Survival outcomes after rescue extracorporeal cardiopulmonary resuscitation in pediatric patients with refractory cardiac arrest

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Objectives: We report our experience with extracorporeal cardiopulmonary resuscitation with extracorporeal membrane oxygenation in children having cardiac arrest refractory to conventional cardiopulmonary resuscitation and explore predictors for favorable outcome (survival with grossly intact neurologic status).

Methods: We reviewed all patients who required extracorporeal cardiopulmonary resuscitation from 2000 to 2005. Multivariable regression analysis determined factors associated with favorable outcome and time-related survival.

Results: Eighty children, median age 150 days (range: 1 day–17.6 years), required venoarterial extracorporeal cardiopulmonary resuscitation. There were several categories of disease among the patients: postcardiotomy (n = 39), unoperated congenital heart disease (n = 17), cardiomyopathy (n = 12), respiratory failure (n = 9), or myocarditis (n = 3). Cannulation sites were neck (n = 45) or chest (n = 36). Median duration of extracorporeal membrane oxygenation was 4 days (range: 1–22). Extracorporeal membrane oxygenation was successfully discontinued in 42 (54%) patients: wean (n = 35), heart transplantation (n = 7). Survival till hospital discharge was 27 (34%) patients. Most common cause of death was ischemic brain injury (n = 17). Twenty-four (30%) patients had a favorable outcome. Median duration of cardiopulmonary resuscitation for patients with favorable versus unfavorable outcome was 46 minutes (range: 14–95; interquartile range: 29–55) versus 41 minutes (range: 19–110; interquartile range: 30–55), $P = .916$. According to the logistic regression model, none of the following factors was a significant predictor of favorable outcome: age, weight, sex, etiology (cardiac vs noncardiac), duration of cardiopulmonary resuscitation, cannulation site, timing, or location of extracorporeal membrane oxygenation institution.

Conclusions: Acceptable survival and neurologic outcomes (30%) can be achieved with extracorporeal cardiopulmonary resuscitation in children after prolonged cardiac arrest (up to 95 minutes) refractory to conventional resuscitation measures. Heart transplantation is often needed for successful extracorporeal cardiopulmonary resuscitation exit strategy. Lack of predictors of poor outcome support aggressive attempts to initiate extracorporeal cardiopulmonary resuscitation in all patients, followed by subsequent assessment of organ salvage.

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In-hospital cardiac arrest is associated with high mortality and subsequent morbidity in surviving children.[1-9] Additionally, increased duration of cardiopulmonary resuscitation (CPR) is associated with higher mortality and permanent central nervous system damage. After CPR duration lasting more than 30 minutes, survival with conventional CPR measures ranges between 0% and 5%.[1,2]

Abbreviations and Acronyms
CCU = critical care unit
CPR = cardiopulmonary resuscitation
ECMO = extracorporeal membrane oxygenation
ECPR = extracorporeal cardiopulmonary resuscitation
IQR = interquartile range
OHTX = orthotopic heart transplantation

Extracorporeal cardiopulmonary resuscitation (ECPR) is the rapid deployment of extracorporeal membrane oxygenation (ECMO) to provide immediate cardiovascular support for patients who have cardiac arrest unresponsive to conventional CPR measures.[2,9-18]

Several case series reported the use of ECPR in pediatric and adult cardiac patients, with a rate of survival to hospital discharge of 30% to 80%.[2,9-18] The use of ECPR in cardiac arrest for noncardiac medical conditions has been reported less frequently and has been associated with worse outcome.[2] Several series reported that mechanical assistance with ECMO in children having cardiac arrest refractory to conservative CPR measures is a significant factor for improved survival.[1-9] Survival may vary between different programs on the basis of patient selection and the capability to institute ECMO in a timely fashion. Since 2000, we have established a rapid resuscitation ECMO program at the Hospital for Sick Children in Toronto using a preassembled and preprimed ECMO circuit. The aim of this program is to re-establish cardiac output and organ perfusion and to prevent permanent end-organ injury while awaiting reversal of cardiac and other organ disease process or as a bridge to heart transplantation.

In this current series, we report our experience with ECPR over the past 5 years and explore predictors for favorable patient outcome, defined as hospital survival with grossly intact neurologic status.

Patients and Methods

Approval of this study was obtained from the Research Ethics Board at the Hospital for Sick Children in Toronto. From March 2000 to December 2005, 80 children less than 18 years of age required ECPR. Patients were included in the ECPR group if venoarterial ECMO was used as part of the initial active resuscitation from a cardiac arrest. Patients who were in hemodynamically unstable condition and placed on ECMO urgently without active cardiac arrest were not included in this study.

