Postoperative Cerebral and Somatic Near-Infrared Spectroscopy Saturations and Outcome in Hypoplastic Left Heart Syndrome

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Background. **Circulatory vulnerability reflected by low systemic venous oxygen saturation after surgical palliation of hypoplastic left heart syndrome predicts adverse neurologic outcome and reduced survival, and targeting venous saturation may improve outcome. We herein test the hypothesis that near-infrared spectroscopy (NIRS)-derived cerebral and somatic/renal regional saturations can predict survival.**

Methods. **Patient data, from a prospective Institutional Review Board-approved registry of hemodynamic measures after initial palliation of hypoplastic left heart syndrome, were analyzed with logistic and multivariable mixed regression methods to determine relationships between standard hemodynamic measures, direct and NIRS measures of saturation, and outcome. The primary outcome measure was survival through hospital discharge and 30 days.**

Results. **From the entire cohort of 329 patients, complete data for comparative analysis of physiologic predictors were available from 194 patients. The early survival rate was 92.1%; extracorporeal membrane oxygenation was used in 8.8% of patients. The mean arterial pressure, arterial cerebral, and somatic cerebral NIRS saturation differences were significantly higher for survivors versus nonsurvivors. Multivariable analysis found cerebral and somatic NIRS saturations, heart rate, and arterial pressure as predictors of outcome. Bivariate analysis of mean arterial pressure and somatic saturation allowed early identification of low cardiac output and high mortality risk.**

Conclusions. **Continuous noninvasive measurement of regional cerebral and somatic NIRS saturations in the early postoperative period can predict outcomes of early mortality and extracorporeal membrane oxygenation use in hypoplastic left heart syndrome. Because outcomes were strongly determined by NIRS measures at 6 hours, early postoperative NIRS measures may be rational targets for goal-directed interventions.**

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Circulatory vulnerability after surgical palliation of hypoplastic left heart syndrome as reflected by low systemic venous oxygen saturation (Svo_2) predicts adverse neurologic outcome and reduced survival [1–3], and targeting Svo_2 may improve outcome [4, 5]. Venous oxygen saturation monitoring requires intermittent sampling from invasive lines [6] or placement of oximetric catheters for continuous monitoring, and is particularly challenging in neonates, small infants, and in univentricular circulation [7]. Near-infrared spectroscopy (NIRS) monitoring provides continuous noninvasive estimation of regional tissue and venous oxygen saturation, and is thus a candidate to supplement or replace Svo_2 monitoring [8–10].

The use of NIRS-guided, goal-directed intervention has both theoretic and clinical support. We have previously demonstrated a relationship between low cerebral NIRS saturation and adverse neurodevelopmental outcome [3], and somatic NIRS saturation has been related to both renal dysfunction [11, 12] and necrotizing enterocolitis [13]. A linear combination of cerebral and somatic NIRS saturations can predict both Svo_2 [14] and lactate [9, 10]. Because (mixed) Svo_2 is the flow-weighted average of regional venous saturations, which are closely estimated by NIRS, we hypothesized that NIRS-derived oximetric measures could compete with Svo_2 for prediction of outcome. The primary hypothesis was that systemic oxygen status, assessed by continuous cerebral and

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Abbreviations and Acronyms

CPB = cardiopulmonary bypass
$DarSo_2C$ = arteriocerebral saturation difference
$DarSo_2R$ = arteriosomatic saturation difference
$DavSo_2$ = arteriovenous saturation difference
$DrSo_2RC$ = somatocerebral regional oxygen saturation difference
ECMO = extracorporeal membrane oxygenation
Hb = hemoglobin
HLHS = hypoplastic left heart syndrome
HR = heart rate
IQR = interquartile range
MAP = mean arterial pressure
NIRS = near-infrared spectroscopy
$Petco_2$ = end-tidal carbon dioxide tension
ROCA = area under the receiver-operating characteristics curve
rSo_2 = regional oxygen saturation
rSo_2C = cerebral regional oxygen saturation
rSo_2R = somatic regional oxygen saturation
Sao_2 = arterial oxygen saturation
Svo_2 = systemic venous oxygen saturation
SVR = systemic vascular resistance

somatic NIRS saturations in the early postoperative period, could predict survival.

