Extracorporeal Membrane Oxygenation to Aid Cardiopulmonary Resuscitation in Infants and Children

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Background—Extracorporeal membrane oxygenation (ECMO) has been used to support cardiorespiratory function during pediatric cardiopulmonary resuscitation (CPR). We report on outcomes and predictors of in-hospital mortality after ECMO used to support CPR (E-CPR).

Methods and Results—Outcomes for patients aged <18 years using E-CPR were analyzed with data from the Extracorporeal Life Support Organization, and predictors of in-hospital mortality were determined. Of 26 242 ECMO uses reported, 695 (2.6%) were for E-CPR (n=682 patients). Survival to hospital discharge was 38%. In a multivariable model, pre-ECMO factors such as cardiac disease (odds ratio [OR] 0.51, 95% confidence interval [CI] 0.31 to 0.82) and neonatal respiratory disease (OR 0.28, 95% CI 0.12 to 0.66), white race (OR 0.65, 95% CI 0.45 to 0.94), and pre-ECMO arterial blood pH >7.17 (OR 0.50, 95% CI 0.30 to 0.84) were associated with decreased odds of mortality. During ECMO, renal dysfunction (OR 1.89, 95% CI 1.17 to 3.03), pulmonary hemorrhage (OR 2.23, 95% CI 1.11 to 4.50), neurological injury (OR 2.79, 95% CI 1.55 to 5.02), CPR during ECMO (OR 3.06, 95% CI 1.42 to 6.58), and arterial blood pH <7.2 (OR 2.23, 95% CI 1.23 to 4.06) were associated with increased odds of mortality.

Conclusions—ECMO used to support CPR rescued one third of patients in whom death was otherwise certain. Patient diagnosis, absence of severe metabolic acidosis before ECMO support, and uncomplicated ECMO course were associated with improved survival. **(*Circulation*. 2007;116:1693-1700.)**

Key Words: cardiopulmonary resuscitation ■ extracorporeal circulation ■ heart arrest ■ pediatrics

Survival after pediatric cardiopulmonary resuscitation (CPR) for cardiopulmonary arrest conducted either inside or outside healthcare facilities remains poor.[1–3] In 1992, a report by del Nido et al[4] showed that extracorporeal membrane oxygenation (ECMO) support instituted as rescue therapy during CPR (E-CPR) in children with cardiac disease who had cardiopulmonary arrest and failed to respond to conventional CPR promoted survival. Since then, E-CPR has been increasingly used to rescue children with both primary cardiac and noncardiac diseases receiving CPR after conventional resuscitative measures have failed to restore adequate circulation.[4–11] The current American Heart Association pediatric advanced life support guidelines recommend consideration of E-CPR for in-hospital pediatric cardiac arrest patients "if the conditions leading to arrest are reversible, or amenable to heart transplantation."[12] Although favorable survival outcomes for E-CPR have been demonstrated in many reports, ECMO is neither universally available nor accepted into clinical practice, and the current reports on the effectiveness of E-CPR are institution-specific.[10,11] Prognostic features such as patient factors before and during E-CPR use, complications during ECMO that may influence survival, and neurological and long-term outcomes after E-CPR have not been delineated clearly.

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Deployment of E-CPR requires the ready availability of personnel experienced with rapid assembly of an ECMO circuit, and surgical, medical, and nursing teams to initiate and manage patients on ECMO. Because the timing of cardiac arrest is unpredictable, these skilled personnel need to be available 24 hours a day, and often on-site, which makes the maintenance of an E-CPR team expensive.[7,13] Thus, it is imperative to understand survival and long-term outcomes after E-CPR use in pediatric patients to justify its use.

The goals of the present study are to describe the type of pediatric patients treated with E-CPR and to report trends in the use of and survival after E-CPR with data from the Extracorporeal Life Support Organization (ELSO). Furthermore, we evaluated whether in-hospital mortality after E-CPR use was associated with patient demographic factors, diagnosis, and ECMO support details.