Patients were identified according to the institutional ECMO and Surgical Database. Clinical, operative, and outcome data were abstracted from the medical records. Risk factors available before the start of ECPR were analyzed.

ECMO Circuit and Equipment

A preassembled and preprimed ECMO circuit and trained personal are available in the critical care unit (CCU) at all times.

The circuit is composed of ¼-inch internal diameter polyvinyl chloride tubing with Carmeda (Medtronic, Minneapolis, Minn) heparin-bonded biocompatible surface coating. The total prime is approximately 400 mL. The main components are the Jostra Rotaflow centrifugal pump (Maquet, Hirrlingen, Germany) and Hilite 2400 LT oxygenator (Medos, Stolberg, Germany) (Figure E1). This system can support patients up to 20 kg and will provide temporary support for larger patients until a 3/8-inch circuit with an increased surface area oxygenator can be substituted. The circuit is primed with PlasmaLyte 148 (Baxter Corp, Toronto, Ontario, Canada), an unbuffered electrolyte solution, and is usable for 30 days. This safe limit has been determined by multiple periodic sterility testing of prime fluid with aerobic, anaerobic, and fungus cultures, and none of those cultures was positive up to 30 days.

Once ECPR is required, a predefined protocol is initiated. The circuit and all necessary ancillary equipment are brought to the bedside, creating a mini operating room setting in the CCU. A surgical table with sterile ECMO instrument tray, a single bundle of disposable and reusable equipment, a full cannulation cart with cannula size and flow guidelines, emergency albumin, cautery, and headlight are exclusively available to the rescue ECMO program and housed in the CCU.

All cannulations at our institution are performed by a staff cardiac surgeon or with a staff cardiac surgeon assisting. Cannulation site is dependent on the clinical situation. In postcardiotomy patients having postoperative cardiac arrest within the first week after surgery, direct aortic and atrial cannulation through the chest is usually done inasmuch as it provides the most expeditious means of instituting support while allowing the performance of effective open CPR. In patients who have cardiac arrest in settings other than the early postoperative period, neck cannulation is performed in our series of patients. Femoral cannulation can be considered as an alternative peripheral cannulation site in older children and adults.

When ECPR is requested, the blood bank is notified to prepare blood products. However, owing to time limitations, it is often necessary to initiate ECMO support with a clear prime. Heparin 1 U/mL of prime, sodium bicarbonate 15 mEq, and calcium chloride 250 mg are added to the prime before cannulation. Additionally, systemic heparin is administered at a dose of 50 U/kg body weight to maintain an activated clotting time of 180 to 200 seconds.

Once the patient's condition is stable on ECMO, the crystalloid volume is removed and packed red blood cells are added by a one-for-one syringe exchange transfusion process. Platelets and cryoprecipitate are given to correct the inherent coagulation deficiency. For children less than 1 year of age, an infusion of fresh frozen plasma is placed in the circuit at 20 mL/kg every 8 hours. The administration of blood products continues until transfusion targets are reached: hemoglobin 110 g/L, platelet count 100,000/mm^3, fibrinogen 2 g/L, and antithrombin 1 U/mL.

Rescue ECMO Team

The success of an ECPR program is dependent on the quick response of a team of specifically skilled and trained professionals. Individual roles and responsibilities have been identified so that the process can be expedited. A certified ECMO specialist and/or cardiovascular perfusionist are available in-house at all times. The

other members of the team include the CCU attending physician/fellow, cardiovascular staff surgeon and fellow, and cardiac nurse. Additional professional support is provided by cardiology, hematology, respiratory therapy, blood bank, laboratory medicine, and social work.

Registered respiratory therapists and registered nurses enroll in an in-house ECMO training program that consists of a didactic component, wet laboratory simulation, and animal laboratory management sessions. The ECMO specialist must then attain 100 bedside clinical hours. A written examination and subsequent oral and practical evaluation are completed before certification is awarded.

To increase proficiency and accuracy of the team, and to identify any system deficits to improve the ECPR process and minimize response times in critical situations, an intensivist and a senior perfusionist periodically perform random mock rescue ECMO drills, done without warning, in the intensive care unit.

