Title
Duration of Cardiopulmonary Resuscitation before Extracorporeal Rescue: How Long Is Not Long Enough?

Journal
ASAIO Journal, 51(5)

ISSN
1058-2916

Authors
Kelly, Robert B
Porter, Penny A
Meier, Andreas H
et al.

Publication Date
2005-09-01

DOI
10.1097/01.mat.0000171596.39362.7a

Peer reviewed

Case Reports

Duration of Cardiopulmonary Resuscitation before Extracorporeal Rescue: How Long Is Not Long Enough?

Robert B. Kelly,* Penny A. Porter,† Andreas H. Meier,‡ John L. Myers,† and Neal J. Thomas§

Despite the extensive resources required, extracorporeal cardiopulmonary resuscitation (ECPR) has been recognized as an extension of traditional CPR. The reported duration of CPR before ECPR initiation is similar between survivors and nonsurvivors, but the duration of CPR that results in futility of care is unknown. We report two cases of prolonged CPR followed by ECPR resulting in acceptable neurologic outcomes. Ventricular tachycardia developed in a 4-year-old with myocarditis, resulting in a cardiac arrest requiring CPR for 176 minutes before initiation of extracorporeal membrane oxygenation (ECMO). The patient required ECMO for 9 days. He survived neurologically normal. A ventricular arrhythmia developed in a newborn after an arterial switch procedure, leading to cardiac arrest requiring CPR for 97 minutes before ECMO, which lasted for 11 days. Hydrocephalus developed, but the patient is progressing developmentally. The upper limit of CPR duration before ECPR resulting in acceptable neurological outcomes is unknown. Many clinical and biochemical factors are potential predictors of appropriate ECPR utility. The Extracorporeal Life Support Organization registry is a plausible forum to collect data regarding ECPR. We suggest that possible predictive variables be collected. Until then, practitioners must rely on experience and judgment regarding the value of ECPR in children. *ASAIO Journal* 2005; 51:665–667.

Extracorporeal membrane oxygenation (ECMO) has been used as an extension of traditional cardiopulmonary resuscitation (CPR) with resultant patient survival.[1] Although this use of ECMO, also known as extracorporeal cardiopulmonary resuscitation (ECPR), is appealing, extensive medical resources are required, and numerous ethical questions are raised regarding selection of appropriate patients. Criteria that can prospectively identify appropriate candidates for ECPR are presently unknown. Many children who do not receive ECPR may likely benefit from it, and, conversely, there are likely many instances in which ECPR is used in futile cases. Although the Extracorporeal Life Support Organization (ELSO) collects some ECPR data, many data fields vital to the study of the utility of ECPR are lacking. In addition, existing retrospective studies and case reports examining possible predictors of acceptable ECPR outcome may lack the statistical power required to confirm early findings. A number of criteria, including the duration of CPR before initiating ECPR, etiology of the cardiac arrest, and other clinical and biochemical tests, may help in the identification of appropriate ECPR candidates. Studies aimed at identifying these predictor variables would be helpful in ensuring optimal neurologic outcomes and the judicious use of resources. To demonstrate the scope of ECPR in relation to extreme duration of CPR before extracorporeal support, and to address many unanswered questions, we report two cases of prolonged CPR followed by ECPR ultimately leading to survival and acceptable neurologic outcomes.

Case Reports

Case 1

A 4-year-old, previously healthy boy was admitted to the pediatric intensive care unit (PICU) after a new-onset seizure, which was associated with reported apnea. Immediately upon admission to the PICU, he was noted to have ventricular tachycardia that quickly led to a witnessed cardiac arrest. CPR was required for 176 minutes, during which the patient received numerous intravenous doses of epinephrine, amiodarone, atropine, lidocaine, sodium bicarbonate, and calcium chloride. Chest compressions were continued throughout the resuscitation, and defibrillation was utilized numerous times. The CPR continued until placement of internal carotid and internal jugular cannulas and initiation of ECMO. Of note, during operative placement of the cannulas, effectiveness of external cardiac massage was assessed and guided by the surgeon's direct visualization of the carotid artery pulsatility. A dilated cardiomyopathy was discovered by echocardiography, and the myocarditis was ultimately diagnosed. Intravenous gammaglobulin and corticosteroids were administered, and the patient required ECMO for 9 days. The hospital course was complicated by acute respiratory distress syndrome, hepatitis, sepsis, and acute tubular necrosis. Dialysis was required during extracorporeal support, but the renal failure resolved shortly after decannulation. The patient required supportive mechanical ventilation for an additional 4 weeks, and was

From the Departments of *Pediatrics, †Pediatric Cardiothoracic Surgery, ‡Pediatric Surgery, and §Pediatric Critical Care Medicine and Health Evaluation Sciences, Penn State Children's Hospital, Hershey, PA.

Submitted for consideration April 2005, accepted in revised form May 2005.

Presented in part at the First International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion, May 19–22, Hershey, PA, USA.

Reprint Requests: Neal J. Thomas, MD, MSc, Penn State Milton S. Hershey Medical Center, Penn State Children's Hospital, Department of Pediatric Critical Care Medicine, H085, 500 University Drive, Hershey, PA, 17033-0850.

