Neurodevelopmental outcome in hypoplastic left heart syndrome: Impact of perioperative cerebral tissue oxygenation of the Norwood procedure

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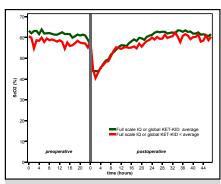
ABSTRACT

Objectives: Patients with hypoplastic left heart syndrome are at risk for neurodevelopmental impairment. Hypoxic-ischemic brain injury during neonatal treatment might be a relevant cause. We evaluated the association between cerebral oxygenation in the perioperative course of the Norwood procedure and neurodevelopmental outcome.

Methods: Cerebral tissue oxygen saturation (ScO₂) was obtained by near-infrared spectroscopy for 24 hours before and 48 hours after surgery in 43 patients. Full-scale, verbal, and performance IQ scores were evaluated with the Wechsler Preschool and Primary Scale of Intelligence at a median of 4.5 years (range, 3.5-6.8 years). Cognitive functions were assessed with the German Kognitiver Entwicklungstest für das Kindergartenalter (KET-KID).

Results: Mean IQ scores and KET-KID percentile ranks were in the lower-normal range (full-scale IQ, 94 \pm 11; verbal IQ, 97 \pm 13; performance IQ, 93 \pm 9; KET-KID global, 42 \pm 27; verbal, 48 \pm 29; nonverbal, 37 \pm 23). Scores were below average (full scale IQ <85 or KET-KID <16th percentile) in 12 cases. Mean preoperative ScO₂ was lower in patients scoring below average (56.8% \pm 7.1% vs 61.7% \pm 5.8%; P = .028) and was correlated with full-scale IQ (r = 0.495; P = .001), verbal IQ (r = 0.524; P = .001), and performance IQ (r = 0.386; P = .012) scores, and with global (r = 0.360; P = .018) and verbal (r = 0.395, P = .009) KET-KID scores. A relationship between IQ or KET-KID scores and postoperative ScO₂ was not found. Gestational age, head circumference z-score, age at surgery, and postoperative length of stay were associated with IQ and KET-KID scores.

Conclusions: Neurodevelopmental outcome was in the lower-normal range. Along with innate patient factors, preoperative cerebral tissue oxygenation is likely an important determinant of cognitive development. (J Thorac Cardiovasc Surg 2016;151:1358-66)



Perioperative cerebral tissue oxygenation compared with neurodevelopmental outcome.

Central Message

Preoperative cerebral tissue oxygenation is related to neurodevelopmental outcome in children undergoing the Norwood procedure.

Perspective

Hypoxic-ischemic brain injury might impair neurodevelopmental outcome in children undergoing the Norwood procedure. Decreased postoperative cerebral tissue oxygenation has been attributed to cognitive impairment. In contrast, only preoperative cerebral tissue oxygenation was related to neurodevelopmental outcome in our study. The impact of preoperative cerebral oxygenation warrants further investigation.

See Editorial Commentary page 1367.

Surgical and perioperative management of patients with hypoplastic left heart syndrome (HLHS) have steadily improved, resulting in substantially increased survival.

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Nonetheless, neurodevelopmental problems, including cognitive impairment, fine and gross motor deficits, and speech and language disorders, are common in children with HLHS. Therefore, identification of risk factors is of great interest for improving long-term neurodevelopmental outcomes. Near-infrared spectroscopy (NIRS) allows noninvasive and real-time measurement of cerebral

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Abbreviations and Acronyms AUC = area under the curve HAWIVA-III = Hannover-Wechsler Intelligence Scale, Third Edition **HLHS** = Hypoplastic left heart syndrome **KET-KID** = Kognitiver Entwicklungstest für das Kindergartenalter **NIRS** = near-infrared spectroscopy ScO₂ = cerebral tissue oxygen saturation SsO₂ = somatic tissue oxygen saturation **SCPA** = superior cavopulmonary anastomosis **TCPC** = total cavopulmonary connection

tissue oxygen saturation (ScO₂) and is being increasingly used for perioperative monitoring of patients with congenital heart disease.⁷

Patients undergoing the Norwood procedure may be at risk for hypoxic-ischemic brain injury, with decreasing ScO_2 observed in the early postoperative course. ⁸⁻¹⁰ Previous studies have reported abnormal findings on magnetic resonance imaging and worse neurodevelopmental outcomes. ^{11,12}

The purpose of this study was to assess the association between perioperative ScO₂ and neurodevelopmental outcomes in survivors of staged palliation for HLHS. In addition, potential risk factors for impaired neurodevelopmental outcome, including innate factors and variables related to surgical palliation, were evaluated.