CCU Management

The pump flow is started initially at 100 mL $\cdot$ kg^{-1} $\cdot$ min^{-1} and adjusted to maintain end-organ perfusion, normalization of arterial blood gases, increase in systemic venous saturation, and clearance of lactic acidosis. Higher flows are needed for infants with single ventricle and an open modified Blalock–Taussig shunt. Cardiac inotropic agents are maintained and adjusted as needed to maintain left heart function and pulsatility. Vasopressors are used to maintain a mean blood pressure of around 60 mm Hg. Afterload-reducing agents such as phenoxybenzamine and nitroprusside are often used to improve cardiac performance. Similarly, nitric oxide (Inotherapeudics, Clinton, NJ), beginning at 20 to 40 ppm and weaned according to protocol, is used in children with refractory pulmonary hypertension. Mechanical ventilation rate is adjusted to maintain oxygenation of blood generated by the native cardiac output and to prevent lung atelectasis. The usual ventilations rate is 10 to 12 breaths/min, with an inspired oxygen fraction of 0.21 to 0.35 and the peak inspiratory pressure maintained under 30 cm H_2O.

After establishment of ECMO, the consciousness level is evaluated every 12 hours after ECPR, aiming to identify persistent severe neurologic insult requiring withdrawal of ECMO support. More recently, mild hypothermic core cooling and application of ice to the patient's head have been used for up to 48 hours after cardiac arrest in an effort to lower metabolic demands as part of a prospectively randomized study to minimize postarrest neurologic insult. Future follow-up and analysis of this study is needed to confirm the benefit of that practice.

Assessment of the underlying cause leading to cardiac arrest is begun soon after patient stabilization, and further intervention is considered to address and treat the underlying cause and optimize the patient for future weaning.

In patients who have had cardiac arrest, follow-up echocardiography is done up to a daily interval to estimate the recovery of the heart, detect residual lesions and thrombus formation in the left ventricle, and to assess the need for heart transplantation in case of failure of heart recovery. Timing of weaning is dependent on the clinical scenario, hemodynamic stability during ECMO support, correction of the underlying cause, and the presence of residual lesions.

In general, weaning for postcardiotomy patients is begun around 72 hours after ECMO support. Transesophageal echocardiography is frequently used to assess myocardial function during the weaning process.

Weaning and separation from ECMO assist is accomplished with optimal ventilator and inotropic support, preferably with an epinephrine requirement of 0.05 μg $\cdot$ kg^{-1} $\cdot$ min^{-1} or less. ECMO flow rates are gradually decreased. When flow rates are approximately 25% of maximal support, the bridge between the arterial and venous systems is unclamped and the circuit allowed to recirculate.

After successful separation from ECMO, the cannulas are usually left in place for 1 to 3 hours, flushed every 10 to 15 minutes, and subsequently removed if hemodynamic stability is maintained. Purse-string sutures are usually left in place and resnared with the chest left open after cannula removal in all postcardiotomy patients. In patients who have had neck cannulation, the vessels are repaired if the tissue was of good quality and the patient required 1 week of ECMO support or less.

Statistical Analysis

Descriptive statistics were reported as median, range, and interquartile range (IQR) for continuous variables and as frequencies and percentages for categorical variables. Unrelated 2-group comparisons were done with unpaired, 2-tailed t tests for continuous variables and the χ^2 or Fisher exact test for categorical data. Potential risk factors that were available before the institution of ECPR were analyzed with a multivariable logistic regression model. The response variable was death or gross neurologic deficit within admission. Long-term time-related survival and freedom from morbid events were estimated by the Kaplan–Meier method. Multivariable Cox regression was used to determine the independent predictors of time-related survival. In all multivariable models, the normality and linearity of continuous variables was assessed and appropriate transformations were used where necessary. All analyses were done with the R statistical package.

Results

Patients Characteristics

A total of 80 patients (47 boys) required ECPR during active cardiac massage. Patients ranged in age from 1 day to 17.6 years, with a median age of 150 days (IQR: 24–787). Median weight was 5.2 kg (range: 1.7-90; IQR: 3.2–10.1) Most patients had cardiac disease (n = 71) including postcardiotomy cardiac arrest (n = 39), unoperated congenital heart disease (n = 17), cardiomyopathy (n = 12), and myocarditis (n = 3). The remaining patients had noncardiac problems (n = 9) including meconium aspiration syndrome, congenital diaphragmatic hernia, drowning, lamp oil aspiration, thoracic lymphoma, pulmonary embolus, adenovirus infection, pneumonia, and complications after adenoidectomy (n = 1 each).