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Methods

The data source for the present study came from the ELSO registry.[14,15] The ELSO registry was founded in 1982 and collects patient data on all extracorporeal techniques used to support cardiorespiratory function in children and adults. Data are collected and sent from the contributing centers with a standardized data sheet that contains patient demographics, diagnosis and procedure information, ECMO technique, complications during ECMO, and patient outcomes. Currently, 110 centers including 14 international centers contribute data to the registry. Each individual member institution approves data reporting through their local institutional review board. Patients who receive E-CPR are reported to ELSO with a distinct indication code and can be easily identified.[14] The ELSO registry defines E-CPR as "extracorporeal cardiopulmonary resuscitation, in which ECLS (extracorporeal life support) was used as part of the initial resuscitation from cardiac arrest. Patients who are hemodynamically unstable and placed on ECLS emergently without a cardiac arrest are not considered E-CPR."[15] Decisions regarding the use of E-CPR and the management and weaning of E-CPR patients are not standardized and thus are subject to practice variability.

Inclusion criteria included data from all E-CPR uses for patients <18 years of age during 1992 to 2005. Variables used included patient age, diagnosis and procedure codes, type and duration of ECMO support, number of ECMO runs per patient, reason for ECMO discontinuation, pre-ECMO mechanical ventilator and patient support details, worst pre-ECMO pH in the 6 hours before ECMO, ECMO support–related complications, and in-hospital mortality.

Data Categorization

We used both primary and secondary diagnosis and procedure ICD-9 CM (International Classification of Diseases, 9th Revision, Clinical Modification) codes to create diagnostic groups that included "cardiac" (including congenital heart disease and myocarditis or cardiomyopathy), "pediatric respiratory disease," "neonatal respiratory disease" (including congenital diaphragmatic hernia, meconium aspiration syndrome, and neonatal respiratory distress syndrome), "sepsis" (neonatal and pediatric), "accidental injury (including poisoning and trauma)" and "miscellaneous" (which included those cases that could not be classified into any of the above categories and those for which the only diagnosis code was cardiac arrest). Patients were categorized into the 5 diagnosis groups independently by 2 authors (RRT and SLB), and disagreement was resolved by consensus. If a subject had multiple diagnosis codes, such as an ICD-9-CM code for congenital heart disease and another for sepsis, they were classified as having a primary cardiac condition. Cannulation sites were categorized as "thoracic" if 1 of the cannulation sites used included the right atrium or aorta and "peripheral" if only peripheral vessels were used. Arterial cannulation sites were classified as "right carotid artery," "aorta," or "other sites" (which included both femoral arteries and the left carotid artery). When >1 arterial site was reported, the arterial site was classified as the site perceived to be the most difficult to cannulate. The right carotid artery was considered the least difficult site for arterial cannulation and the aorta the most difficult. Mode of ECMO was categorized as "venoarterial," "venovenous," or "combination" if a combination of both modes was reported.

Patient complications during ECMO were grouped with complication codes created by the ELSO registry into the following categories and subcategories: (1) brain injury (seizures [clinical or electroencephalogram evidence of seizures], radiological evidence of central nervous system injury [ultrasound or CT scan evidence of hemorrhage or infarction], and brain death); (2) renal injury (serum creatinine >1.5 mg/dL and dialysis use [hemodialysis or continuous arteriovenous hemodialysis]); (3) bloodstream infection, defined as blood culture–proven infection; (4) ECMO support (arterial blood pH <7.2 on ECMO, mechanical failure of the ECMO circuit, thrombus in the ECMO circuit, and cannulation site or surgical site bleeding); (5) respiratory complications (pulmonary hemorrhage and pneumothorax requiring treatment); (6) cardiac complications (arrhythmias during ECMO support that required treatment and CPR during ECMO support); and (7) gastrointestinal complications (gastrointestinal hemorrhage and hyperbilirubinemia [defined as serum direct bilirubin >2 mg/dL, indirect bilirubin >13 mg/dL, or total bilirubin >15 mg/dL]). Data on short- or long-term functional outcomes such as neurological function or quality of life for E-CPR survivors are not collected by the ELSO registry.

Statistical Analysis

Only 1 E-CPR run for each patient was included in the analysis. Thus, if a patient (n=13) had >1 E-CPR run reported, only the first E-CPR run was included. Survival to hospital discharge was defined as discharge from the ECMO center to either home or another facility. Demographic, pre-ECMO, and ECMO support details and ECMO complications were compared for survivors and nonsurvivors. The Mann-Whitney U test was used for continuous data, whereas categorical data were compared with the χ^2 test. The Fisher exact test was used when expected counts in >20% of cells were <5.

