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## SURVIVAL AND LONG TERM FUNCTIONAL OUTCOMES FOR CHILDREN WITH CARDIAC ARREST TREATED WITH EXTRACORPOREAL CARDIOPULMONARY RESUSCITATION

Francesc Torres-Andres, MD<sup>1</sup>, Ericka L. Fink, MD<sup>2</sup>, Michael J. Bell, MD<sup>2</sup>, Mahesh S. Sharma, MD<sup>3</sup>, Eric J. Yablonsky<sup>2</sup>, and Joan Sanchez-de-Toledo, MD, PhD<sup>2,4</sup>

<sup>1</sup>Department of Neonatology, Hospital Clinic-Maternitat, ICGON-BCN natal, Barcelona, Spain

<sup>2</sup>Department of Critical Care Medicine, University of Pittsburgh School of Medicine, Children's Hospital Pittsburgh of UPMC, USA

<sup>3</sup>Department of Cardiothoracic Surgery, University of Pittsburgh School of Medicine, Children's Hospital Pittsburgh of UPMC, USA

<sup>4</sup>Department of Pediatric Cardiology, Hospital Sant Joan de Déu, Barcelona, Universitat de Barcelona, Spain

### Abstract

**Objectives**—To identify patient- and disease-related factors related to survival and favorable outcomes for children who underwent Extracorporeal Cardio-Pulmonary Resuscitation (ECPR) after a refractory cardiac arrest.

**Design**—Retrospective observational study with prospective assessment of long term functional outcome.

**Patients**—Fifty-six consecutive children undergoing ECPR at our institution from 2007 to 2015. Median age at arrest was 3.5 months (IQR 1 – 53).

**Setting**—Tertiary Pediatric University Hospital with a Referral Heart Center.

**Interventions**—Health-related quality of life, and family functioning assessment with the PedsQL and the McMaster Family Assessment Device (MMFAD).

**Measurements and Main results**—Fifty-eight (58) consecutive ECPR episodes were included, with 46 (79.3%) related to primary cardiac conditions. Initial cannulation site was central in 19 (32.8%) and peripheral in 39 (67.2%). Survival to decannulation was 77.6% with survival at hospital discharge and at the end of the follow-up period being 65.5% and 62.1%, respectively. Time to follow-up was 38 months [IQR 19–52]. Patients who survived tended to be younger (3.5 mo [1m – 2y] vs. 7 mo [1.25 mo – 17y],  $p = 0.3$ ) with decreased ECPR times (28 min [15–47] vs 37.5 min [28.5 – 55],  $p = 0.04$ ). Those who received therapeutic hypothermia

Address Correspondence to: Joan Sanchez de Toledo MD., PhD., Cardiac Intensive Care Division, Department of Critical Care Medicine, University of Pittsburgh, 4401 Penn Ave, Pittsburgh, PA 15224, joansdt@gmail.com.

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tended to have higher hospital survival (21/28 (75%) vs 16/29 (55%)  $p=0.08$ ). Follow-up assessments of survivors demonstrated good quality of life and family functioning (PedsQL 84 [76–89.5]; MMFAD 1.62 [1.33–1.83]).

**Conclusions**—In this series, ECPR was associated with relatively high survival rates and a good health-related quality of life and family functioning. Larger series are needed to assess whether this technique should be more broadly available in the pediatric critical care community.

### Keywords

cardiopulmonary resuscitation; extracorporeal life support; cardiac arrest; quality of life; neurologic outcomes

## Introduction

Survival rate after pediatric cardiopulmonary resuscitation (CPR) for children undergoing cardiac arrest (CA) remain low. In addition to survival, understanding the development of new neurological disabilities after cardiac arrest remains challenging (1).

Extracorporeal Cardiopulmonary Resuscitation (ECPR), defined by the initiation of extracorporeal life support during active chest compressions, has the potential to offer survival and favorable neurological recovery (2). In the early 1990's extracorporeal membrane oxygenation (ECMO) support instituted as rescue therapy during CPR promoted survival in children with cardiac disease who had cardiopulmonary arrest and failed to respond to conventional CPR (3). Since then, ECPR has been increasingly used as a method to improve survival in patients with refractory CA due to cardiac and non-cardiac etiology (4,5). An ELSO registry report which reviewed data from 2004 to 2016 showed an important increase of pediatric ECPR, but did not demonstrate improved survival (6).

Current pediatric advance life support guidelines recommend that ECPR may be considered for children with underlying cardiac conditions who have an in-hospital CA, when appropriate protocols, expertise, and equipment are available (Class IIb, LOE C-LD). Pediatric out-of-hospital cardiac arrest (OHCA) was not considered for the 2015 ILCOR systematic review (7).

