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Intermediate-Term Results of Extracorporeal Membrane Oxygenation Support Following Congenital Heart Surgery

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Abstract

Background: Although there are considerable data regarding in-hospital results of congenital heart surgery (CHS) patients requiring postoperative extracorporeal membrane oxygenation (ECMO) support, there is limited information on intermediate-term outcomes. **Methods:** A single-institution retrospective review of 25 consecutive postoperative CHS patients who required ECMO and survived to hospital discharge between January 2003 and June 2008. Survival was estimated by the Kaplan-Meier method. **Results:** At a median follow-up of 3.3 years (interquartile range: 1.2-5.9 years), there was one death which occurred at six months postsurgery. Kaplan-Meier-estimated survival at three years was 95% (95% confidence interval: 90%-100%). Indications for ECMO included extracorporeal cardiopulmonary resuscitation (48%), systemic hypoxia (4%), postoperative low-cardiac output syndrome (28%), and intraoperative failure to wean off cardiopulmonary bypass (20%). Following ECMO support, 65% of patients had unplanned cardiac reinterventions (three requiring operative interventions, six requiring percutaneous interventions, and four requiring both), and 47% of patients required unplanned hospitalizations. In all, 29% of patients developed neurological deficits and 12% of patients developed chronic respiratory failure. No patients developed renal failure. Overall, systemic ventricular (SV) function normalized in 83% of patients, whereas 17% of patients had persistent mild-to-moderate SV dysfunction. **Conclusions:** Intermediate-term patient survival of ECMO following CHS is encouraging. However, neurological impairment and unplanned cardiac reinterventions remain significant concerns. Further delineation of risk factors to improve patient outcomes is warranted.

Keywords

extracorporeal membrane oxygenation, ECMO, congenital heart surgery, cardiac critical care

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Introduction

In patients undergoing palliative congenital heart surgery (CHS), extracorporeal membrane oxygenation (ECMO) was first described as a method of resuscitation and support in 1970[1] and is now a well-accepted and cost-effective modality for the treatment of patients with significant cardiac or respiratory compromise.[2] The overall survival to discharge of neonatal and pediatric patients placed on ECMO for cardiac indications is 40% and 49%, respectively.[3] Survival of patients requiring ECMO for respiratory indications is more favorable than for patients requiring ECMO for cardiac support.[4] Although the indications for ECMO have broadened since its inception, the survival rates reported have been constant over the years. Post-ECMO morbidity remains a significant concern, and long duration of ECMO support, acidemia, low-urine output in the first 24 hours, renal failure, and neurological impairment have been established as some of the risk factors associated with short-term morbidity and mortality.[5,6]

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Abbreviations and Acronyms

AICD	automatic implantable cardioverter defibrillator
CHS	congenital heart surgery
ECMO	extracorporeal membrane oxygenation
SV	systemic ventricular

Although recent studies have reported survival rates of up to 55% in neonatal and pediatric patients receiving ECMO for cardiac indications, 40% to 60% of these survivors have new neurological deficits.[7] These high long-term morbidity and mortality rates, as well as the high resource utilization associated with ECMO, raise concerns about the overly aggressive use of ECMO in CHS patients. Although short-term morbidity and mortality are well established, there are few data available on the intermediate- and long-term outcomes for these patients to help guide clinical decision making. This study seeks to examine the intermediate-term outcomes for patients who receive ECMO after CHS.

Patients and Methods

After obtaining institutional review board approval, a retrospective medical record review was performed to identify all patients who required post-CHS ECMO support and survived until hospital discharge at Children's National Medical Center from January 2003 to June 2008. Twenty-five patients were identified and selected for further review. Both inpatient and outpatient records were analyzed for demographic and outcomes data. Statistical analyses were performed using IBM SPSS Statistics (version 21.0, IBM, Armonk, New York). Continuous variables are expressed as median and interquartile range. Kaplan-Meier survival analysis was utilized to assess patient survival with a 95% confidence interval based on Greenwood's formula. New neurological deficits were defined as motor and cognitive abnormalities diagnosed following post-CHS ECMO support. Chronic respiratory failure was defined as tracheostomy/ventilator dependence at one year following discharge. Unplanned cardiac reinterventions were defined as any interventions (other than planned, staged single ventricle palliation) following complete operative repair, including interstage interventions in single-ventricle disease. Unplanned hospitalizations were defined as any hospitalizations not related to planned, staged single-ventricle palliative procedures. Renal failure was defined as the need for hemodialysis or peritoneal dialysis.

