Clinical outcome score predicts the need for neurodevelopmental intervention after infant heart surgery

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Objective: Our goal was to determine if a clinical outcome score derived from early postoperative events is associated with 18- to 24-month Psychomotor Developmental Index (PDI) score among infants undergoing cardiopulmonary bypass surgery.

Methods: We included infants aged ≤6 weeks who underwent surgery during 2002-2006, all of whom were referred for neurodevelopmental evaluation at age 18 to 24 months. We excluded children with chromosomal abnormalities, hearing loss, cerebral palsy, or a Bayley III assessment. The prespecified clinical outcome score had a range of 0 to 7. Lower scores indicated a more rapid postoperative recovery. Patients requiring extracorporeal membrane oxygenation were assigned a score of 7.

Results: Ninety-nine subjects were included. Surgical procedures were arterial switch (n = 36), Norwood (n = 26), repair of total anomalous pulmonary venous connection (n = 16), and other (n = 21). Four subjects had postoperative extracorporeal membrane oxygenation. Clinical outcome scores were highest in the Norwood group (mean 4.1 ± 1.4) compared with the arterial switch group (1.9 ± 1.6) ($P < .001$), total anomalous pulmonary venous connection group (1.6 ± 2.0) ($P < .001$), and other group (3.3 ± 1.6, P = not significant). A mean decrease in PDI of 10.9 points (95% confidence interval, 4.9-16.9; $P = .0005$) was observed among children who had a clinical outcome score ≥3, compared with those with a clinical outcome score <3. Time until lactate ≤2.0 mmol/L increased with increasing clinical outcome score ($P = .0003$), as did highest 24-hour inotrope score ($P < .0001$).

Conclusions: Clinical outcome scores of ≥3 were associated with a significantly lower PDI at age 18 to 24 months. This score may be valuable as an end point when evaluating novel potential therapies for this high-risk population. (J Thorac Cardiovasc Surg 2013;145:1248-54)

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Mortality from congenital heart disease has decreased significantly during the past 3 decades.[1,2] This is particularly true for infants undergoing complex cardiac surgical procedures.[2] As a consequence, neurodevelopmental morbidity has become an increasingly relevant outcome. However, neurodevelopmental outcomes are difficult to predict in early childhood, and interventions in infancy that may affect neurodevelopment are challenging to evaluate given a time lag between intervention and neurodevelopmental assessment that may be 2 years or longer. Many innovative therapies for infants undergoing cardiopulmonary bypass (CPB) surgery have been evaluated in recent years and will continue to evolve, yet selection of primary end points for clinical trials remains challenging. These issues speak to the potential value of surrogate outcomes that reliably predict neurodevelopmental sequelae and can be measured early in the postoperative course.

In pediatric patients undergoing cardiac surgery, several scoring systems have been developed that predict mortality.[3,4] However, correlation with neurodevelopmental outcomes has not been a focus of publications to date. Mackie and colleagues[5] developed a composite clinical outcome score for neonates undergoing complex aortic arch reconstruction that discriminated patients receiving intravenous postoperative tri-iodothyronine from those receiving placebo. This score is objective and measurable in intensive care units (ICUs) at no cost. Possible scores range from 0 (reflecting least morbidity) to 7 (reflecting death or use of postoperative mechanical circulatory support).

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Disclosures: Authors have nothing to disclose with regard to commercial support.
Received for publication Jan 16, 2012; revisions received March 23, 2012; accepted for publication April 13, 2012; available ahead of print Sept 10, 2012.

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0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2012.04.029

Abbreviations and Acronyms

CPB = cardiopulmonary bypass
ICU = intensive care unit
PDI = Psychomotor Developmental Index
LOS = length of stay
BSID-II = Bayley Scales of Infant Development, 2nd edition
MDI = Mental Developmental Index
TAPVC = total anomalous pulmonary venous connection

However, the full range of potential scores was not observed among patients in that initial validation study.[5] Therefore, a modification of this score was developed. The objective of our study was to examine the performance of this modified score. We hypothesized that the modified clinical outcome score would correlate with Psychomotor Developmental Index (PDI) score at age 18 to 24 months. A secondary objective of this study was to determine the correlation between this modified clinical outcome score and other important perioperative events, namely time to normalization of postoperative lactate, postoperative inotrope score, postoperative ICU length of stay (LOS), and total hospital LOS.

