline value as in a prior study (21). For example, when a patient with baseline renal NIRS at 80% dropped renal NIRS down to 64%, this event is calculated as a 20% drop from the baseline. Sensitivity and specificity of NE as a diagnostic test of LCO was performed using 2 × 2 table. Receiver operating curve (ROC) analysis was then performed to determine whether any other percent drop from baseline in NIRS values was a better predictor of LCO. Sensitivity analyses were performed using a limited LCO definition without fluid bolus as well as for subjects below 5 months of age. Summary data are described as range, interquartile range, or 95% confidence interval (CI). All analyses were performed with Stata version 11 (Stata, College Station, TX).

RESULTS

We enrolled 20 patients for the study, and three were excluded due to technical challenges in obtaining complete NIRS data. The remaining 17 patients provided 828 hrs of postoperative measurements. Demographics and surgical background data are summarized in Table 1. There were six univentricular lesions – one with pulmonary atresia status post Blalock-Taussig shunt, two with tricuspid atresia and pulmonary atresia status post Blalock-Taussig shunt, two with hypoplastic left heart syndrome, and one with double outlet right ventricle. There were 11 biventricular lesions – one with secundum atrial septal defect, one with transposition of great arteries with intact ventricular septum, six with tetralogy of Fallot, two with large perimembranous ventricular septal defect, and one with common atroventricular canal defect. Six patients underwent intraoperative transesophageal echocardiograms, all of which demonstrated good ventricular function. Baseline postoperative data are summarized in Table 2. Using a cutoff of ≥20% drop in SrSO₂ and/or RrSO₂ from baseline during any study hour for NE,
Table 1. Demographic and surgical data of the patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Median</th>
<th>Range (Interquartile Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>5</td>
<td>0.06–180 (1.2–8.0)</td>
</tr>
<tr>
<td>Gender</td>
<td>Not applicable</td>
<td>Male 14, Female 3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>5</td>
<td>2–63 (3.6–63)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>55</td>
<td>43–150 (51–66.5)</td>
</tr>
<tr>
<td>Risk Adjustment for Congenital Heart Surgery-1</td>
<td>3</td>
<td>1–6 (2–3)</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (min)</td>
<td>120</td>
<td>45–300 (92.5–225)</td>
</tr>
<tr>
<td>Cross-clamp time (min)</td>
<td>88</td>
<td>17–157 (54–108)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>Not applicable</td>
<td>Univentricular 6 Biventricular 11</td>
</tr>
</tbody>
</table>

273 NEs and 31 episodes of LCO were observed in 17 patients. Figure 1 shows an example of NE and LCO episodes during a 24-hr record of SrSo₂ and RrSo₂ in one of the patients.

Of 31 LCO episodes observed, 17 were in the form of fluid boluses, two were oliguria, five were the occurrence of metabolic acidosis, and seven were an escalation of inotropic support. Among seven LCO events that were identified as escalation of inotropic support, two were in the form of escalation of epinephrine infusion (change in inotrope score from 14.5 to 15.5 and 13 to 14, respectively), two as escalation of dopamine infusion (change in inotrope score from 11 to 13 and 5 to 7, respectively), one as escalation of milrinone infusion (change in inotrope score from 5 to 7.5), and two as restarting of the dopamine infusion (change in inotrope score from 0 to 5 in each). NEs were observed with 48% (15 of 31) of LCO events. The sensitivity and specificity for LCO were 48.3% (95% CI: 30.5%–66.6%) and 67.6% (95% CI: 64.2%–70%), respectively. Table 3 presents sensitivity, specificity, positive predictive value, and negative predictive value of NE as a diagnostic test for LCO using NE cutoff as ≥25%, 10%, 15%, 20%, 30%, and 40% drop from the baseline. ROC analysis revealed that neither splanchnic nor renal NE had a significant area under the curve (AUC) for prediction of LCO (splanchnic: AUC 0.45, 95% CI 0.30–0.60; renal: AUC 0.51, 95% CI 0.37–0.65). The diagnostic ability of NIRS (with ≥20% drop from baseline as cutoff value) did not change when we used a limited LCO definition after eliminating fluid bolus as a criterion for LCO (sensitivity, 42.8% [95% CI 18–70], specificity, 67.1% [95% CI 63–70]), and also when we performed analysis of data for subjects below 5 months of age only (n = 8) (AUC for splanchnic NE = 0.51 [95% CI 0.33–0.69], AUC for renal NE = 0.48 [95% CI 0.31–0.65]). When we used ≥20% drop in NIRS saturation as a cutoff for detection of LCO, only 5.4% (95% CI 3.2–9.0) of NEs had an association with clinical LCO, whereas 97.1% (95% CI 95.2–98.2) of NEs were not associated with clinical LCO events. There was one patient out of the 17 patients with a high baseline lactate level of 9.33 mmol/L and low renal and splanchnic baseline NIRS values of 27 and 30, respectively. This patient belonged to Risk Adjustment for Congenital Heart Surgery category 2, with a CPB time of 120 mins and baseline inotrope score of 10. There was no intraoperative transesophageal echocardiogram record available for this patient, however. The remaining 16 patients had baseline lactate level <3 mmol/L. A sensitivity analysis with and without this patient did not change the direction or significance of our findings. The diagnostic characteristics did not improve when we used an absolute NIRS measurement cutoff instead of a relative percent drop from baseline values (AUC for splanchnic NIRS: 0.58 [95% CI 0.43–0.73], AUC for renal NIRS: 0.50 [95% CI 0.37–0.63]).