Candidate variables for inclusion in a multivariable logistic regression model to evaluate factors associated with in-hospital mortality for E-CPR users were chosen from the bivariate analysis, and the criterion for variable selection was set at a probability value ≤0.1. A forward-selection procedure was used for entry of variables into the model, and criteria for variable inclusion in the model were set at a probability value ≤0.05. Variables containing continuous data were only retained in the model if assumption of linearity was met. Variables not meeting the linearity assumption were divided into categories and included in the model as categorical variables. For example, worst arterial blood pH before E-CPR was trichotomized into pH <6.9, 6.9 to 7.17, and >7.17. The cutoff values were chosen on the basis of the lower 25th quartile and median pH among children who died. Because many diagnostic groups were small, we combined some groups for meaningful inclusion in the multivariable model. Among diagnostic groups, patients in the cardiac and neonatal respiratory failure groups had the best survival outcomes, and the remaining diagnosis groups were collapsed into a single diagnosis group, "other," for inclusion in the multivariable model. SPSS version 14.0 software (SPSS Inc, Chicago, Ill) was used for the analysis. Data are reported as frequency (n) with proportion (%) or median values with interquartile range (25th percentile, 75th percentile). Statistical significance was set at a probability value <0.05.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Study Population

Six hundred eight-two patients used E-CPR during the years of the study (1992–2005). Median age of the study population was 3 months (1, 28), and median weight was 4.6 kg (3.2, 12); diagnostic groups included cardiac disease (n=499, 73%; congenital heart disease [n=398], myocarditis and cardiomyopathy [n=101]), sepsis (n=54, 8%), pediatric respiratory failure (n=43, 6%), miscellaneous (n=35, 5%), neonatal respiratory failure (n=34, 5%), and accidental injury (n=17, 2%). The vast majority of E-CPR patients were managed with venoarterial ECMO (n=615, 90%). A combination mode was used in 56 patients (8%), and only 6 patients were managed with venovenous ECMO. Overall, 261 patients (38%) survived to hospital discharge.

Trends in E-CPR Use

E-CPR use increased significantly over time (linear association χ^2 probability value <0.001); however, survival did not significantly improve over the 14 years of study (linear

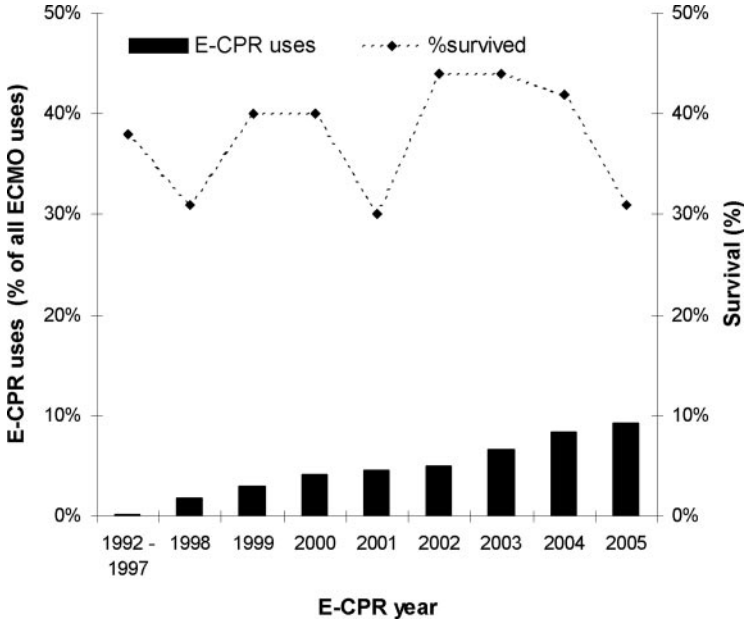

Figure 1. Trends in E-CPR use and survival: 1992 to 2005.

association χ^2 probability value=0.96; Figure 1). In 2005, almost 10% of ECMO use among pediatric patients was for E-CPR. Trends in the use of E-CPR based on diagnosis groups (cardiac versus noncardiac) are shown in Figure 2, with cardiac indications making up the majority of cases.