DOI: 10.1097/01.mat.0000171596.39362.7a

subsequently discharged after a 2-month hospitalization. He received inpatient rehabilitative care and, later, physical therapy briefly after discharge. At discharge, the patient was feeding orally and speaking at an age-appropriate level. The patient is presently neurologically normal and is attending school.

Case 2

A term newborn boy with a diagnosis of transposition of the great vessels presented to the PICU after an arterial switch procedure. Soon after his arrival, a ventricular arrhythmia and progressive hypotension led to a witnessed cardiac arrest with asystole requiring closed-chest, then open-chest CPR. During the resuscitation, the patient received multiple doses of epinephrine, atropine, sodium bicarbonate, and calcium chloride with no sustainable return of spontaneous circulation. The total time of CPR was 97 minutes, culminating in ECMO initiation with direct intracardiac cannulation. The patient required ECMO support for 11 days, during which ultrafiltration was initiated secondary to fluid overload. After decannulation, the patient had some left-sided weakness and was diagnosed with a right middle cerebral artery hemorrhagic infarct. A ventriculo-peritoneal shunt was subsequently placed secondary to hydrocephalus. On follow-up outpatient evaluations, the patient was feeding orally and was noted to have mild speech delay and mild motor delay. Presently, however, the patient is walking without assistance and is progressing developmentally.

Discussion

The upper limit of CPR duration before ECPR resulting in acceptable neurologic outcomes is unknown. The two cases described in this report demonstrate that acceptable neurologic outcomes are possible despite prolonged CPR of up to 3 hours. Clearly, given the data presented in our cases and in the literature, one or more factors other than CPR duration would better predict successful ECPR outcome. This is particularly true in the context of a cardiac arrest witnessed in a PICU, where practitioners are generally very experienced with resuscitation of children. Given the current lack of a clear link between duration of CPR and acceptable survival after ECPR, more investigation is needed.

Whether survival and acceptable neurologic recovery of patients who are rescued with ECPR depends on the duration of traditional CPR is unclear in the adult and pediatric literature. A retrospective report by Morris and colleagues[2] found no significant difference between survivors and nonsurvivors regarding length of CPR before ECPR cannulation. In this report, survivors received CPR for a median of 50 minutes (range, 5–105 minutes), whereas nonsurvivors received CPR for a median of 46 minutes (range, 15–90 minutes). In addition, Parra and colleagues[3] found no significant difference between CPR duration less than or greater than 20 minutes and survival, but only a portion of these children received ECPR. Clearly, the duration of CPR in these reports is much less than the 3 hours reported in our 4-year-old patient. Duncan and colleagues[4] investigated the use of "rapid-resuscitation ECMO" in an effort to decrease CPR duration and therefore increase survival. Although there was a trend toward better survival rates among those who underwent rapid-resuscitation ECMO, the findings were not statistically significant. This was likely because CPR durations between those given rapid-resuscitation ECMO and those who were not were not significantly different, thus negating the main hypothesized impact of the rapid-resuscitation ECMO team.

In contrast, Chen and colleagues[5] reported in the adult literature that significantly more patients survived ECPR if their initial CPR duration was less than 60 minutes. In one mixed pediatric and adult study, there was a significant difference between survivors and nonsurvivors regarding CPR duration before cannulation.[6] Survivors received CPR for an average of 21 minutes, whereas nonsurvivors received an average of 43 minutes. In this report by Younger and colleagues, however, all three of the included children died. In the absence of ECPR, Slonim and colleagues[7] found that survivors had a significantly shorter duration of CPR, and that patient demise versus length of CPR was significantly linear. Survivors received CPR for an average of 22.5 minutes, whereas nonsurvivors received CPR for an average of 24.8 minutes. As in the other studies, the duration of CPR is much shorter than the cases that we report. The etiology of the cardiac arrest and the location of the cardiac arrest are also important variables to study. In the cases we present, both children were rescued from a cardiac arrest that occurred in the intensive care unit due to an underlying arrhythmia. Practitioners should use caution when extrapolating this data to other causes of cardiac arrest.

Some investigators have postulated that certain laboratory factors may contribute to ECPR survival. The partial pressure of arterial oxygen (Pa_{O_2}) before ECPR has been postulated as a possible predictor of positive neurologic outcome in adult ECPR patients.[8] Of the nine adult patients examined, those who regained consciousness during ECPR had a Pa_{O_2} between 132 and 442 mm Hg, whereas those who did not regain consciousness during ECPR had a Pa_{O_2} between 34 and 58 mm Hg. Research in children, however, has not significantly implicated arterial blood gas values as predictors of ECPR survival.[9]

Because data are limited regarding survivors and nonsurvivors of ECPR, important predictive parameters of ECPR may be extrapolated from reports of CPR without extracorporeal rescue. Horisberger and colleagues[10] provided some important data regarding predictors of survival after CPR without ECPR rescue. The authors note that initial base deficit was related to survival in pediatric patients. Although not all patients had initial blood gases for this report, only 10% of CPR recipients with a base deficit > 20 survived one year, compared with a survival rate of 86% in CPR recipients with a base deficit less than or equal to 15. Therefore, metabolic acid-base status may be an important predictor of survival after ECPR. Other possible predictors of survival included site of CPR, primary diagnosis, and etiology of the cardiac arrest. Again extrapolating from CPR without ECMO rescue, prehospital CPR and severity of illness are important predictors of survival,[7] and it seems intuitive that cardiac arrest witnessed by practitioners skilled in resuscitation (such as in the PICU) should lead to better outcomes. Whether these data can be extrapolated to ECPR patients is of critical interest, and this underscores the importance of studying multiple possible predictors through a large, multicenter database such as is present with the ELSO registry.