Patients and Methods

A registry of 48-hour hemodynamic measures after stage 1 palliation of neonates with hypoplastic left heart syndrome (HLHS) has been maintained with approval of the Children's Hospital of Wisconsin Institutional Review Board since May 1996. Standard perioperative monitoring has included heart rate (HR) by electrocardiography, invasive mean arterial pressure (MAP) and right/common atrial pressure (RAP), continuous pulse oximetry (arterial oxygen saturation [Sao_2]), and superior vena cava venous saturation (Svo_2), end-tidal carbon dioxide tension ($Petco_2$), with intermittent arterial or venous blood gas and hemoglobin (Hb) concentration analysis. For the past decade, standard monitoring has included cerebral regional saturation (rSo_2C) and somatic regional saturation (rSo_2R) by NIRS. The arteriovenous saturation difference ($DavSo_2$), arteriocerebral saturation difference ($DarSo_2C$), arteriosomatic saturation difference ($DarSo_2R$), and somatocerebral regional oxygen saturation (rSo_2) saturation difference ($DrSo_2RC$) were calculated by temporally synchronous subtraction (details in Supplemental Table A1).

Patients underwent standardized management. An opioid-based, volatile-supplemented perioperative anesthesia technique was used for stage 1 palliation [15, 16]. Cardiopulmonary bypass (CPB) utilized pH-stat cooling, limited hemodilution, and limited deep hypothermic circulatory arrest, as previously described [16, 17]. Shunt type was determined by randomization during clinical trials [18] or by surgeon discretion. Systemic vascular resistance was modulated by phenoxybenzamine or phentolamine in most patients [19–22]. Postoperative management targets included MAP greater than 50, Svo_2 greater than 50, and rSo_2C greater than 40 [1, 3, 5, 16, 17, 23–27].

The primary outcome measure was survival though 30 postoperative days and hospital discharge [28]. Use of extracorporeal membrane oxygenation (ECMO) use was analyzed as a secondary outcome. Descriptive summary statistics and analyses were performed on the entire cohort, and in subgroups determined by use of Svo_2 or NIRS monitors; patients with both monitors comprised the comparison subgroup. Data were summarized as mean ± SD or median (interquartile range [IQR]) if normality testing failed, and 5% to 95% confidence intervals or percentiles. We used panel or mixed-effects univariable and multivariable regression to analyze relationships between demographic and physiologic measures and outcome in the comparison group, using stepwise parameter selection with p greater than 0.20 for removal and p less than 0.1 for entry. The area under the receiver-operating characteristics curve (ROCA) was used to assess prediction accuracy; optimal cutpoints were defined by the maximum production of sensitivity and specificity [29]. All statistical calculations were performed with STATA software (version 14; StataCorp, College Station, TX).

Results

Population and Monitoring Demographics

The study cohort included 329 patients (mean weight 3.2 ± 0.58 kg, median 3.2 kg [IQR: 0.6], confidence interval: 2.3 to 4.1 kg; mean age 8.8 ± 13 days, median 7 [IQR: 4], confidence interval: 3 to 22) at stage 1 palliation. Overall, 301 patients (91%) had Svo_2 monitoring, 214 (65%) had NIRS monitoring, 321 (98%) had either Svo_2 or NIRS, and 194 (59%) had both Svo_2 and NIRS, comprising the comparison group. Patients with NIRS monitoring were smaller and younger than patients with Svo_2 only (Table 1). The Svo_2 catheters were not used in 22 patients because of unusual superior vena cava anatomy, low weight, or technical problems. Data availability for attached devices over 48 hours was 47.1 ± 1.2 hours for electrocardiogram/HR, 47.5 ± 1.6 hours for MAP, 47.1 ± 2.9 hours for Sao_2, 46.9 ± 1.1 hours for rSo_2C, 46.8 ± 1.5 hours for rSo_2R, and 45.4 ± 6.3 hours for Svo_2.

Overall Survival and Morbidity

Inhospital and cumulative survival was, respectively, 92.1% and 80% for all 329 patients at median follow-up of 9.4 years; survival was 94.4% and 73% for 301 patients with Svo_2 monitoring, 90.7% and 83.3% for 214 patients with NIRS monitoring, and 91.2% and 84% for 194 patients with Svo_2 and NIRS, with no differences from the whole population. In the entire cohort, patients who died had lower weight and longer CPB and deep hypothermic circulatory arrest time. The 20 patients monitored with NIRS only were significantly smaller than the rest of the population (2.83 ± 0.69 kg versus 3.21 ± 0.58 kg,