METHODS

Patient Population

Children age 3.5 to 7 years who underwent staged palliation for HLHS or similar lesions were eligible to participate in this study. A total of 86 patients underwent the Norwood procedure between September 2006 and December 2010. Of these, 71 survived until Fontan surgery. Late death occurred in 2 cases. In addition, 7 patients with incomplete NIRS data and 2 non–German-speaking children were excluded. In 17 patients, testing was still pending or the parents denied participation. The remaining 43 patients were included in the analysis. Patients with genetic anomalies were not enrolled. Patient characteristics and surgical data were obtained from an institutional research database. Head circumference *z*-scores at birth were calculated adjusted for gender and gestational age based on reference data presented by Voigt et al. ¹³ Microcephaly was defined as head circumference *z*-score of -2 or less.

Perioperative Management

In the preoperative period, all patients were treated according to a standardized protocol consisting of afterload reduction with sodium-nitroprusside or phentolamine, low-dose prostaglandin E1, furosemide, enteral feeding, and avoidance of mechanical ventilation or inotropic support. ¹⁴

In the postoperative period, systemic afterload reduction therapy with sodium nitroprusside or with the alpha-blocker phentolamine was provided

in all patients. In addition, patients received the phosphodiesterase-III inhibitor enoximone or milrinone. Inotropic support was achieved with epinephrine. Analgesia and sedation were controlled with morphine.

NIRS was part of the perioperative routine monitoring. Institutional protocols in terms of a goal-directed therapy did not exist, however. Preoperative and postoperative therapy and interventions were guided primarily by arterial oxygen saturation, arterial pO_2 and pCO_2 levels, acid-base status, arterial blood pressure, central venous saturations, and echocardiographic right ventricular function. Transfusion of red blood cells was provided to keep hemoglobin levels >14 g/dL.

Data Collection

Routine perioperative monitoring included continuous measurement of arterial oxygen saturation (SaO_2) , invasive arterial blood pressure and central venous pressure in the superior vena cava. Hemodynamic monitoring was performed using the IntelliVue system (Philips Healthcare, Best, The Netherlands). Arterial blood gas measurements were obtained at 1- to 2-hour intervals. Central venous blood gases were sampled from the superior vena cava and analyzed at 4-hour intervals for the first 48 postoperative hours.

NIRS probes were placed on the patient's midline forehead and slightly to the right of midline on the T10-L2 posterior flank. Cerebral oxygen saturation (ScO₂) and somatic tissue oxygen saturation (SsO₂) data were stored digitally with the INVOS 5100 system (Covidien, Mansfield, Mass) and were matched to the hemodynamic and respiratory data for 24 hours preoperatively and for 48 hours postoperatively. Mean values for hemodynamic, respiratory, and NIRS data were calculated for the last 24 preoperative hours (baseline), for the first 4 postoperative hours (early postoperative course), and the entire 48-hour postoperative period. A cutoff value of 40% was chosen to define periods of diminished ScO₂. The absolute duration of ScO₂ <40% was evaluated. The area under the curve (AUC) of ScO₂ <40% was calculated to indicate the extent of desaturation below the threshold of 40%, using the following equation: AUC = ScO₂ <40% × duration in minutes. To estimate cerebral oxygen extraction, the difference between SaO₂ and ScO₂ was calculated for the preoperative and postoperative measurements ($\Delta SacO_2 = SaO_2 - ScO_2$).

Norwood Procedure

Surgical technique has been described in detail previously. ¹⁵ Pulmonary blood flow was established using a modified Blalock-Taussig shunt. Surgery was performed with deep hypothermia and selective antegrade cerebral perfusion via the modified Blalock-Taussig shunt during aortic arch reconstruction with a pump flow of approximately 15% of the target total bypass flow. The ph-stat method was used for cooling to a minimum temperature of 18°C, and was continued during bypass and antegrade cerebral perfusion. Patients were rewarmed with the alpha-stat method. Hemofiltration was routinely used before weaning from bypass. Primary chest closure was attempted in all patients.

Subsequent Procedures

Subsequent procedures included a superior cavopulmonary anastomosis (SCPA) using the hemi-Fontan technique, followed by a total cavopulmonary connection (TCPC) with a fenestrated intra-atrial tunnel. Data on age and weight at surgery and duration of cardiopulmonary support were collected. As a rough measure for complexity of the entire surgical palliation, cumulative cardiopulmonary bypass times and cumulative length of hospital stay were calculated for all 3 surgical procedures.

Assessment of Neurodevelopmental Outcomes

Two different tests were administered and analyzed by a single psychologist. Verbal IQ, performance IQ, and full-scale IQ were

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