Two–year survival, mental, and motor outcomes after cardiac extracorporeal life support at less than five years of age

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Supplemental material is available online.

Objective: Comprehensive outcome assessment of children receiving cardiac extracorporeal life support.

Methods: From 2000 to 2004, 39 consecutive children (aged 1 day to 4.4 years) had cardiac extracorporeal life support. Neurodevelopmental follow-up of all survivors was performed more than 6 months after life support (aged 53 ± 12 months). Developmental delay was defined as a score of less than 70 on the Bayley Scales of Infant Development II or Wechsler Preschool and Primary Scale of Intelligence. Predictor variables for mortality (at 2 years' follow-up) and delay were examined by univariate and multivariate analyses.

Results: Indications for extracorporeal life support were progressive low cardiac output in 14 (36%), failed weaning from cardiopulmonary bypass in 13 (33%), cardiac arrest in 9 (23%), and hypoxia in 3 (8%). Cardiac anatomy was single ventricle in 16 (41%), biventricular in 21 (54%), and myocarditis in 2 (5%). Survival was 18 (46%) at hospital discharge and 16 (41%) at 2 years. In survivors, mental score was 73 ± 16 (normal 100 ± 15), and 8 (50%) had mental delay. Initiating extracorporeal life support during cardiopulmonary resuscitation and duration of this resuscitation were not associated with death or mental delay. On multivariable Cox regression, lactate on admission to the pediatric intensive care unit (hazard rate 1.13; 95% confidence intervals 1.08–1.27) and single ventricle anatomy (hazard rate 3.93; 95% confidence intervals 1.62–9.49) were associated with death at 2 years. Stepwise multiple regression found time for lactate to normalize on extracorporeal life support, highest inotrope score during 120 hours of life support, and chromosomal abnormality explained 76.7% of the variance in mental score.

Conclusion: Cardiac extracorporeal life support had a 41% 2-year survival. Potentially modifiable variables (time for lactate to normalize and highest inotrope score early during extracorporeal life support) explained 69% of mental score variance.

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Extracorporeal life support (ECLS) has become an accepted therapeutic modality for neonates and children with progressive respiratory and/or cardiac failure that is refractory to conventional management.[1] The first use of ECLS to provide cardiac assistance after surgery for congenital heart disease was reported in 1970, but since the early years of ECLS, the predominant application has been for neonatal respiratory failure.[2] Over the past decade, however, there has been a significant increase in the use of cardiac-related ECLS reported to the Extracorporeal Life Support Organization international registry. Currently, ECLS is used as a bridge to recovery in patients with severe low cardiac output syndrome after surgery for congenital heart disease and in nonsurgical conditions such as myocarditis and dysrhythmias. As well, ECLS is used as a bridge to cardiac transplantation in children with

Abbreviations and Acronyms

CI = confidence intervals
CPB = cardiopulmonary bypass
CPR = cardiopulmonary resuscitation
ECLS = extracorporeal life support
HR = hazard rate
MAHSC = The Multiattribute Health Status Classification System
OR = odds ratio
PICU = pediatric intensive care unit
SD = standard deviation

cardiomyopathy and patients who have not had significant recovery of cardiac function postoperatively.

More than 20,000 neonates worldwide have undergone ECLS for respiratory failure in the past 20 years, and many publications are available regarding the outcome of these neonates.[1] These data reveal an overall survival of approximately 75% with an incidence of long-term neurologic dysfunction in survivors of between 15% and 30%.[3-5] Less than half as many neonates and children worldwide have received ECLS for cardiac indications,[1] with some recent single-center reports of survival between 30% and 55% (overall 40%).[6-8] The long-term neurodevelopmental outcomes of these cardiac ECLS patients have not been widely studied, although some series have described an incidence of long-term neurologic deficits in 40% to 60% of survivors.[9-11]

Our objective was to evaluate the long-term neurodevelopmental outcome in young patients receiving cardiac-related ECLS over a 5-year period and to identify any predictors of adverse neurologic outcomes or death in these patients.