ECPR was initiated in the CCU in the majority of the cases (n = 71), followed by the catheterization laboratory (n = 6) and the operating room (n = 3). Children having cardiac arrest in the emergency room or the regular ward

TABLE 1. Descriptive statistics for patients with cardiac and noncardiac underlying pathologic conditions

	Cardiac disease (n = 71)	Noncardiac disease (n = 9)	All patients (n = 80)	*P* value
Age (mo)	4.9 (0.8–17.1)	25.4 (1.9–127.6)	4.9 (0.8–25.8)	.3
Weight (kg)	4.8 (3.2–10)	13.9 (3.1–41.3)	5.2 (3.2–10.1)	.3
Sex				
Female	38%	67%	41%	.1
Male	62%	33%	59%	
Cannulation site				
Thoracic	49%	11%	45%	.5
Neck	51%	89%	55%	
ECPR location				
ICU	87%	100%	89%	.5
Cath lab	8%	0%	8%	
OR	4%	0%	4%	
ECPR timing				
Weekday	35%	12%	32%	.03
Weeknight	41%	75%	44%	
Weekend	25%	12%	23%	
Anatomy precluding effective CPR	4%	0%	4%	.5
ECMO exit by heart transplantation	11%	0%	10%	.3
Pre-ECMO CPR duration (min)	42 (30–55)	41 (39–50)	41 (30–55)	.6
ECMO duration (d)	4 (2.5–8)	1 (1–4)	4 (2–8)	.09
Hospital survivor	37%	11%	34%	.1
Favorable outcome	32%	11%	30%	.2

Continuous variables presented as median (25th quartile-75th quartile). *ECPR*, extracorporeal cardiopulmonary resuscitation; *ICU*, intensive care unit; *Cath lab*, catheterization laboratory; *OR*, operating room; *CPR*, cardiopulmonary resuscitation; *ECMO*, extracorporeal membrane oxygenation.

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were promptly transferred to the CCU after initiation of CPR so that ECPR could be started in the CCU. The timing of ECPR initiation was during weekdays (8 AM–5 PM) (n = 25), weekends (n = 18), and weeknights (5 PM–8 AM) (n = 34). Cannulation sites were intrathoracic in 35 patients, neck cannulation in 44 patients, and both neck and intrathoracic cannulation in 1 patient owing to inadequate flows after neck ECMO. The median interval between the beginning of CPR and the initiation of ECMO (CPR duration) was 41 minutes (range: 14–110; IQR: 30–55; mean ± SD = 44 ± 19). The complete demographic data for all the patients treated with ECPR are listed in Table 1.

Early Results

ECMO was successfully discontinued (ie, children were able to maintain adequate hemodynamics >24 hours after ECMO discontinuation) in 42 (53%) patients. This was accomplished by successful weaning (n = 35) or by orthotopic heart transplantation (n = 7). Twenty-seven (34%) patients survived to hospital discharge. The causes for mortality included ischemic brain injury (n = 17, 32% of deaths), multiorgan failure (n = 13, 25%), failure of cardiac recovery (n = 11, 21%), sepsis (n = 7, 13%), and intraventricular hemorrhage (n = 5, 9%). Twenty-four (30%) patients had favorable outcome (hospital survival with grossly intact neurologic status). The median ECMO duration for the whole group was 4 days (range: 1–22; IQR: 2–8).

Risk Factors for Unfavorable Outcome

Variables available before initiation of ECPR were analyzed to test whether or not they were significant predictors of an unfavorable outcome. Those factors included the age, weight, and sex of the patients; the location and timing of ECPR initiation; the cannulation site; the underlying cardiac etiology; the presence of factors that would prevent effective CPR, such as blocked aortopulmonary shunts or dislodged interventional Fontan stents placed in the catheterization laboratory; and finally CPR duration before ECMO initiation and the duration of ECMO. None of those factors was significantly different between the 2 groups (Table 2), and none was found to be independently predictive of an unfavorable outcome by multivariable regression (Table E1).

Of special interest, the median CPR duration before ECMO initiation for patients with favorable versus unfavorable outcome was 46 minutes (range: 14–95; IQR: 29–55) versus 41 minutes (range: 19-110; IQR: 30–55), $P = .9$. (Figure 1). Moreover, median duration of ECMO for patients with favorable versus unfavorable outcome was 4 days (range: 1–18; IQR: 3–6) versus 4 days (range: 1–22; IQR: 2–8), $P = .9$ (Figure E2).