ECPR requires significant expertise and resource utilization and is thus not universally available. Skilled personnel for rapid assembly of an ECMO circuit, alongside surgical, medical and nursing teams are needed to initiate and manage patients on ECMO successfully. In addition, around the clock availability of such a specialized team is a considerable expense and as such, survival and long-term outcomes must justify this strategy. Until recently, data about neurological outcomes and morbidity has been limited due to a lack of rapid and reliable assessment tools applicable to the wide age range of pediatric patients. Multiple functional and neurological scales have been used in prior studies such as the Pediatric Overall Performance Category (POPC), the Pediatric Cerebral Performance Category (PCPC) and the Functional Status Scale (FSS) (8–9). The Pediatric Quality of Life Inventory (PedsQL) measurement model is a modular approach to measuring health-related quality of life (HRQOL) in healthy children and adolescents and those with

acute and chronic health conditions. The 23-item PedsQL Generic Core Scales were designed to measure the core dimensions of health - physical, emotional and social - as delineated by the World Health Organization, as well as role (school) functioning (10). Also, the McMaster Family Assessment Device (MMFAD) has been validated as a single index measure to assess family functioning (11).

The aim of our study is to identify factors related to survival to hospital discharge and describe health-related quality of life for children who had either in-the-hospital CA (IHCA) or witnessed OHCA and who underwent in-hospital ECPR at a single-center using the PedsQL and the MMFAD.

## Materials and methods

This study was approved by the University of Pittsburgh Institutional Review Board. All children who received ECPR for sudden and refractory CA at Children's Hospital of Pittsburgh of UPMC between May 2007 and July 2015 were included. We retrospectively analyzed data collected from 56 pediatric patients who suffered from sudden and refractory cardiopulmonary arrest and were placed on rescue ECMO during this period of time. Patient demographics, etiology and location of arrest, ECPR duration (defined as the time between initiation of chest compressions and ECMO flow started), pediatric risk of mortality (PRISM) score prior to ECMO cannulation was calculated for all medical patients. Laboratory data prior to and after ECMO cannulation were also obtained. Health-related quality of life and family functioning were assessed with the Pediatric Quality of Life Inventory (PedsQL) and the McMaster Family Assessment Device (MMFAD) obtained by scheduled phone interview performed by a research coordinator. Additionally, diagnostic neurologic evaluation of all children undergoing ECPR was assessed by computed tomography, ultrasonography, or magnetic resonance imaging.

## Patients

The inclusion criteria for determining patients' candidacy for rescue ECMO at our institution included: (1) witnessed in-hospital CA (IHCA) or witnessed out-of-hospital cardiac arrest (OHCA); (2) receipt of advanced CPR; (3) no recovery of spontaneous circulation (ROSC) within 15 minutes of CPR; and (4) no contraindication to mechanical circulatory support, such as pre-existing severe neurologic abnormality, renal failure, CHD not correctable by conventional surgery or transplantation and gestational age less than 35 weeks. Exclusion criteria were contraindication to mechanical circulatory support or anatomic constraints precluding successful cannulation for extracorporeal support.

## ECPR Protocol

Our practice is to initiate activation of the emergency ECMO team if ROSC is not achieved within 5 min of well-performed CPR when a potentially reversible underlying pathology is considered. Patients were treated with veno-arterial (VA) ECMO with a standard circuit including a centrifugal pump and an oxygenator.

Before starting ECPR, patients received one dose of Heparin (100 U/kg) followed by a continuous infusion to maintain an activated clotting time (ACT) of 180–200 s. Inotropic

support was weaned to minimal levels as tolerated to keep mean arterial blood pressure at age appropriate/targeted levels. Flow rates of 2.5–3 l/m<sup>2</sup>/min were maintained depending on the hemodynamic state, serum lactate levels, and mixed venous oxygen saturation. Mechanical ventilation was continued using low ventilatory rates, PEEP of 7–10 cm H<sub>2</sub>O and 30–40% FiO<sub>2</sub>, with all settings adjusted accordingly to minimize barotrauma to the lungs. All patients were given neuromuscular blocking agents, minimal sedation and narcotic analgesia to permit adequate neurological evaluation.

Cardiac function was assessed by serial transthoracic echocardiography and hemodynamic stability at reduced rescue ECMO flow. The flow rate was reduced when there was sufficient recovery of cardiac function.