Table 1. Summary of Patient Demographics and Characteristics.[a]

Variable	Total Patients, N = 25
Male gender, no (%)	13 (52)
Female gender, no (%)	12 (48)
Age at ECMO, days	124 (5-437)
Weight, kg	3.5 (2.9-8.5)
Cannulation site, no (%)	
Neck	4 (16)
Chest	19 (76)
Groin	2 (8)
Concurrent genetic syndromes, no (%)	4 (16)
Duration of hospitalization, days	48 (33-74)
Duration of follow-up, years	3.3 (1.2-5.9)

Abbreviations: ECMO, extracorporeal membrane oxygenation; no, number.
[a] Continuous variables are median (interquartile range).

Table 2. Summary of Patient Cardiac Diagnoses.

Cardiac Diagnosis	Total Patients, N = 25
Cyanosis with increased PBF, no (%)	3 (12)
Cyanosis with decreased PBF, no (%)	12 (48)
Left-sided obstructive lesions, no (%)	5 (20)
Left-to-right shunt, no (%)	2 (8)
Hypoplastic left heart syndrome, no (%)	2 (8)
Anomalous origin of coronary artery, no (%)	1 (4)

Abbreviations: PBF, pulmonary blood flow; no, number.

Table 3. Clinical Summary.

Variable	Total Patients, N = 25
Indications for ECMO, no (%)	
E-CPR	12 (48)
Post-operative low-cardiac output	7 (28)
Intra-operative failure to wean from CPB	5 (20)
Hypoxia	1 (4)
Secondary end points, no (%)	
Neurological deficits	5[a] (22)
Chronic respiratory failure	3 (12)
Unplanned cardiac reinterventions	13[a] (65)
Unplanned hospitalizations	9[a] (39)
Renal failure	0 (0)
Normalization of SV function	19[a] (83)

Abbreviations: CPB, cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; E-CPR, extracorporeal cardiopulmonary resuscitation; SV, systemic ventricular; no, number.
[a] Neurological deficits, unplanned hospitalizations, and normalization of SV function are based on 23 patients available for follow-up; unplanned cardiac reinterventions are based on 20 patients available for long-term follow-up.

Results

In this single-institution retrospective review, 25 consecutive post-CHS ECMO patients who survived to hospital discharge were followed for a mean period of 3.3 years (interquartile range: 1.2-5.9 years; Table 1). Of the 25 patients, 18 (72%) underwent biventricular surgical repair and 7 (28%) underwent single-ventricle palliation. A summary of the cardiac diagnoses of the study patients is documented in Table 2. Median age at the time of ECMO initiation was four months. Indications for the use of ECMO in these patients included extracorporeal cardiopulmonary resuscitation (48%), postoperative low-cardiac output syndrome (28%), intraoperative failure to wean off cardiopulmonary bypass (20%), and hypoxia (4%; Table 3). In all, two patients were lost-to-follow-up immediately following discharge (one was a foreign national who returned to her home country; one for unknown reasons); three additional patients

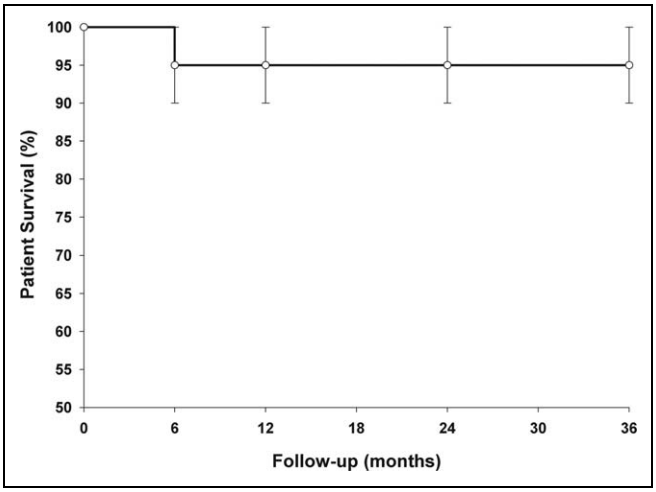

Figure 1. Kaplan-Meier survival curve based on 25 patients (one death at six months post-surgery). Error bars denote 95% confidence intervals based on Greenwood's formula.