TABLE 2. Descriptive statistics for patients with favorable and unfavorable outcome after ECPR

	Favorable outcome (n = 24)	Unfavorable outcome (n = 56)	*P* value
Age (mo)	4.8 (0.6–16)	5.1 (0.9–29)	.7
Weight (kg)	5.2 (3.2–8.9)	5.2 (3.2–11.5)	.9
Sex			
Female	29%	46%	.2
Male	71%	54%	
Pathology			
Cardiac	96%	86%	.2
Noncardiac	4%	14%	
Cannulation site			
Thoracic	50%	43%	.6
Neck	50%	57%	
ECPR location			
ICU	92%	88%	.5
Cath lab	8%	7%	
OR	0%	5%	
ECPR timing			
Weekday	39%	30%	.6
Weeknight	43%	44%	
Weekend	17%	26%	
Anatomy precluding effective CPR	0%	5%	.3
ECMO exit by heart transplantation	25%	2%	<.001
Pre-ECMO CPR duration (min)	46 (29–55)	41 (30–55)	.9
ECMO duration (d)	4 (3–6)	4 (2–8.3)	.9

Continuous variables presented as median (25^{th} quartile-75^{th} quartile). *ECPR*, extracorporeal cardiopulmonary resuscitation; *ICU*, intensive care unit; *Cath lab*, catheterization laboratory; *OR*, operating room; *CPR*, cardiopulmonary resuscitation; *ECMO*, extracorporeal membrane oxygenation.

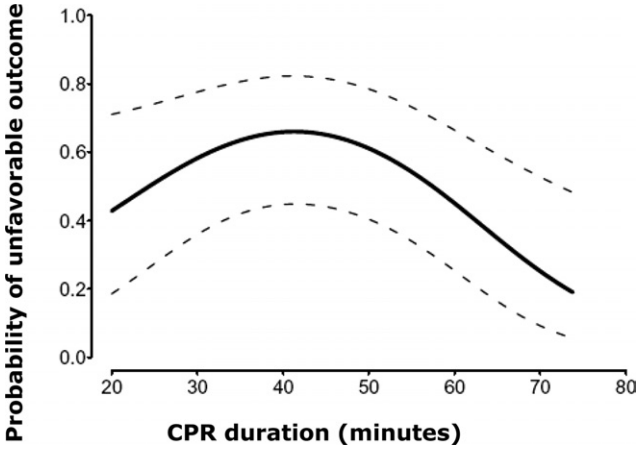

Figure 1. Graph showing the relationship between the probability of unfavorable outcome (death or stroke) as related to pre-ECMO CPR duration.

Time-related Survival Results

Time-related survival at 1 and 3 years was 29% and 27%, respectively (Figure E3). On multivariable analysis, none of the studied variables was a significant risk factor for diminished survival (Table E2).

Discussion

Although the use of ECMO support to treat pediatric patients with cardiac arrest refractory to routine resuscitation measures has been reported by several centers, little information exists regarding the outcome predictors of this approach in this difficult group of patients.

The most important factor for achieving favorable outcome with ECPR is the prompt establishment of adequate organ perfusion. Decision to institute ECMO support in children who have not responded to traditional resuscitative measures must be made early. At our hospital, we have adopted criteria to determine which patients are candidates for ECPR. Those criteria include any child having a witnessed arrest, with lack of recovery of cardiac function within 5 to 10 minutes of the initiation of CPR, and the absence of coexisting conditions that will preclude survival or lifestyle such as pre-existing severe neurologic or genetic anomaly or significant end-organ injury. Once the decision is made, we aim to institute mechanical support within a short period of time (usually 25–40 minutes).

In this series, we reviewed different demographic and clinical variables aiming to identify those that significantly affect outcome.

CPR Duration

We were unable to demonstrate a significant effect of the duration of chest compressions before the institution of ECMO on survival or on the prevention of ischemic brain injury. The duration of CPR was comparable between patients with favorable and unfavorable outcome. More important, we identified 7 patients in whom chest compression was performed for almost 1 hour before ECPR, up to a maximum of 95 minutes, and who survived without any gross neurologic deficit.

Most of the patients in this retrospective series had a witnessed arrest with conventional CPR started immediately, especially the postcardiotomy group and other patients with cardiac disease who were closely monitored in the hospital before their cardiac arrest; however, this analysis may be contaminated by data from patients who had prolonged arrest before initiation of CPR, for example, the drowning child or other children with noncardiac disease, and that may explain the worse outcome in this group of patients. Nonetheless, the important message is that in a child with a witnessed arrest who received immediate and

adequate resuscitation, we were unable to determine a CPR duration beyond which ECMO support is futile. Similar to our experience, others have reported intact neurologic outcomes in ECPR survivors after prolonged chest compression up to 176 minutes.[2,14]