E-CPR Survivors Versus Nonsurvivors

Demographic Data

Table 1 shows demographic features of survivors compared with nonsurvivors after E-CPR use. Patient age, weight, and gender and year of E-CPR use did not vary significantly between survivors and nonsurvivors. Children identified with white race were more likely to survive than children of other races. Indication for E-CPR was significantly associated with in-hospital mortality. Mortality was lower in children with neonatal respiratory disease and cardiac disease than with the other diagnostic categories.

Pre-ECMO and ECMO Support Data

Clinical features related to pre-ECMO and initial ECMO parameters are presented in Table 2. Pre-ECMO ventilator settings, duration of ventilation before ECMO, and use of respiratory support therapies such as inhaled nitric oxide or high-frequency oscillatory ventilation before ECMO were similar for survivors and nonsurvivors. Children who survived to hospital discharge had significantly higher median Pao_2 and arterial blood pH before ECMO than children who died.

Mortality after E-CPR use was not associated with mode of ECMO support (Table 2). Mortality was also not associated with the use of peripheral or open-chest thoracic cannulation technique, percutaneous cannulation technique, or site used for arterial cannulation. Children who survived were supported for significantly more hours with ECMO and had longer length of hospital stay than children who died.

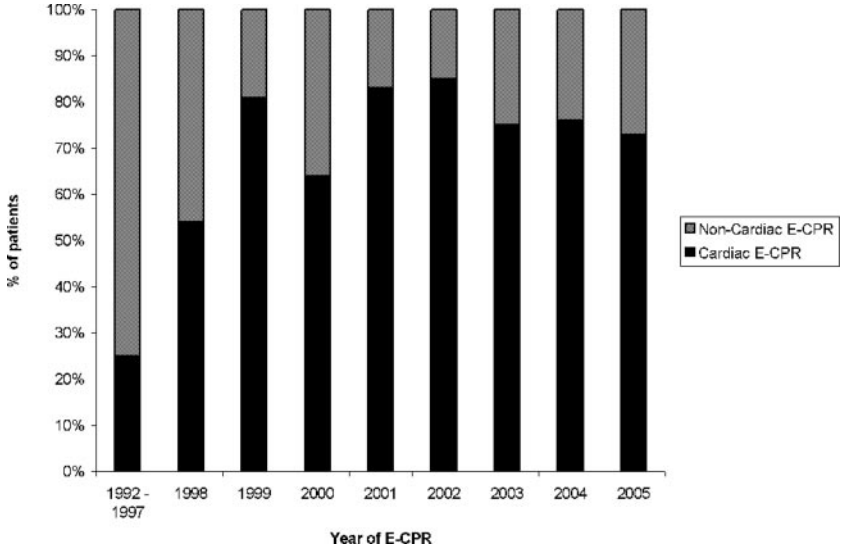

Figure 2. Trends in E-CPR use based on diagnostic groups: 1992 to 2005.

Table 1. Demographic Features of Survivors and Nonsurvivors After E-CPR Use

Variable	Survivors (n=261)	Nonsurvivors (n=421)	P
Age, mo	3 (0–16)	4 (1–36)	0.09
Gender	...	...	0.6
Male	152 (58)	246 (58)	...
Female	107 (41)	174 (41)	...
Body weight, kg	4.3 (3.2–9.5)	4.8 (3.1–9.5)	0.34
Race	...	...	0.01
White	171 (65)	234 (56)	...
Other	90 (34)	187 (44)	...
Diagnostic groups	...	...	<0.001
Cardiac disease	211 (81)	288 (68)	...
Sepsis	12 (5)	42 (10)	...
Pediatric respiratory disease	9 (3)	34 (8)	...
Neonatal respiratory disease	17 (7)	17 (4)	...
Accidental injury	3 (1)	14 (3)	...
Miscellaneous	9 (3)	26 (6)	...
E-CPR year	...	...	1.0
1992–1999	35 (13)	57 (14)	...
2000–2002	90 (34)	146 (35)	...
2003–2005	136 (52)	218 (52)	...

Data are presented as median (interquartile range) or n (%).

ECMO Complications and E-CPR Survival

As expected, several complications that developed after initiation of E-CPR were associated with increased risk of death (Table 3). These complications included radiological evidence of central nervous system injury, renal injury, arterial blood pH <7.2 on ECMO support, pulmonary hemorrhage, pneumothorax that required treatment, occurrence of arrhythmias, need for CPR during ECMO support, gastrointestinal hemorrhage, and hyperbilirubinemia. Of note, seizures while on ECMO, bloodstream infection, mechanical complications, thrombus in the ECMO circuit, and surgical or cannula site bleeding did not differ between children who survived and those who died.