Separation from ECMO was accomplished by gradual flow reduction while increasing inotropic and ventilatory support. Once the patient was off complete support, hemodynamic stability was monitored and tissue perfusion was assessed by serial arterial blood gases with serum lactate, base deficit values and mixed venous oxygen saturation. For those patients with central cannulation (transthoracic ECMO) delayed sternal closure was performed two to three days after decannulation when catecholamine support was minimal or withdrawn. No fundamental changes were instituted in the ECPR protocol during the study period.

### **Management of body temperature after CA**

Therapeutic hypothermia was utilized at the discretion of the multidisciplinary care team. When hypothermia was employed, patients were actively cooled between 34–35°C. In those patients who were not cooled, controlled normothermia was performed avoiding body temperature above 37°C with antipyretic drugs or devices.

### **Statistical analysis**

All data were analyzed with the SPSS program. Patient demographics, cardiac arrest and ECPR time, ECMO details, survival outcomes, and testing data were analyzed descriptively. Demographic data are expressed as absolute and percentage values and continuous data as mean and standard deviation or median and interquartile range (IQR), as appropriate. The Chi-square, Fisher exact and Mann-Whitney tests were used to compare parametric and non-parametric variables, respectively. A *p*-value < 0.05 was considered statistically significant. A multivariable logistic regression to determine variables associated with survival to hospital discharge was conducted. The variables with a *p* value less than 0.2 were fitted into the model.

## **Results**

### **Patient characteristics**

Between May 2007 and July 2015, 56 patients were cannulated during ongoing chest compressions because of refractory cardiac arrest, with a total of 58 ECPR episodes. Only three out of 58 episodes (5.2%) were OHCA, with 55 (94.8%) being witnessed IHCA.

Median age at arrest in our cohort was 3.5 months (IQR 1 – 53). Twenty-three patients were female (39.6%) and the median weight was 6 kg (IQR 3 – 20.7) (Table 1).

Among the 58 ECPR episodes included in the analysis, 46 (79.3%) occurred in patients with primary cardiac condition (32 (55.2%) being structural heart disease and twelve (20.7%) in patients suffering from non-cardiac conditions). Twenty-four episodes of CA followed cardiac surgery. The rest of episodes of CA were not related to surgery (32 (55.2%) related to myocardial failure).

Of those 55 IHCA, 29 (53%) occurred in the cardiac intensive care unit (CICU), 14 (25.5%) in the pediatric intensive care unit (PICU), 5 (9%) in the operating room, 3 (5.3%) in the emergency department, 2 patients (3.6%) in the catheterization laboratory, and finally 2 (3.6%) in the neonatal intensive care unit (NICU).

Cannulation site was central in 19 patients (32.8%) and peripheral in 37 patients (63.8%): cervical cannulation in 32 patients (55.2%) and multi-site (cervical and femoral) in 5 patients. Two patients (3.4%) required central cannulation due to failure of initial peripheral cannulation (Table 1). Only one circuit change was required during the study due to evidence of circuit thrombosis. That patient successfully survived decannulation and no abnormal results were reported on the follow up imaging studies. No other circuit failures were reported during the study period.

Survival to ECMO decannulation was 45/58 (77.6%); survival to hospital discharge was 38/58 (65.5%) and survival at the end of the follow-up period was 36/58 (62.1%). Median time of follow-up was 3 years (IQR 1.5 – 4.5). Hospital survival in OHCA was 1/3 (33.3%). None of the patients that underwent OHCA survived to the follow-up period (table 1). Among the non-survivors, withdrawn of life sustaining therapies was related to multi organ failure in 13 patients (59.1%), brain death in 6 patients (27.3%), severe brain injury in 2 patients (9.1%), and extracorporeal support withdrawn by family request in 1 patient (4.5%) (Table 2).

### **Risk factors associated with hospital mortality**

Patients who survived were younger than those who did not survive, but these differences did not reach significance (3.5 months (1m – 2 years) vs. 7 months (1.25m – 17 years),  $p=0.3$ ). No patients undergoing more than one ECPR episode survived at hospital discharge (Table 1).

Survival among patients with underlying cardiac conditions was 31/46 (67.4%), compared to 5/12 (41.6%) of those with a non-cardiac condition ( $p = 0.09$ ). Based on the cannulation location, patients cannulated in the operating room had an 85.7% of hospital survival, compared to 63% in the CICU, 54% in the PICU, 50% in the catheterization laboratory, and 0% in the emergency department. Survival based on cannulation site was 12/19 (63%) with central cannulation, and 23/37 (62%) with peripheral cannulation. Patients who required central cannulation on top of an initial peripheral approach achieved 1/2 (50%) survival (Table 3).