The performance of effective CPR during the dissection and the cannulation stages is essential for good outcome. Chest compression is often interrupted for brief periods during neck dissection or cannulation. Similarly, if chest cannulation is performed, open heart massage may frequently become compromised. Surgeons should avoid prolonged pauses in chest compression and should be able to make an early decision to change the cannula size or the cannulation site when having difficulties accessing the neck vessels. Unfortunately, the adequacy of chest compression was hard to assess in this retrospective review, and identifying patients who had poor resuscitation was not always possible. In a few anecdotal cases, inability to cannulate the neck vessels resulted in frequent interruptions of conventional CPR and a delay in establishment of ECMO and were associated with poor neurologic outcomes.

Moreover, several factors can affect the quality of resuscitation and oxygen delivery to the brain and other organs. Patients with blocked aortopulmonary shunts are at a high risk for the development of ischemic brain injury despite adequate blood pressure achieved with chest compressions. In addition, 1 patient in our current series had a Fontan conduit placed by the interventional cardiology service in the catheterization laboratory, complicated by dislodgment of the stented graft and cardiac arrest. Despite obtaining adequate cardiac output with chest compression for a CPR duration of 25 minutes until ECMO was initiated via neck cannulation, she had fatal irreversible ischemic brain injury complicating her cardiac arrest owing to the lack of adequate blood flow and oxygen delivery to the brain. All 3 patients in our series with cardiac anatomy precluding effective augmentation of blood flow during CPR died of ischemic brain injury although that was not statistically significant, likely owing to the small sample size.

ECMO Duration

Multiple series in the literature showed that prolonged duration of ECMO and the emergence of complications were all factors that have a significant negative impact on survival.[11,12,19-21] The pattern of ECMO duration requirement after cardiac arrest is unique. Mechanical support was often discontinued early in the first 48 hours owing to the emergence of irreversible ischemic brain injury or other severe end-organ injury such as lethal intestinal necrosis without any attempts to assess patients for cardiac recovery. On the other hand, similar to postcardiotomy ECMO, patients requiring prolonged duration of ECMO with failure of cardiac function recovery are at high risk for the development of complications such as intracranial hemorrhage, coagulopathy, sepsis, and multiorgan system failure and will die unless they undergo heart transplantation. The median duration of ECMO in the favorable and unfavorable groups was similar. However, that is likely due to the high incidence of early withdrawal of support in those with severe end-organ injury after cardiac arrest.

After cardiac arrest and ECPR institution for postcardiotomy patients, prompt evaluation of any residual lesion that may require reintervention should be performed. In this series, 7 patients underwent reoperation to address their residual lesions, but only 1 infant survived with a favorable outcome. This infant had complex second-stage reconstruction of single-ventricle disease complicated by severe cyanosis and cardiac arrest requiring ECPR. She underwent surgical revision with takedown of the bidirectional cavopulmonary anastomosis and placement of a modified Blalock–Taussig shunt.

If no residual lesions were present and the postcardiotomy patient continued to show no evidence of recovery of cardiac function within an average of 72 hours, the patient was assessed for candidacy to receive orthotopic heart transplantation (OHTX). In our current series, OHTX was often required for successful ECMO exit strategy. Among all ECPR patients, 7 required OHTX with 6 survivors and only 1 mortality owing to graft failure and unsuitability of the patient for retransplantation.

Underlying Pathologic Conditions

We studied the influence of underlying pathologic conditions on clinical outcome. Although the majority of patients had underlying cardiac disease, 9 children required ECPR for the noncardiac problems listed in the Results section. Only 1 neonate who had meconium aspiration syndrome survived, whereas the remaining 8 did not (89% mortality compared with 63%; $P = .13$) (Figure E3). This finding may be explainable by the presence of severe multiple organ dysfunction in children with noncardiac conditions leading to cardiac arrest and acknowledgement of the possibility that those children did not have a real witnessed arrest with potential delays in initiation of CPR. Although the difference did not reach statistical significance, this may be due to the small sample size. Similar to our findings, another large series from Philadelphia showed that children with isolated heart disease were more likely to survive after ECPR than were children with a cardiac arrest complicating other medical conditions.[2]

Seventy-one patients had underlying cardiac problems. Favorable outcomes were achieved in 50% of those with cardiomyopathy, 67% of those with myocarditis, 36% of those having had cardiotomy, and 6% of patients with unoperated congenital heart disease. Although the likelihood of recovery of cardiac function in myocarditis and

some forms of cardiomyopathy probably increases their chance of survival, the role of OHTX cannot be underestimated as a favorable exit strategy for appropriate candidates.