Multivariable Logistic Regression Models Predicting Survival for E-CPR Users

Two separate models were developed, 1 to determine pre–E-CPR factors, including demographic variables, and another model to evaluate factors that occurred while receiving ECMO that were associated with in-hospital mortality (Table 4). Pre–E-CPR and demographic factors independently associated with mortality included diagnostic groups, race, and pre-ECMO arterial blood pH. The adjusted OR for in-hospital mortality was lower for patients with cardiac disease and neonatal respiratory disease than for those with other indications. Other factors that were associated with reduced adjusted odds of in-hospital mortality included white race compared with other races and patients whose pre–E-CPR arterial blood pH was >7.17 compared with those whose pre–E-CPR arterial blood pH was <6.9. Patient age, arterial blood oxygen and carbon dioxide levels, and use of surfactant as adjunct respiratory support before ECMO initiation were not independently associated with mortality.

The second model explored the association of ECMO complications (excluding brain death) and in-hospital mortality after adjustment for duration of ECMO support. Several ECMO complications, including radiological evidence of neurological injury, pulmonary hemorrhage, CPR while on ECMO, and persistent metabolic acidosis with arterial blood pH <7.2 during ECMO support, significantly increased the odds of mortality before hospital discharge. Other complications, such as bloodstream infection, gastrointestinal hemorrhage, occurrence of arrhythmias, pneumothorax, and hyperbilirubinemia during ECMO support, were not independently associated with mortality.

E-CPR Nonsurvivors

Of 421 E-CPR nonsurvivors, 221 patients (52%) died within 72 hours of ECMO initiation and were more likely to meet brain-death criteria (85% versus 15%. $P<0.001$) and to have a pre-ECMO pH <6.9 (61% versus 39%, $P=0.04$) than those who died after >72 hours of ECMO support. The incidence of renal failure (serum creatinine >1.5 mg/dL) was more frequent in those whose ECMO support lasted >72 hours than in those who died ≤72 hours after ECMO initiation (59% versus 41%, $P=0.01$).

Discussion

In the present cohort of children with cardiopulmonary arrest, the use of ECMO to aid ongoing CPR salvaged over one third of patients (38%) who failed conventional CPR and whose prognosis was otherwise dismal. E-CPR use has increased significantly over the last 14 years, and E-CPR is used to augment CPR in pediatric patients with cardiac and noncardiac diseases. Newborn infants with respiratory failure and patients with cardiac disease had significantly better survival than children with other diseases such as pediatric respiratory failure. Mortality after E-CPR was also associated with the presence of severe metabolic acidosis before the initiation of ECMO and with race. In addition to these pre-ECMO factors, clinical status during ECMO, such as the persistence of metabolic acidosis during ECMO, which indicated inadequate circulatory support, and ECMO complications increased the odds of death before hospital discharge. Although survival rates for E-CPR use reported here are higher than those reported for conventional CPR, data on neurological outcomes or quality of life after hospital discharge for E-CPR survivors were not available, which is an important limitation of these analyses.[16,17]

Survival after conventional CPR has been shown to be influenced by patient age, patient diagnosis, reversible nature of the event leading to cardiac arrest (such as ventricular dysrhythmias compared with pulseless rhythms), presence of multisystem organ failure, patient location (out of hospital versus intensive care unit), technical skills and equipment available to the provider, and characteristics of the institution where CPR was conducted.[1,2,8,16–19] Many of the factors that influence survival after conventional CPR continue to influence survival when E-CPR is used. For example, we found

