Predictive value of near-infrared spectroscopy on neurodevelopmental outcome after surgery for congenital heart disease in infancy

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Objective: To explore the relationship between intraoperative regional cerebral oxygen saturation (rSO_2) measured by near-infrared spectroscopy (NIRS) and neurodevelopmental outcome in children after cardiac surgery.

Methods: Cross-sectional neurodevelopmental evaluation at 2 years of age was performed in a cohort of young infants who had surgery for congenital heart disease in 2007. The third edition of Bayley Scales of Infant and Toddler Development (Bayley-III) was used to assess cognitive, language, and motor functioning. Clinical and perioperative data were collected, including intraoperative rSO_2 nadir, rSO_2 percent decrease from baseline, and cumulative minutes of at least 20%, 30%, and 40% decrease from baseline.

Results: Twenty-seven patients without chromosomal abnormality were included in analyses. Mean Bayley-III scores fell within 1 standard deviation of the normative mean. Stepwise regression analyses of patient- and procedure-related variables, including rSO_2, demonstrated that cognitive ability was predicted by length of hospital stay and premature birth (58.1% of variance), receptive communication was predicted by length of hospital stay and rSO_2 nadir (40.2% of variance), expressive communication was predicted by birth weight (26.2% of variance), fine motor functioning was predicted by duration of cardiac intensive care unit stay (41.4% of variance), and gross motor functioning was predicted by the presence of a significant comorbidity (43.5% of variance).

Conclusions: In a contemporary cohort of infants undergoing surgery for congenital heart disease, neurodevelopmental outcomes at 2 years of age are largely influenced by patient-related characteristics. Although receptive communication appears to be influenced by rSO_2 nadir, the predictive value of NIRS remains unclear. (J Thorac Cardiovasc Surg 2012;143:118-25)

With the dramatic decline in mortality among children with congenital heart disease (CHD), attention has been directed toward functional outcomes. Neurodevelopmental impairment is the most common morbidity among survivors with CHD, limiting academic achievement, employability, and overall quality of life.[1] Intraoperative regional cerebral oxygen saturation (rSO_2) has been identified as a potential contributor to neurodevelopmental outcomes among children undergoing cardiac surgery.[2] Monitoring of rSO_2 with near-infrared spectroscopy (NIRS), a noninvasive optical technique that monitors brain tissue oxygenation through measurement of oxyhemoglobin and deoxyhemoglobin concentrations, is gaining acceptance.[3-5] However, technical issues in the measurement of cerebral oxygen,

methodologic limitations of previous studies, and a lack of evidence correlating NIRS values with neurodevelopmental scores or demonstrating that NIRS data can be used to improve outcomes are commonly cited as obstacles to embracing NIRS monitoring as routine in pediatric cardiac surgery.[6] Only a few published reports examine the relationship between perioperative oxygenation and later neurodevelopmental functioning,[7-9] and unfortunately these studies have used inconsistent methods and, commonly, very small sample sizes. Therefore, the existing data cannot provide the necessary confirmation about the usefulness of this tool. This study seeks to examine the predictive value of NIRS by evaluating the relationship between rSO_2 data obtained using intraoperative NIRS and neurodevelopmental outcome at 2 years of age.

METHODS

Participants and Study Design

The current investigation is a retrospective cross-sectional study examining the relationship between intraoperative rSO_2 measured by NIRS and neurodevelopmental outcome in young children with CHD. Participants were 27 children without chromosomal abnormalities who underwent surgery for CHD at our institution in 2007. All patients were under the age of 12 months at the time of the operation and 24 ± 3 months at the time of study participation. Patients who were unable to undergo neurodevelopmental testing or were non–English speaking were excluded from

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Abbreviations and Acronyms
Bayley-III = Bayley Scales of Infant and Toddler
            Development, Third Edition
CHD       = congenital heart disease
CICU      = cardiac intensive care unit
DHCA      = deep hypothermic circulatory arrest
NIRS      = near-infrared spectroscopy
PDI       = Psychomotor Development Index
rSO₂      = regional cerebral oxygen saturation
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enrollment. The Nemours Institutional Review Board approved the study, and informed consent and parental permission were obtained from the parents or legal guardians before study participation.

A total of 79 patients under the age of 12 months underwent open cardiac operations for a cardiac defect using NIRS monitoring in 2007. There were 62 English-speaking survivors at the time of study enrollment, and 43 of their families provided informed consent. Nineteen families did not consent owing to factors such as family relocation or lack of interest. Of those who did consent, 39 were tested. Twelve of the tested patients had a documented chromosomal abnormality and were excluded from the present analyses, resulting in a final sample size of 27.