ECMO support has been used successfully to salvage neonates with a functional single ventricle from refractory low cardiac output syndrome postoperatively. In our series, 44% of postcardiotomy patients had single-ventricle pathology. Favorable outcome was achieved in 47% of those patients compared with 27% of patients with 2-ventricle pathology. These results are encouraging and equivalent to results of ECMO support done in nonemergency settings in patients with single ventricle.

Study Limitations

Certain trends and anecdotes have been identified and may have affected outcome either positively (ability to offer heart transplantation in cases of failure of cardiac recovery) or negatively (unwitnessed arrest, noncardiac disease, frequent pauses in chest compression, blocked shunts, prior ECMO during the same admission, and so on). Nonetheless, this case series is subject to many limitations inherent in all retrospective observational studies, such as selection bias and lack of randomization. Most important, there has been no complete or uniform appraisal of neurologic function and deficit by an independent pediatric neurology specialist. Finally, the small cohort size, the high incidence of patients with an unfavorable outcome, and the multiple variables in this heterogeneous group of patients preclude sophisticated statistical analyses and limit the power of the study to identify clinically significant risk factors.

Conclusions

ECMO support of children with intractable cardiac arrest can result in a favorable outcome in almost one third of the patients. Acceptable survival and neurologic outcomes can be achieved in children having prolonged cardiac arrest up to 95 minutes. Heart transplantation is often needed for a successful ECPR exit strategy. Timely application of mechanical support and judicious patient selection may be necessary for improved results. However, the lack of predictors for poor outcome supports aggressive attempts to initiate ECPR in patients with refractory cardiac arrest and no comorbidities that severely limit their lifestyle or survival, followed by subsequent assessment of organ salvage given the extremely dismal outcome after prolonged conventional CPR in children with conditions refractory to traditional interventions. Multi-institutional study with standardization of protocols and analysis of all variables may be necessary to achieve statistical power to determine significant risk factors and to help establish useful selection guidelines for establishment of ECPR. Nonetheless, in this particular case of ECPR, it might be difficult to carry out such a study with interpretable results from separate programs. This is largely due to the large differences in manpower availability, the technical approaches to cannulation, and the overall philosophy toward this type of support. Finally, consideration should be made toward expanding the application of ECPR to the adult population. Adults may hold the advantages of having easier vascular access with the ability to perform peripheral femoral cannulation without interruption of CPR. Finally, adult patients who survive the insult of cardiac arrest can be offered various exit strategies, such as a ventricular assist device, as a longer-term bridge to recovery or to transplantation that may be associated with improved outcome.

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Notice of Correction

Kernstine KH, DeArmond DT, Karimi M, Van Natta TL, Campos JH, Yoder MR, Everett JE. The robotic, 2-stage, 3-field esophagolymphadenectomy. *J Thorac Cardiovasc Surg* 2004;127:1847-9.

The middle initial of author Dr Javier Campos was inadvertently printed as "C" by the publisher. The correct middle initial is "H," as shown in the corrected author line above.

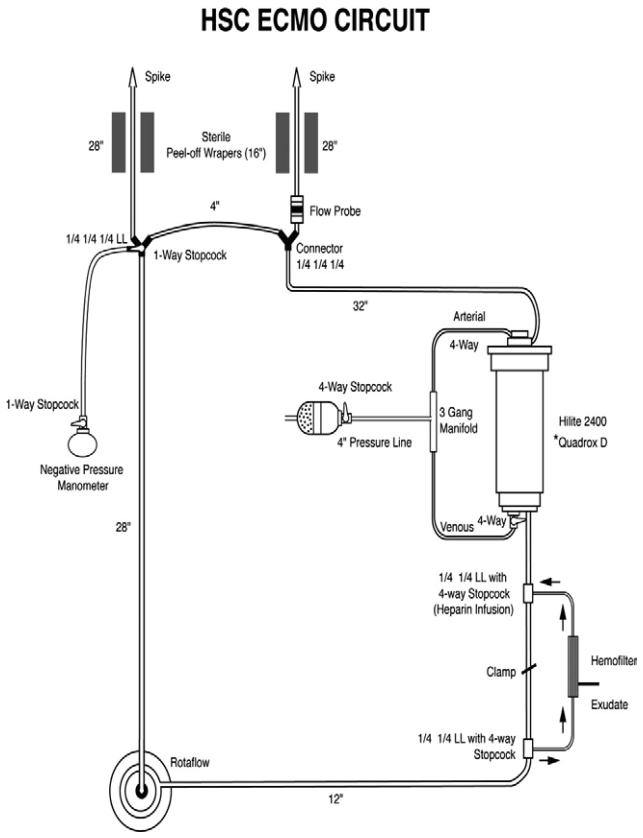

Figure E1. Schematic diagram of the basic ECMO circuit used for ECPR at the Hospital for Sick Children *(HSC)* in Toronto. *Quadrox D used with 3/8-inch circuit. *ECMO,* Extracorporeal membrane oxygenation; *ECPR,* extracorporeal cardiopulmonary resuscitation.