**DISCUSSION**

To our knowledge, this is one of the few studies that examined the sensitivity and specificity of NIRS splanchnic and/or renal tissue oxygenation monitoring for detection of LCO in children following surgery for both single- and two-ventricle reconstruction of CHDs. Since splanchnic and/or renal tissue hypoxemia can be an early indicator of LCO, NIRS regional oxygen monitoring has been proposed as an early marker of LCO. Our data, however, show that NIRS monitoring for renal and splanchnic oxygenation has poor predictive validity as an indicator of LCO. This result is surprising because previous studies demonstrated a better correlation between somatic NIRS and indirect measures of CO, such as mixed venous saturation (17, 18) and lactate levels (19).

Explanations for our differing results from other studies include the possibility that somatic SrSo₂ measurements using current sensors are not accurate. Greisen (22) recently described a lack of accuracy of the currently available NIRS instruments in measurement of cerebral SrSo₂. Commercial NIRS sensors have a signal-to-noise ratio of 2%–3%, higher than that of pulse oximetry. According to Greisen (22), averaging the absolute cerebral NIRS tissue oxygenation index measurements over a minute can provide an accurate mean value and overcome the problem of large signal-to-noise ratio. Mean values differ, however, based on site of sensor placement, as much as 15%. This expert review concluded that the precision of currently available NIRS instruments is insufficient for clinical use (22). There are also concerns that abdominal wall thickness may exceed the sampling depth (1.5–2 cm) of currently used NIRS probes in patients above 4 yrs for renal and 6 yrs for splanchnic measurements (23). We therefore performed an analysis of data for subjects younger than 5 months of age (n = 8) with no improvement in sensitivity and specificity.

It is also possible that the previously used threshold of a 20% drop in NIRS values is not an appropriate cutoff for
Currently, data on the normal range of NIRS rSo\textsubscript{2} exist only in healthy term newborns (24). Similar to several studies (25–28), we observed substantial between-subject variability in baseline NIRS rSo\textsubscript{2} values (baseline SrSo\textsubscript{2} values ranged from 30 to 90 and baseline RrSo\textsubscript{2} values ranged from 27 to 90). We performed the ROC analysis to evaluate the discriminative ability of the NIRS measurement and to identify an appropriate cutoff for the postoperative NIRS measurement. We were not able to identify any appropriate cutoff for LCO, however. To address the issue of baseline variability in NIRS rSo\textsubscript{2} values, we also ran a ROC analysis for the absolute rSo\textsubscript{2} values instead of the relative percent drop from baseline as a sensitivity analysis. This strategy also did not improve the diagnostic characteristics of the NIRS-derived splanchnic and/or renal regional oxygenation for LCO.

One other possibility is that our surrogate markers inadequately represent LCO. As is usually the case in clinical practice in pediatrics, we did not have a continuous CO measurement to correlate with somatic NIRS values. We defined LCO using clinical (oliguria, need of fluid bolus, or escalation of inotrope support) and/or laboratory (occurrence of metabolic acidosis) criteria as have previously published studies (7, 8). Because clinicians’ decisions to provide a fluid bolus could conceivably be affected by factors other than a diagnosis of LCO, we conducted a sensitivity analysis with a more limited definition of LCO excluding fluid boluses. This yielded similar results.

In recent years there has been increased interest in NIRS as a monitoring device in various clinical settings (15–17, 29-32), but there are gaps in the understanding of NIRS regional oxygenation monitoring. One study provided normal NIRS values of cerebral and renal rSo\textsubscript{2} in a small population of healthy term newborns (24), but baseline preoperative rSo\textsubscript{2} in children with cyanotic and noncyanotic heart defects are not known. Also, the effects of palliative or corrective surgery for these lesions on the rSo\textsubscript{2} are unknown.