METHODS

Design

This study is part of a larger multiprovince inception cohort that was established to evaluate neurodevelopmental outcomes of infants aged ≤6 weeks who undergo cardiopulmonary bypass surgery in western Canada.[6] This inception cohort prospectively collected preoperative, intraoperative, and postoperative variables, as previously described.[7]

Subjects

Inclusion criteria were infants ≤6 weeks of age who underwent cardiopulmonary bypass surgery at the Stollery Children's Hospital in Edmonton, Alberta, Canada, between January 2002 and February 2006, all of whom received multidisciplinary neurodevelopmental assessments including the Bayley Scales of Infant Development (BSID-II)[8] through a developmental clinic with the exception of 1 child who was lost to follow-up. Developmental clinics were located in Edmonton and Calgary, Alberta; Regina and Saskatoon, Saskatchewan; Vancouver, British Columbia; and Winnipeg, Manitoba, Canada. We excluded children with known chromosomal abnormalities (eg, Trisomy 21 or deletion 22q11.2), cerebral palsy, or moderate to severe hearing loss, and those who had a Bayley III assessment rather than a BSID-II, because the two are not equivalent.[9] The inception cohort follow-up had ethics board approvals from each site. All parents/guardians provided written informed consent. The Health Research Ethics Board at the University of Alberta approved the study.

Early Childhood Assessments

Children were evaluated at age 18 to 24 months. Certified pediatric psychologists and psychometrists administered the BSID-II,[8] yielding separate Mental Developmental Index (MDI) and PDI standardized scores. The MDI assesses memory, problem solving, number concepts, vocalization, language, and social skills. The PDI assesses gross motor and fine motor skills. The mean score for both the MDI and PDI is 100 ± 15. Pediatricians experienced in neurodevelopmental assessment examined each child for evidence of cerebral palsy or visual impairment, defined as corrected visual acuity in the better eye of <20/60. Hearing was evaluated by experienced certified pediatric audiologists in soundproof environments as has been described.[6] Hearing loss was defined as binaural sensorineural hearing loss of more than 40 dB at any frequency from 250 to 4000 Hz. Maternal education was determined by years of schooling.

Clinical Outcome Score

The original clinical outcome score developed by Mackie and colleagues[5] is shown in Table 1. The components of the clinical outcomes score were derived with the intent of using variables that could be recorded objectively and early in the postoperative course, that are clinically meaningful (eg, time to first extubation) and that reflect hemodynamic status. No subjects in our study or the original publication had a score of 5 or 6. To improve the distribution of subjects across the range of possible scores (0 to 7), a modified clinical outcome score was developed (Table 1) using the same variables as the previous score, but with a modified score weighting. The score was calculated by adding the subscore of each individual component (range, 0 to 2 each). Subjects requiring postoperative extracorporeal membrane oxygenation were assigned a score of 7, the highest possible score, to reflect the most severe morbidity.

Inotrope Score

The postoperative inotrope score was calculated as per Wernovsky and colleagues.[10] The highest 24-hour postoperative inotrope score for a given patient was recorded for the purpose of correlation with the clinical outcome score.

Lactate

Serum lactate was measured postoperatively in the ICU with a frequency that was determined by the responsible intensivist. All blood gases analyzed in the ICU have a point of care lactate result, and are usually done during the first postoperative day at least every 4 hours, as previously described.[11] The time interval between weaning from cardiopulmonary bypass to first lactate ≤2.0 mmol/L was measured in hours.

Statistical Analysis

Categorical data are presented as proportions. Continuous data are expressed as mean ± standard deviation or median with interquartile range. One-way analysis of variance with Tamhane's multiple comparisons and Fisher exact test were used to compare surgical groups; Bonferroni correction was applied. Descriptive variables for outcomes were analyzed with Student t test, χ^2 test, and Fisher exact test. Correlations between clinical outcome score and other outcome variables were examined using Spearman rank order correlation coefficient. Subjects with a clinical outcome score of 6 or 7 were grouped together due to small sample size in these groups. Exploratory data analyses supported the use of multiple indicators for the clinical outcome score, with the lowest score being the reference category. Multiple linear regression analysis included clinical outcome score and any other potential predictor variables having $P < .10$ on univariate linear regression analysis, and after checking for multicolinearity. Potential predictor variables considered were birth weight, gestational age at birth, age at surgery (in days), year of surgery, number of preoperative days of ventilation, duration of cardiopulmonary bypass, duration of deep hypothermic circulatory arrest, lowest flow rate on cardiopulmonary bypass, palliative procedure (eg, Norwood) versus complete biventricular repair, mother's years of schooling, and antenatal diagnosis (yes/no). All analyses were 2-sided. Statistical analyses were performed using SPSS version 17 (2008; IBM Co, Armonk, NY) and SAS version 9.1 (2007; SAS Institute, Cary, NC), and R version 2.30 (2009; Institute for Statistics and Mathematics, Vienna University, Vienna, Austria).