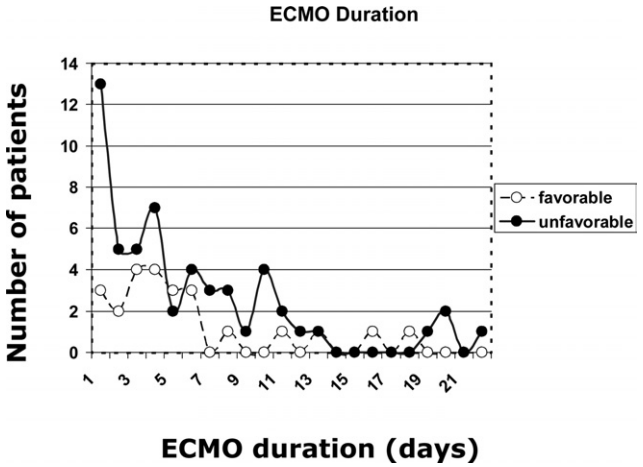

Figure E2. A graph showing the duration of ECMO requirement for patients having favorable and unfavorable outcome after ECPR. *ECMO,* Extracorporeal membrane oxygenation; *ECPR,* extracorporeal cardiopulmonary resuscitation.

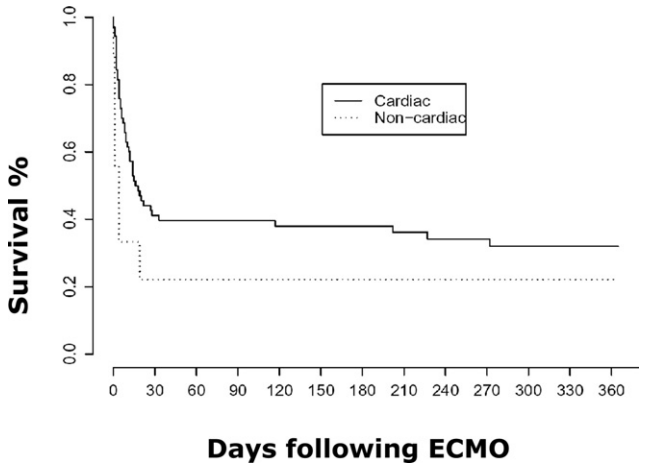

Figure E3. Time-related survival curves for ECPR patients stratified by cardiac and noncardiac pathologic conditions. *ECMO,* Extracorporeal membrane oxygenation; *ECPR,* extracorporeal cardiopulmonary resuscitation.

TABLE E2. Multivariable Cox regression analysis using Wald statistics for time-related survival after ECPR

	χ^2	*df*	*P* value
Age	0.16	1	.7
Sex	1.61	1	.2
Weight	0.03	1	.9
Pre-ECMO CPR duration	0.26	1	.6
Cannulation site	0.09	1	.8
Anatomy precluding effective CPR	3.39	1	.07

ECPR, extracorporeal cardiopulmonary resuscitation; *df*, degrees of freedom; *ECMO*, extracorporeal membrane oxygenation; *CPR*, cardiopulmonary resuscitation.

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TABLE E1. Multivariable logistic regression analysis using Wald statistics for unfavorable outcome (death or gross neurologic injury) after ECPR

	χ^2	*df*	*P* value
Age*	3.84	4	.4
Sex	0.14	1	.7
Weight*	3.55	4	.5
Pre-ECMO CPR duration*	2.47	2	.3
ECPR timing	2.3	3	.5
Cannulation site	0.58	1	.5
ECPR location	0.14	2	.9
Anatomy precluding effective CPR	0.01	1	.9

ECPR, extracorporeal cardiopulmonary resuscitation; *df*, degrees of freedom; *ECMO*, extracorporeal membrane oxygenation; *CPR*, cardiopulmonary resuscitation. *Continuous variables modeled with a nonlinear transformation to account for lack of linearity. The *P* value presented is representative of the overall effect.