Hoffman et al (17) evaluated the correlation between regional (cerebral and renal) NIRS measures and mixed venous saturations in neonates after stage 1 palliation for single-ventricle lesions. The intrapatient correlation among rSo\textsubscript{2} and mixed venous saturation was higher ($r^2 = .53$) than interpatient correlation ($r^2 = .46$). Therefore, the authors concluded that the NIRS measure is a reliable noninvasive indicator of mixed venous saturations. Another study by Chakravarti et al (19) showed a correlation between NIRS measurements and lactate levels among children with LCO. Currently, data on the normal range of NIRS rSo\textsubscript{2} exist only in healthy term newborns (24). Similar to several studies (25–28), we observed substantial between-subject variability in baseline NIRS rSo\textsubscript{2} values (baseline SrSo\textsubscript{2} values ranged from 30 to 90 and baseline RrSo\textsubscript{2} values ranged from 27 to 90). We performed the ROC analysis to evaluate the discriminative ability of the NIRS measurement and to identify an appropriate cutoff for the postoperative NIRS measurement. We were not able to identify any appropriate cutoff for LCO, however. To address the issue of baseline variability in NIRS rSo\textsubscript{2} values, we also ran a ROC analysis for the absolute rSo\textsubscript{2} values instead of the relative percent drop from baseline as a sensitivity analysis. This strategy also did not improve the diagnostic characteristics of the NIRS-derived splanchnic and/or renal regional oxygenation for LCO.

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double-ventricle physiology undergoing repair of CHD. In this study, they evaluated the diagnostic values of cerebral, splanchnic, renal, and muscle rSO₂ using blood lactate as a surrogate standard for LCOs. Measured rSO₂ at each point was averaged over 1 hr before a blood draw. They measured lactate levels at 0, 2, 4, 6, 8, 10, 12, 14, and 24 hrs after surgery. By using this methodological approach, they probably missed an unknown number of changes in NIRS rSO₂ values and lactate levels. Our study monitored blood lactate every hour with other clinical signs of LCO, and the NE was defined as a drop in rSO₂ below baseline every hour. We believe our approach is more realistic and close to the clinical application. In a case series of children who underwent cardiac surgery, the authors stated that NIRS may herald deterioration and that there may be a “threshold” effect that NIRS may usefully detect (33). Our study, using ROC analysis, failed to detect any meaningful threshold value of either renal or splanchnic NIRS measurement to detect early deterioration (LCO). It appears that NIRS events are overwhelmingly associated with no change in clinical CO status, demonstrated by an extremely low positive predictive value. Therefore, our study results cannot support the routine use of regional NIRS as an indicator that reliably heralds LCO.

Our study has several limitations. This is a prospective observational study with a small sample size from a single PICU, and the majority of patients belonged to low Risk Adjustment for Congenital Heart Surgery categories. Since the definition of LCO may be problematic, future multicentered studies may benefit from continuous CO or mixed venous saturation measurement to compare to rSO₂. We cannot exclude the possibility that they may have responded to the values on the display with interventions to potentially improve CO, although clinicians caring for our study subjects were not formally trained to interpret data from the NIRS monitor. If this occurred, however, it would have increased the likelihood that a fall in NIRS values would be associated with clinician interventions, biasing toward a positive result, which we did not find. Therefore, this is unlikely the case. We also used a landmark approach to place NIRS probes to detect splanchnic and renal rSO₂. This might have decreased the validity of the NIRS measures in older patients, although those were few in our study population. Also, if it were possible to continuously monitor lactate, base deficit, and instantaneous glomerular filtration rate, then there may have been other transient episodes of LCO that the clinical criteria missed. We acknowledge this is a methodological challenge when we compare an intermittent diagnostic test with continuously measured parameters.

Some physicians have recommended NIRS as “standard of care” in children for postoperative management (34), recognizing that “regional saturation measured by the NIRS technology may provide an early indication of oxygen deficits associated with impending shock states and anaerobiosis” (35). Our study results, however, suggested that NIRS measurements of splanchnic and renal regional oxygenation have limited capability to detect LCO. Further study is needed to delineate where the NIRS technology plays an important role to manage critically ill infants and children.

CONCLUSIONS

Splanchnic and/or renal tissue hypoxemia as detected by NIRS may not be highly sensitive or specific for clinical LCO after open-heart surgery in children.

ACKNOWLEDGMENTS

We thank the PICU staff at Children’s Hospital of New Jersey for their assistance with NIRS monitoring. We also extend our special thanks to children and their parents for their willingness to contribute to the science.

REFERENCES