Operative Management

Patients were managed preoperatively and postoperatively in a dedicated cardiac intensive care unit (CICU). Perfusion management included pH-stat strategy during cooling with a target hematocrit value of 30%, as well as fresh whole blood and a single dose of methylprednisolone in the cardiopulmonary bypass prime. Deep hypothermic circulatory arrest (DHCA) was used at the discretion of the surgeon. No variation in perfusion practices or personnel occurred during the study period. Perioperative management decisions were not made on the basis of NIRS data.

NIRS

Regional cerebral oxygenation with NIRS (INVOS 5100B; Somanetics, Troy, Mich) was routinely recorded during surgery for CHD by placement of a probe on the forehead in the midline position. The INVOS is a continuous-wave near-infrared spectrometer that uses 2 wavelengths of light (730 and 810 nm) to measure the ratio of oxyhemoglobin to total hemoglobin to derive oxygen saturation, the scale unit of which is percent. This information was then used to calculate (1) the lowest saturation level during the operative period (nadir), (2) the percent decrease from baseline to nadir, (3) rSO_2 nadir below 40%, 30%, and 20% (yes/no variables), (4) 20%, 30%, and 40% decrease from baseline (yes/no variables), and (5) cumulative minutes at 20%, 30%, and 40% decrease from baseline. We examined both absolute and relative measures of rSO_2. In addition to comparing the neurodevelopmental outcomes of patients above and below the levels suggested to be associated with increased risk (rSO_2 of 40% or 20% decrease from baseline),[5] comparison of patients falling above and below alternative levels was performed given the lack of empirical data correlating any specific level with neurodevelopment outcomes. NIRS data were unavailable for 1 participant; therefore, sample size was 26 for regression analyses involving NIRS variables.

Neurodevelopmental Testing

Children were administered the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III)[10] by a clinical psychologist according to standardization. The Bayley-III assesses the developmental functioning of infants and young children between the ages of 1 month

and 42 months through items administered to the child in a structured play format. As compared with the Bayley-II, this updated measure allows for the calculation of separate cognitive, receptive communication, and expressive communication scaled scores (previously combined into the Bayley-II Mental Development Index) and separate fine motor and gross motor scaled scores (previously combined into the Bayley-II Psychomotor Development Index [PDI]). Scaled scores have a mean of 10 and a standard deviation of 3. After the evaluation, families who expressed interest in obtaining feedback regarding the results of their child's evaluation were provided with a brief verbal debriefing. We were able to obtain only partial neurodevelopmental data for 7 of the 27 patients owing to child fussiness or refusal to complete testing. All available data for these patients were included in analyses.

Analytic Strategy

Exploratory univariable analyses assessed the relationships of patient- and procedure-related characteristics and NIRS variables to neurodevelopmental scores. Procedure-related characteristics referred to the operation with NIRS monitoring in 2007, with the exception of history of multiple cardiac procedures, history of multiple procedures with DHCA, and cumulative exposure to DHCA. Associations with sociodemographic variables were also examined. For multivariable analysis, only those variables associated with each neurodevelopmental outcome at $P < .05$ were considered in forward stepwise regression analyses. The entry criterion was set at $P < .05$ and the removal criterion was set at $P \geq .10$. Explained variance for all models was calculated by adjusted R^2 values.

To further examine the predictive value of NIRS on neurodevelopmental outcome, we performed secondary analyses in which all patients were stratified into 2 groups for each neurodevelopmental domain: delayed and nondelayed. Patients were considered delayed if their score was more than 1 standard deviation below the normative mean. All other patients were considered nondelayed. Independent samples t test (for continuous variables) and Fisher's exact test (for dichotomous variables) were used to compare the 2 groups.

The Nemours Foundation was not involved in data interpretation.

RESULTS
Baseline Characteristics

Cardiac procedures for the 27 patients included in analyses were Fontan or hemi-Fontan (n = 6), arterial switch (n = 3), Ross-Konno (n = 2), Norwood (n = 2), orthotopic heart transplantation (n = 2), and repair of a ventricular septal defect (n = 5), right ventricular outflow tract obstruction (n = 3), tetralogy of Fallot (n = 2), truncus (n = 1), and coarctation/ventricular septal defect (n = 1). Table 1 reports patient- and procedure-related characteristics for these 27 patients and for the 16 eligible patients without chromosomal abnormalities who did not enroll or participate in neurodevelopmental testing. Table 2 reports sociodemographic information for the study sample. Patients who did not enroll or participate in testing were more likely to be of an ethnic minority group than those who did participate in testing (56% vs 26%; $P = .047$). Table 3 reports descriptive data for the NIRS variables in this sample.

Neurodevelopmental Outcomes

Receptive communication (9.2 ± 3.5), expressive communication (9.5 ± 3.4), and fine motor (9.3 ± 3) development were comparable with that of the general