Table 2. Pre–E-CPR Support and ECMO Variables in E-CPR Users

Variable	Survivors (n=261)	Nonsurvivors (n=421)	*P*
Ventilator parameters before E-CPR*			
PEEP, mm Hg	5 (4–7)	5 (5–8)	0.51
Mean airway pressure, mm Hg	13 (9–20)	12 (9–18)	0.36
Arterial blood gas values pre E-CPR*			
$PaCO_2$, mm Hg	47 (35–63)	49 (37–77)	0.06
PaO_2, mm Hg	46 (32–73)	40 (26–70)	0.04
Arterial pH	7.26 (7.06–7.38)	7.17 (6.9–7.36)	0.001
Adjunct respiratory support			
Inhaled nitric oxide	37 (14)	51 (12)	0.44
High-frequency oscillatory ventilation	18 (7)	36 (9)	0.44
Surfactant	5 (1)	9 (3)	0.04
Duration of mechanical ventilation before ECMO, h	14 (3–47)	18.5 (3–74)	0.17
Mode of ECMO	...	...	0.36
Venoarterial	257 (98.4)	374 (89)	...
Venovenous	1 (0.4)	5 (1)	...
Combination mode	1 (0.4)	39 (9)	...
Missing	2 (0.8)	3 (1)	...
Thoracic cannulation	88 (34)	143 (34)	0.95
Percutaneous cannulation	10 (4)	25 (6)	0.20
Arterial cannulation site†	...	...	0.23
Right carotid artery	150 (57)	213 (51)	...
Aorta	88 (34)	143 (34)	...
Other site	17 (7)	40 (10)	
Missing	5 (2)	20 (5)	
Initial ECMO flow, $mL \cdot kg^{-1} \cdot min^{-1}$	100 (80–121)	102 (80–131)	0.52
Duration of ECMO support, h	88 (51–140)	66 (26–157)	0.01
Length of hospital stay, d	33 (19–59)	11 (3–24)	<0.001

Data are presented as median (interquartile range) or n (%).
*Missing data: ventilator parameters (53% to 66%); arterial blood gas values (17% to 19%).
†Excludes patients supported on venovenous ECMO.

that patients with neonatal respiratory disease and cardiac disease had better survival after E-CPR use than those with pediatric respiratory failure and sepsis. It is likely that patients with neonatal respiratory disease and cardiac disease had a more easily reversible event that led to cardiac arrest and were less likely to have had multisystem organ failure, which resulted in improved survival. In addition, although the ELSO database does not include information about pre-ECMO invasive monitoring and location of the patient at the time of arrest, many patients in the present cohort had E-CPR after recent cardiac surgery. These patients are likely to have vascular access for monitoring during and after CPR and to be cared for in an intensive care unit with rapid assessment and response capability, thus improving their odds of survival. The influence of hospital E-CPR experience on survival outcome is difficult to evaluate because of the nature of data reported to ELSO. We speculate that institutions that use E-CPR frequently are more likely to have systems and processes in place for rapid deployment during CPR, and whether such influences are important should be studied in the future.

An important finding in the present analysis was the association of higher pre-ECMO arterial pH (pH >7.17 compared with pH <6.9) with survival to hospital discharge. In the present analysis, we used arterial blood pH as a surrogate for the adequacy of cardiac output, respiratory function, and tissue perfusion before cardiopulmonary arrest and during CPR. The severity of metabolic acidosis based on arterial blood gas pH before ECMO has been shown to be associated with risk of central nervous system injury among all pediatric patients treated with ECMO.[20] In the present report, we found that 52% of the E-CPR nonsurvivors died within 72 hours of ECMO initiation, which included both the majority of patients who met brain-death criteria and nonsurvivors whose pre-ECMO pH was <6.9. In these patients, inadequate cardiac output and tissue perfusion or inadequate gas exchange before and during CPR may have led to death, rather than complications related to ECMO support. Duration of CPR and therapies used during CPR before ECMO are not reported to the ELSO registry, so a maximum duration of CPR beyond which E-CPR therapy is not beneficial could not be determined. Furthermore, although pre-ECMO arterial

Table 3. ECMO Complications in E-CPR Survivors and Nonsurvivors

Variable	Survivors (n=261), n (%)*	Nonsurvivors (n=421), n (%)*	*P*
Brain injury			
Seizures	30 (11)	53 (13)	0.67
Radiological findings of CNS injury	16 (6)	65 (15)	<0.001
Brain death	0	74 (18)	<0.001
Renal injury			
Serum creatinine >1.5 mg/dL	29 (11)	90 (21)	0.001
Dialysis use	15 (6)	54 (13)	0.003
Bloodstream infection	15 (6)	41 (10)	0.07
ECMO support			
Arterial blood pH <7.2 on ECMO	16 (6)	72 (17)	<0.001
Mechanical failure of ECMO circuit	21 (8)	56 (13)	0.04
Thrombus in ECMO circuit	48 (18)	70 (17)	0.55
ECMO cannula and surgical site bleeding	67 (26)	121 (29)	0.38
Respiratory			
Pulmonary hemorrhage	11 (4)	53 (13)	<0.001
Pneumothorax	2 (0.8)	16 (4)	0.02
Cardiac			
Arrhythmias during ECMO support	36 (14)	83 (20)	0.05
CPR during ECMO support	9 (3)	47 (11)	<0.001
Gastrointestinal			
Gastrointestinal hemorrhage	1 (0.4)	20 (5)	0.001
Hyperbilirubinemia	6 (2)	27 (6)	0.02

