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Determining comorbidities and quality of life among pediatric survivors of extracorporeal life support☆,☆☆

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ABSTRACT

Purpose: The purpose of this study is to describe health-related quality of life (HRQoL) and the prevalence of comorbidities in pediatric survivors of extracorporeal life support (ECLS) and to determine risk factors for poor HRQoL.
Materials: The study design was a retrospective cohort and prospective follow-up study of patients who received ECLS in the pediatric intensive care unit at Egleston Children's Hospital from 2006 to 2013. Quality of life was measured using the Pediatric Quality of Life Inventory (PedsQL 4.0) completed by either parent proxies or the survivors themselves. Clinical data were obtained via review of electronic medical records.
Results: Surveys were sent to 37 parent proxies or survivors with a response rate of 43.2%. Survivors ranged in age from 2 to 21 years with follow-up range of 1 to 7.5 years. Primary respiratory failure due to pneumonia was the reason for ECLS in 81.3%. Mean total PedsQL scores were 73.9 (±21.3) with 11 survivors (69.8%) having a normal quality of life. None of the clinical characteristics (including age, ECLS length, or length of stay) correlated with PedsQL scores. The most commonly reported comorbidities included readmission les than 1 year after ECLS (46.7%) and "problems with school" (25%).
Conclusions: Survivors of pediatric extracorporeal membrane oxygenation can exhibit good HRQoL scores yet may be at risk for long-term adverse effects, such as lower psychosocial functioning and problems with school. A rigorous prospective investigation of the long-term follow-up of this patient cohort is needed to further evaluate these conclusions and to work toward the best possible outcomes for recipients of this resource-intensive therapy.

1. Introduction

For more than 25 years, extracorporeal life support (ECLS) has been used as life-sustaining therapy for pediatric patients with severe respiratory and/or cardiac failure. Traditionally, survival outcomes have served as the only metric of success in the pediatric population. According to the most recent report from the Extracorporeal Life Support Organization, survival of those placed on ECLS for respiratory disease is around 58% [1]. The observed trend over the last 2 decades has been an initial rise in survival followed by a plateau from 1993 to present. Extracorporeal life support utilization for pediatric respiratory indications has steadily increased from 200 cases per year (1993-2004) to 331 to 448 per year (2008-2012), with evidence of increasing ECLS use for children with preexisting comorbidities [2,3].

Unfortunately, other than the dichotomous variable of "survival," few existing articles describe other meaningful outcomes such as residual comorbidities or quality of life in pediatric, noncardiac ECLS survivors. In a 3-year multicenter study using the California Patient Discharge Database, Jen and Shew [4] describe a 16% prevalence of seizures and/or developmental delay in pediatric respiratory extracorporeal membrane oxygenation (ECMO) survivors with a 62% hospital readmission rate. In 21 surviving pediatric patients treated with ECMO for refractory sepsis, 62% had no disability at a median 5-year follow-up with zero patients demonstrating severe disability [5]. Among a cohort of children with primary pulmonary parenchymal disease, 5 of 13 survivors demonstrated no disability when evaluated by telephone interview using Pediatric Outcome Performance Category scores [6]. A retrospective evaluation of Pediatric Cerebral Performance Category (PCPC) and Pediatric Outcome Performance Category scores in ECLS survivors was published in 2005, but only 3 survivors received pediatric respiratory ECLS [7].

Obviously, a lack of prospective outcomes research exists regarding survivors of pediatric respiratory ECMO. Studies with actual personal contact with ECLS survivors rather than preestablished data collection from databases is rare. In addition, data collection involving more than basic categorical neurologic outcomes scores that rate disability does not exist. Unlike the neonatal and cardiac populations, pediatric respiratory ECLS survivors are usually not followed by either their previous intensive care unit (ICU) caregivers or a dedicated follow-up clinic;

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therefore, a more in-depth evaluation of outcomes variables goes unassessed. According to a recent 2014 article by Bone et al [8], ECMO is an independent risk factor for functional and/or cognitive disability in pediatric patients, highlighting the importance of addressing the posthospital recovery of these patients. Potential measurable long-term outcomes include neurodevelopmental assessments, descriptions of persistent comorbidities, and health-related quality of life (HRQoL), which have all been reported in survivors of neonatal and cardiac ECLS [9-14].

Measuring HRQoL has become a reliable, feasible metric for children with critical illness who survive to hospital discharge [15-17]. The concept of HRQoL and its determinants have evolved since the 1980s to encompass those aspects of overall quality of life that can be clearly shown to affect physical and mental health. This can include physical and mental health perceptions and their correlates—including health risks and conditions, functional status, social support, and socioeconomic status [18]. The Pediatric Quality of Life Inventory (PedsQL 4.0) is a validated tool that evaluates HRQoL as subsets of emotional, psychologic, physical, and school functioning and is applicable across multiple ages and health conditions [19,20].

The purpose of this study is to describe HRQoL and the prevalence of comorbidities in pediatric, noncardiac survivors of ECLS and to determine risk factors for impaired HRQoL.