Patients and Methods

This study uses data from an interprovincial inception cohort outcomes study conducted in three provinces in Western Canada. All patients under 5 years of age who received ECLS from January 2000 through December 2004 were identified at the time of ECLS. In all cases, ECLS was performed at the Stollery Children's Hospital, Edmonton, Alberta, Canada.

Demographic and some overall hospitalization variables that were previously agreed on were collected prospectively.[12] Several pre-ECLS, ECLS, and post-ECLS variables (Table E1) were added to the database by retrospective chart review. Long-term follow-up was discussed with parents or guardians once survival was probable. With their consent, contact was made with their respective follow-up clinics at the tertiary site of origin.

Patients

All consecutive patients given venoarterial cardiac-related ECLS at an age of less than 5 years over the 5-year period were registered. There were no exclusion criteria. All survivors received multidisciplinary neurodevelopmental assessments through existing neonatal follow-up clinics in Edmonton and Calgary, Alberta; Regina and Saskatoon, Saskatchewan; and Winnipeg, Manitoba. Ethics board approvals were obtained from each site before onset of the study. All parents or guardians signed individual consent forms.

Early Childhood Assessments

Outcomes assessment was completed at least 6 months after ECLS. At assessment, a research nurse recorded history of hospitalizations, illnesses, medication use, and need for supplemental oxygen. Physical measurements were obtained as has been described.[12] The family socioeconomic status was determined by the Blishen Index, a formula considering the relative income, needed education, and prestige factor of employment with a population mean and standard deviation (SD) of 43 (13).[13] Maternal education was indicated by years of schooling. Pediatricians experienced in neurodevelopmental follow-up examined each child for evidence of cerebral palsy[14] or visual impairment, defined as corrected visual acuity in the better eye of less than 20/60.[12] Hearing was evaluated by experienced certified pediatric audiologists in soundproof environments, as has been described.[12] Hearing impairment was defined as binaural sensorineural hearing loss of more than 40 dB hearing level at any frequency from 250 to 4000 Hz for children under 2 years; for older children, bilateral responses greater than 25 dB hearing level within the same frequencies were considered impaired. Motor or sensory disability was defined as cerebral palsy, visual impairment, or sensorineural hearing impairment as defined herein. Certified pediatric psychologists and psychometrists administered The Bayley Scales of Infant Development II in those assessed at 42 months of age or less (n = 5).[15] This is a widely accepted standardized outcome measure used in neonatal follow-up clinics yielding a mental standardized score (developmental quotient) with a mean of 100 and an SD of 15. A developmental quotient of less than 70 (2 SD below the mean) indicates mental delay. Within a normative sample, 2.27% of children have scores of less than 70. The full scale intelligence quotient of the Wechsler Preschool and Primary Scale of Intelligence (third edition[16]) was used for those assessed after 48 months of age. This is a widely accepted standardized score with a mean of 100 and an SD of 15.[16] An intelligence quotient of less than 70 (2 SD below the mean) indicates mental delay. The parent completed Adaptive Behavior Assessment System, second edition, for children before the sixth birthday. General Adaptive Composite score with a mean of 100 and an SD of 15 was used to support the tested findings. The Multiattribute Health Status Classification System (MAHSC) parental questionnaire with each of 8 domains coded as normal or abnormal was recorded.

Statistics

Demographic variables included age at time of ECLS, weight on admission to the pediatric intensive care unit (PICU), gender, chromosomal abnormality, socioeconomic status, and mother's year of schooling. Pre-ECLS variables included the following: cardiac diagnoses, cardiopulmonary resuscitation (CPR), seizure, plasma lactate, inotrope score,[17] pediatric logistic organ dysfunction score,[18] cardiopulmonary bypass (CPB) time, aortic crossclamp time, and deep hypothermic circulatory arrest time for those having cardiac surgery before ECLS, whether ECLS was used after cardiac surgery or not, and indication for ECLS (failure to wean off CPB in the operating room, progressive low cardiac output syndrome, progressive low cardiac output syndrome with refractory hypoxia, or ongoing failed CPR). ECLS variables were recorded daily for up to 120 hours