Given the complexity of CPR, ECPR, and human physiology in response to cardiac arrest, reasons for survival and acceptable neurologic outcome after ECPR are likely numerous.

Whether the difficulty in identifying these potential predictors is related to a lack of power due to small sample sizes or, perhaps, to additional factors that are presently unknown, further investigation is required so that ECPR can be reserved for those most likely to benefit from such intervention. The collection of such data at a single institution level would not be feasible because of the rare occurrence of cardiac arrests culminating in ECMO in children.

Because appropriate patients are possibly already being excluded from ECPR, all potentially predictive variables are important to study. For example, some authors have suggested that "relative contraindications" to ECPR are cardiac arrest $>$ 30 minutes or a blood pH of $<$ 7.0.[7] If this were true, the two children we describe in this case series possibly would not have received ECPR and, likely, would not have survived. Clearly, more definitive criteria are needed to determine appropriate use of this costly technique. However, if the boundaries of the use of ECPR are extended, allocation of limited resources becomes an important issue.

As evidenced by the current uncertainty in the literature, the ELSO registry is a plausible forum to collect multiinstitutional data regarding ECPR survival. Specifically related to ECPR, ELSO presently collects only limited data, including demographics, diagnoses, procedures, broad pre-ECMO support categories, and worst pre-ECMO blood gas, ventilator setting, and hemodynamics. In addition, limited complication and outcome data are collected.[11] We suggest the addition of the following data fields to the registry: CPR duration, multiple blood gas values during CPR, average mean arterial pressure during CPR (in the case of witnessed arrest with continuous arterial blood pressure monitoring), CPR medications, and specific neurologic outcomes after discharge. In addition, further thought should be given to other biologically plausible predictive measures that can be prospectively collected. After extensive review of these variables, the identity of appropriate clinical and laboratory parameters that will help predict candidates who will have meaningful survival after ECPR will likely emerge. Until then, practitioners must rely on experience and judgment regarding the value of ECPR in children suffering cardiac arrest.

References

1. del Nido PJ, Dalton HJ, Thompson AE, Siewers RD: Extracorporeal membrane oxygenator rescue in children during cardiac arrest after cardiac surgery. *Circulation* 86: II300–304, 1992.
2. Morris CM, Wernovsky G, Nadkarni VM: Survival outcomes after extracorporeal cardiopulmonary resuscitation instituted during active chest compressions following refractory in-hospital pediatric cardiac arrest. *Pediatr Crit Care Med* 5: 440–446, 2004.
3. Parra DA, Totapally BR, Zahn E: Outcome of cardiopulmonary resuscitation in a pediatric cardiac intensive care unit. *Crit Care Med* 28: 3296–3300, 2000.
4. Duncan BW, Ibrahim AE, Hraska V, *et al*: Use of rapid-deployment extracorporeal membrane oxygenation for the resuscitation of pediatric patients with heart disease after cardiac arrest. *J Thorac Cardiovasc Surg* 116: 305–311, 1998.
5. Chen Y-S, Chao A, Yu H-Y, *et al*: Analysis and results of prolonged resuscitation in cardiac arrest patients rescued by extracorporeal membrane oxygenation. *J Am Coll Cardiol* 41: 197–203, 2003.
6. Younger JG, Schreiner RJ, Swaniker F, *et al*: Extracorporeal resuscitation of cardiac arrest. *Acad Emerg Med* 6: 700–707, 1999.
7. Slonim AD, Patel KM, Ruttimann UE, Pollack MM: Cardiopulmonary resuscitation in pediatric intensive care units. *Crit Care Med* 25: 1951–1955, 1997.
8. Kurose M, Okamoto K, Sato T, *et al*: The determinant of severe cerebral dysfunction in patients undergoing emergency extracorporeal life support following cardiopulmonary resuscitation. *Resuscitation* 30: 15–20, 1995.
9. Doski JJ, Butler J, Louder DS, *et al*: Outcome of infants requiring cardiopulmonary resuscitation before extracorporeal membrane oxygenation. *J Pediatr Surg* 32: 1318–1321, 1997.
10. Horisberger T, Fischer JE, Fanconi S: One-year survival and neurological outcome after pediatric cardiopulmonary resuscitation. *Intensive Care Med* 28: 365–368, 2002.
11. Extracorporeal Life Support Organization. *ECLS Registry Form [Extracorporeal Life Support Organization web site]*. Available at: http://www.elso.med.umich.edu/WordForms/ELSORegistryForm.pdf. Accessed April 7, 2005.