2. Materials and methods

2.1. Study design

Approval for the study was obtained from the Emory Institutional Review Board with waiver of written consent. The study was a 2-part design with a retrospective chart review to obtain clinical data and a prospective cohort portion used to obtain survivor outcomes. Potential study subjects were identified through querying the Children's Healthcare of Atlanta (CHOA) ECMO Database for survivors of ECMO admitted to the pediatric ICU (PICU) between January 2006 and June 2013. Children's Healthcare of Atlanta is a 30-bed PICU in a tertiary level children's hospital with one of the largest ECMO programs in the country, performing approximately 60 cases per year. Patients were included if they were older than 30 days and younger than 18 years at the time of ECMO and survived to hospital discharge. Patients were excluded if they had an underlying diagnosis of cyanotic and/or unrepaired congenital heart disease or if ECMO was initiated but cannulation was not successful.

For the retrospective portion of the study, pertinent study subject data including demographics, clinical data, and predischarge outcomes were obtained via review of electronic medical records. Primary and secondary diagnoses were attained via review of patient problem lists entered by the primary medical team. Pre-ECMO neurologic status was described using the PCPC scale where 1, normal; 2, mild disability; 3, moderate disability; 4, severe disability; and 5, coma or vegetative state, and was based on the admitting physician history and physical examination.

Clinical data included pre-ECMO as well as post-ECMO data points. Mechanical ventilation days reflected the period from intubation to ECMO cannulation. Oxygenation index was calculated based on the equation: Paw (mean airway pressure) * fraction of inspired oxygen/Pao_2. Cardiac dysfunction was determined through qualitative assessment of ventricular function as described on an echocardiogram by the attending cardiologist. Inotropic scores and vasoactive-inotropic scores were calculated using the formulas:

$$\mathrm{IS} = \text{dopamine dose } (\mu g/kg/\min) + \text{dobutamine dose } (\mu g/kg/\min) + 100 \times \text{epinephrine dose } (\mu g/kg/\min)$$

[21]

$$\mathrm{VIS} = \mathrm{IS} + 10 \times \text{milrinone dose } (\mu g/kg/\min) + 10\ 000 \times \text{vasopressin dose } (U/kg/\min) + 100 \times \text{norepinephrine dose } (\mu g/kg/\min)$$

Acute kidney injury was deemed present if included by the attending ICU physician in the daily problem list. Pre-ECMO and post-ECMO neurologic dysfunction was established through an abnormal clinical examination by the critical care attending or an abnormal diagnostic study such as electroencephalogram, computed tomographic scan, cranial ultrasound, or magnetic resonance imaging. Outcome variables such as length of ECMO, ICU length of stay, hospital length of stay, and disposition were also extracted from the electronic medical record.

For the prospective follow-up portion of the study, survivors and/or survivor families were contacted via telephone to explain the purpose of the study and to obtain informed consent. Contact information for all ECMO survivors is maintained by the ECMO specialist service. Survivors or survivor families that consented for the study were given the option of completing the ECMO Survivor Follow-up Study via a Web-based or traditional paper format. The ECMO Survivor Follow-up Study consisted of 2 parts: (1) the PedsQL 4.0 and (2) a comorbidities survey.

The PedsQL 4.0 is a validated 23-item tool made up of 4 separate subscales that measure physical functioning (8 items), emotional functioning (5 items), psychosocial functioning (5 items), and school functioning (5 items) [19]. Each subscale can be evaluated separately or as a compilation of the 3 summary scores: total scale score, physical health summary score, and psychosocial health summary score. Each section quantifies how much of a problem the items represent to the study subject on a scale of 0 ("never a problem") to 4 ("almost always a problem"). The score for each subscale is determined by transforming the responses to a 100-point scale where 0 is equal to 100; 1, 75; 2, 50; 3, 25; and 4, 0, and then taking the mean of the item responses in that particular subscale. In general, higher scores indicate fewer problems and a "better" quality of life than lower scores. The PedsQL 4.0 offers separate forms for various age categories and separate forms for child vs parent-proxy report.

The comorbidities survey was used to better understand the current, ongoing problems facing ECMO survivors. It included items such as timing and number of readmissions after ECMO, development of new medical problems after ECMO, types of chronic equipment used at home (ie, supplemental oxygen and feeding pump), and outpatient therapies that the survivor actively receives.

Study data were collected and managed using Research Electronic Data Capture electronic data capture tools hosted at CHOA [22]. Research Electronic Data Capture is a secure Web-based application designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry, (2) audit trails for tracking data manipulation and export procedures, (3) automated export procedures for seamless data downloads to common statistical packages, and (4) procedures for importing data from external sources.

2.2. Statistical analysis

Statistical analyses were performed using SAS 9.3 (Cary, NC). Statistical significance was assessed at an $\alpha < .05$ level of significance. Baseline demographic and clinical variables and quality-of-life scores were summarized and described using means and SDs or counts and percentages, when appropriate. Continuous variables were assessed for normality using graphics plots and tests of normality. When the data appeared nonnormal, the median and interquartile range (IQR) were used in place of the mean and SD. Two-sample t tests or Wilcoxon rank sum tests were used to compare PedsQL scores between patient subgroups (ie, disposition after ECMO, comorbidities, and requirement of nasogastric tube feeds at discharge). Spearman rank order correlation coefficient and associated 95% confidence intervals were used to assess the relationship between continuous patient variables and quality-of-life scores.

3. Results

A total of 154 patients received ECMO in the PICU at CHOA from January 2006 to June 2013. Of this cohort, 98 survivors were identified (63%