CNS indicates central nervous system.
*Percentage of patients with the event in the 2 groups.

blood pH was strongly associated with outcome, 12% of children who survived after E-CPR use had a pre-ECMO pH <6.9. Thus, a lower limit of acceptable pre-ECMO arterial blood pH for withholding ECMO support cannot be prescribed. However, we can conclude that severe metabolic acidosis is a marker of poor outcome in these patients and that the utility of E-CPR should be considered carefully in those who have profound metabolic acidosis (arterial blood pH <6.9 before E-CPR), because these patients are at risk of neurological injury and are very unlikely to survive. The shorter duration of ECMO support and length of hospitalization in E-CPR nonsurvivors are likely to be related to the withdrawal of ECMO after the occurrence of catastrophic complications such as brain death.

We expected transthoracic cannulation among patients after cardiac surgery to be associated with better survival because it allows for open cardiac massage before cannulation and may allow more rapid ECMO deployment.[21] However, we did not find a survival benefit to this approach and speculate that similar outcomes after open-chest cannulation compared with peripheral vessel cannulation for ECMO may be due to the need to withhold CPR for a period of time during direct cannulation of the aorta and right atrium and possibly to a higher risk of bleeding after open-chest cannulation.[12] The reason for improved hospital survival associated with white race is uncertain; however, better outcomes for white patients have been reported for children undergoing cardiac surgery and other pediatric critical care illnesses.[22,23] Alternatively, this may be associated with patient demographics served by a given hospital, confounding the association between white race and E-CPR outcome.

Complications that develop during ECMO are generally accompanied by increased mortality for all applications of ECMO and also influence survival after E-CPR.[20,24–26] Inadequate cardiac support, reflected by persistent acidosis during ECMO, and cardiac arrest during ECMO were significantly associated with death. Renal failure, use of dialysis, and the development of multisystem organ failure have been associated with increased mortality among pediatric ECMO patients after cardiac surgery,[24,27] which was also demonstrated in the present cohort. Cerebral or other organ hemorrhage (pulmonary or gastrointestinal) frequently forces withdrawal of ECMO in an effort to stop anticoagulation, which limits the time for myocardial and patient recovery.[20] Thus, if a patient placed on ECMO to aid CPR has persistent metabolic acidosis despite ECMO support, has bleeding complications, or has a deteriorating course with development of multisystem organ dysfunction during ECMO, then the family should be advised that survival is very unlikely.

Survival to hospital discharge after E-CPR use has not improved over time. One reason for this may be the increasing inclusion of patients with noncardiac diagnoses and of those with other nonsurvivable comorbidities for E-CPR support because of lack of clear consensus or guidelines

Table 4. Multivariable Regression Models Showing Predictors of Death in E-CPR Users

Variable	OR	*P*, df	95% CI
Pre-ECMO factors*			
Diagnostic groups			
Other diagnosis	1.0	0.004, 2	Reference group
Neonatal respiratory disease	0.28	...	0.12–0.66
Cardiac disease	0.51	...	0.31–0.82
Pre-ECMO arterial blood pH	...	0.03, 2	...
<6.9	1.0	...	Reference group
6.9–7.17	0.62	...	0.35–1.10
>7.17	0.50	...	0.30–0.84
White race	0.65	0.02, 1	0.45–0.94
Factors related to ECMO use†			
ECMO support factors			
CPR during ECMO	3.06	0.004, 1	1.42–6.58
Arterial blood pH <7.2 on ECMO	2.23	0.009, 1	1.23–4.06
ECMO complications			
Radiological evidence of CNS injury	2.79	0.001, 1	1.55–5.02
Pulmonary hemorrhage	2.23	0.025, 1	1.11–4.50
Renal injury	1.89	0.009, 1	1.17–3.03
Duration of ECMO support, d	1.02	0.123, 1	0.99–1.05