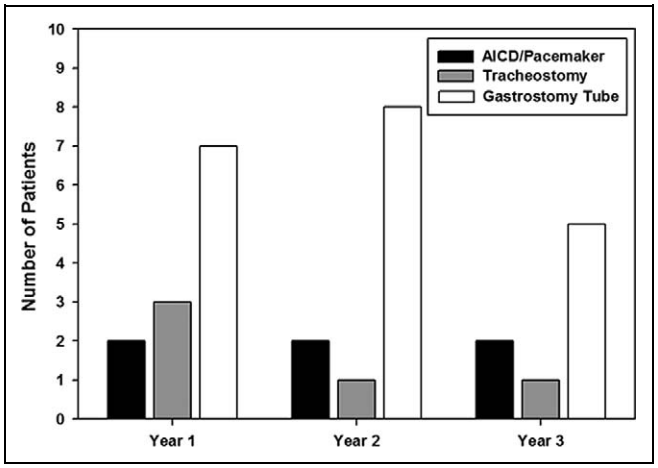

Figure 2. Medical technology dependence, defined here as reliance on specialized equipment on a day-to-day basis, among survivors of ECMO support following congenital heart surgery.

were lost to follow-up within the first year following discharge (two were foreign nationals returning to their home countries; one for unknown reasons), and a single patient died at six months postsurgery. In summary, 23 patients had follow-up after discharge, and a total of 20 patients had long-term (greater than nine months) follow-up. Overall, Kaplan-Meier estimated survival was 95% at three years postdischarge (95% confidence interval: 90%-100%; Figure 1).

Regarding long-term morbidities, 22% (n = 5) of patients developed new neurological deficits after ECMO, and 12% (n = 3) of patients were tracheostomy/ventilator dependent following discharge. In all, 39% (n = 9) of patients with follow-up had unplanned hospitalizations, and 65% (n = 13) of patients with long-term follow-up had unplanned cardiac interventions: three required surgical interventions, six required percutaneous interventions, and four required both percutaneous and surgical interventions. No patients developed renal failure following post-CHS ECMO support. Systemic ventricular (SV) function normalized in 83% (n = 19) of patients with follow-up, while the remaining 17% (n = 4) of patients had persistent mild-to-moderate SV dysfunction (Table 3).

Medical technology dependence, defined here as reliance on specialized equipment on a day-to-day basis, varied during the follow-up period (Figure 2). Over the three-year course of this study, dependence on tracheostomy included three patients at one year, and one patient at two and three years, whereas dependence on gastrostomy tube feeding varied from five to eight patients. At each time point, two patients required automatic implantable cardioverter defibrillator (AICD)/pacemakers.

Comment

Since its early use, ECMO has become an important tool in the modern critical care armamentarium to aid the exceptionally ill patients when cardiopulmonary support is required. There are many advantages to the use of ECMO in pediatric cardiac patients, including both cardiac and pulmonary support, support for various cardiac anatomies, rapid implementation, versatility, and current extensive experience. However, this technology is not without significant potential associated morbidities, including the risk of hemorrhagic or thrombotic complications, transfusion requirements, and neurological deficits.[8] These potential complications typically limit the safe and effective duration of ECMO to days or weeks and have raised concerns regarding the possibility of overly aggressive use of this technology.

Within the pediatric cardiac patient population, ECMO is typically used as a form of extended resuscitation for patients who have potentially reversible causes of cardiac dysfunction but are refractory to standard resuscitation attempts.[9] The specific indications for ECMO in the present study are similar to those reported previously.[10] However, morbidity following ECMO has been a major concern since its inception. Although these patients may survive the period of ECMO support and survive to hospital discharge, they often have persistent medical problems that require further intervention or long-term care. This is reflected in several of the outcomes examined in this study. The rates of further unplanned cardiac interventions and hospitalizations were 65% and 39%, respectively, within our cohort, similar to previously reported data.[11-14] In our cohort, 12% of patients had chronic respiratory failure, with all of these patients being tracheostomy dependent at one-year post-discharge. In addition, ongoing neurologic dysfunction, a long-established ECMO-associated morbidity, was noted to be present in five of our patients, again similar to previously reported results.[6,10] Although not associated with higher mortality, neurological complications represent a source of great morbidity for this population,[15] and the associated costs, long-term care requirements, and strain on caregivers can be tremendous and must be acknowledged when considering initiation of ECMO. Long-term quality-of-life implications due to these morbidities, especially new neurologic dysfunction,