CNS indicates central nervous system.
*Model 1 characteristics: n=557; Nagelkerke R^2=0.066.
†Model 2 characteristics: n=682; Nagelkerke R^2=0.106.

regarding patient selection for E-CPR use.[10] Furthermore, decisions to use E-CPR are frequently made at a time when the probability of mortality is very high, and information regarding prognosis and comorbidities may not be readily available. Although E-CPR is reported to be cost-effective and has been shown to be life-saving, the maintenance of an E-CPR team is expensive, and thus, it may be beneficial to define risk factors and diagnostic groups who are good candidates for E-CPR in guiding future use of this therapy.[13]

This report has several limitations. As discussed previously, the most important limitation is the lack of information regarding long-term neurological and health-related quality-of-life outcomes for E-CPR survivors. Because neurological deficits have been reported in many studies after the use of E-CPR, collection of data on neurological outcomes and health-related quality of life could help guide E-CPR use and refine patient selection for E-CPR use in the future.[10,11,28,29] The exact indication for E-CPR use, patient diagnosis, and duration and details of therapies used during CPR before ECMO are not reported to the ELSO registry. The ELSO registry reporting sheets are not specific with regard to the collection of data on CPR techniques or other adjunct therapies such as total body hypothermia that previously have been shown to promote survival after CPR. Thus, the influence of these therapies on E-CPR outcomes cannot be evaluated.

Many children had multiple diagnosis and procedure codes, and it was difficult to determine their primary diagnosis with certainty. Some patients only had a diagnosis code for "cardiac arrest" without other supporting diagnosis or procedure codes and were coded as "other," and thus, we may have introduced misclassification bias. Furthermore, missing data limited the use of many pre-ECMO support variables for analysis. Thus, important features that may be associated with survival could have been missed. Finally, we did not have data on ECMO center characteristics to evaluate E-CPR outcomes based on center experience or to evaluate how many of the 110 reporting ECMO centers provided E-CPR.

In conclusion, we found that use of ECMO to aid CPR in children salvaged more than one third of children in whom death was otherwise certain. The use of E-CPR is increasing and is being extended beyond patients with primary cardiac disease. Neonates with respiratory failure and children with cardiac disease are more likely to survive to hospital discharge. Pre–E-CPR acidosis is associated with greater odds of mortality. Persistent metabolic acidosis despite ECMO, development of renal insufficiency, pulmonary bleeding, and neurological injury during ECMO are likewise associated with death. We hope the present report generates further prospective investigation of E-CPR use to improve outcomes for children using E-CPR.

Disclosures

Dr Bratton received an honorarium from the American College of Chest Physicians in 2006 for a lecture on ECMO to aid CPR. The remaining authors report no conflicts.

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CLINICAL PERSPECTIVE

Extracorporeal membrane oxygenation (ECMO) to provide cardiorespiratory support (E-CPR) during cardiopulmonary resuscitation (CPR) in infants and children can rescue those who have failed to respond to conventional CPR therapies and who face imminent death. Because E-CPR teams are not universally available and are expensive to maintain, it is important to understand who may benefit from E-CPR use. In this article, we report that 38% of children supported with E-CPR survived to hospital discharge. Compared with other disease groups, patients who had neonatal respiratory or cardiac disease had improved odds of survival. In addition, those with higher arterial blood pH (pH $>$7.17 compared with $<$6.9) had better survival odds, which indicates that severity of illness and management strategies before and during CPR may influence survival for E-CPR users. The persistence of metabolic acidosis during ECMO support and need for CPR during ECMO decrease the odds of survival. This indicates that therapies to improve cardiorespiratory function and close monitoring of cardiorespiratory function should be continued even during ECMO support to improve survival among E-CPR users. ECMO complications such as renal failure, pulmonary hemorrhage, or neurological injury that are known to influence survival for all ECMO users also influence survival in E-CPR users. Management strategies aimed at reducing these complications may help promote survival of E-CPR users. E-CPR should be considered in infants and children with cardiopulmonary arrest who have failed to establish an adequate circulation despite adequate CPR but have a recoverable underlying cause that led to the cardiac arrest.

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