have yet to be examined, and further study to establish the long-term impact that these morbidities have is warranted.

A number of patients in our study cohort had medical technology dependence during the follow-up period (Figure 2). Not surprisingly, AICD/pacemaker dependence was ongoing throughout this period. We speculate that the observed changes in medical technology dependence over time likely reflect a global improvement in function for these patients, and freedom from these technologies may be seen as a surrogate marker for improved quality of life. At the very least, it is a marker of decreased dependence on medical intervention and also represents a decrease in caregiver burden. However, as complete functional assessments and quality-of-life measurements were not undertaken, these results are speculative. Further study is needed to fully understand the effects that these changes have over time in an effort to better determine the ultimate quality of life that these patients attain on a long-term basis.

Finally, our data indicate that, within our population, the majority (83%) of patients went on to regain SV function. The persistent dysfunction present in the remaining patients was of mild-to-moderate severity. As this study did not examine the level of cardiac function for those patients who did not survive to discharge, this result may be due, in part, to the fact that those who had a return of cardiac function were more likely to survive to discharge. These results are, however, encouraging in that they suggest that long-term cardiac function does not appear to be negatively affected by the use of ECMO.

This study has several limitations. Due to the relative infrequency of ECMO utilization post-CHS at our institution, our sample size is small. Specifically, at our institution the incidence of ECMO use in pediatric patients following CHS as a percentage of the total number of all congenital heart operations performed during the study period was as follows: 2003—3.4%, 2004—1.0%, 2005—3.8%, 2006—1.9%, 2007—4.7%, and 2008—4.3% (mean overall annual incidence during the study period—3.2%). In the published literature, the reported incidence of ECMO support following CHS is 1% to 5%,[16] with some centers reporting an incidence as high as 8.5%.[17] Of note, our institution's use of ECMO following CHS (as a percentage of the total number of all congenital heart operations performed) has decreased significantly in 2011 (1.4%) and 2012 (0.9%).

A meaningful assessment of risk factors for intermediate-term morbidity in the study patients was not feasible as the sample size was too small to allow for sufficient power for statistical comparison and multivariate logistic regression analysis. Likewise, we could not analyze the risk factors for mortality for a given cardiac diagnosis due to low statistical power. However, although our patient sample size is small, we believe that our study results are clinically important as there are very limited data available on the intermediate- and long-term outcomes of patients who survive ECMO following CHS. We feel that our study demonstrates the need and may provide impetus for a large, multi-institution study that is sufficiently powered to definitively evaluate intermediate- and long-term outcomes and risk factors for morbidity and mortality based on specific cardiac diagnoses in this critically ill patient population.

As part of our data collection, we administered a well-validated quality-of-life questionnaire by telephone and mail (specifically, the PedsQL Measurement Model, utilizing both the PedsQL Pediatric Quality of Life Inventory Version 4.0 [validated in healthy children and adolescents and those with acute and chronic health conditions][18] and the PedsQL Cardiac Module Version 3.0 [validated in patients with heart disease][19]). However, the participation/response rate in this questionnaire was very low and, hence, we were unable to determine patient-reported assessments of quality of life. As many of the study patients have relocated away from our institution's geographic area, bringing these patients back to our institution for in-person quality-of-life assessments was not feasible.

Overall, further study is needed to better understand how, from the patient and caregiver perspectives, morbidities affect patients in the long term. This will better establish the ongoing quality of life that these individuals experience and help identify the obstacles they face going forward. Ultimately, we continue to believe that ECMO is a valuable clinical tool for management of the critically-ill CHS population, and it will continue to remain an essential part of our treatment strategy in caring for these complex and challenging patients.

Declaration of Conflicting Interests

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