Patients who survived had shorter CPR times compared to those who did not survive (28 min [15–47] vs 37.5 min [28.5 – 55],  $p = 0.04$ ) (Table 1). Patients who survived had lower levels of post-ECMO lactate (mmol/L) compared to those who did not survive (9 (5–12.5) vs

15 (6 – 26),  $p = 0.05$ ). No statistical differences were found in relation to lactate levels prior to neither ECMO cannulation nor ECMO duration between survivors and non-survivors. Within non-surgical patients, Pre-ECPR PRISM scores did not reveal significant differences. In addition, those patients cooled after CA tended to have lower hospital mortality compared to those not cooled (21/28 (75%) vs. 16/29 (55%)  $p = 0.08$ ) (Table 3). In a multivariate logistic regression analysis, none of the variables were independently associated with hospital mortality.

### Patient and family outcomes

Brain imaging studies after ECMO decannulation were obtained in 42 out of 58 episodes at a median of 5 days (IQR 1 – 29) post-ECPR (table 4). Those studies revealed evidence of intracranial injuries in 15/30 (50%) among survivors compared to 7/12 (58.3%) among non-survivors ( $p = 0.7$ ). Among those studies 8 (36%) revealed acute ischemia, 6 (28%) intracranial hemorrhage, 3 (14%) cerebral venous thrombosis and five (22%) studies revealed diffuse white matter injury (Table 4).

**Among survivors, 6 (16.7%) were discharge on anti-epileptic drugs**—Median age at PedsQL and MMFAD evaluation was 4 years (IQR 2 – 7). Median PedsQL score was 84 (76 – 89.5) and MMFAD was 1.62 (1.33–1.83). Those children with a normal brain imaging at the time of ECMO decannulation had statically higher values of physical health and total scores on the PedsQL evaluation (86 [82 – 90] vs 78.5 [61.5 – 81.5],  $p = 0.048$  for Total score; 88 [83 – 94] vs 73.5 [41.75 – 87],  $p = 0.024$  for Physical Health) (Table 5). Nevertheless, no statistical differences were found on the Psychosocial field of the PedsQL and MMFAD among children with normal brain imaging compared to those with abnormal brain imaging (Table 5). No significant statistical differences were found on the PedsQL or MMFAD scores between patients managed with or without hypothermia (Table 5). Among survivors with abnormal brain imaging post-decannulation, those with hemorrhagic changes had lower PedsQL scores compared to those having ischemic changes, specifically on the Physical scores (88 [83 – 94] vs. 73.5 [41.75 – 87],  $p=0.024$ ) (Table 6). No significant correlations were found between PedsQL and MMFAD scores and time of ECPR and ECMO duration.

### Discussion

Overall, our study shows a hospital survival to ECPR of 65.5% and a 3-year follow-up survival of 62.1%, numbers that are relatively higher than those reported in previous ECPR studies and the latest ELSO Registry (6, 12–13). The most recent ELSO registry data reveals that in last decade the use of pediatric ECPR has increased tenfold, however hospital survival rates have remained consistent, from 39% in 2004 to 41% in 2016 (6). In addition, two recent ECPR publications also showed lower rates of hospital survival compared with our data. In 2010 Raymond et al., in a multicenter study from the American Heart Association National Registry including neonates, children and infants, reported a 44% survival to hospital discharge, with higher survival achieved in patients with cardiac diagnosis (12). Most recently Garcia Guerra et al., reported a 49% survival to hospital discharge and a 43% survival at follow-up in a single-center study including a cohort of 55



patients with a mean age of 34.7 months (13). Our patient population was younger (median age of 3.5 months) which in our analysis conferred a survival advantage. These differences in cohorts could have contributed to the better outcomes reported in our study.

In our study, the majority of our population suffered from a witnessed IHCA from primary cardiac condition. Although differences in survival rates between cardiac patients and non-cardiac patients did not reach statistical significance, these patients tended to have higher survival rates (67.4% vs. 41.6%,  $p = 0.09$ ). Similarly, Joffe et al., published in 2012, a review of studies about ECPR finding that patients with a non-cardiac disease were more likely to die (14). It remains unclear why cardiac patients respond better to extracorporeal support than non-cardiac diagnoses. Although further investigations are needed to establish appropriate guidelines, it is noteworthy that the latest American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care, strongly supports the use of ECPR in patients with IHCA and those suffering from a cardiac condition (7).

Similar to other pediatric studies, our data demonstrates better survival for those children suffering from IHCA compared to those with OHCA (67.2% vs. 33.3%). Moreover, none of the patients suffering from OHCA survived to follow-up. On the other hand, our IHCA ECPR survival rates are better than those reported in IHCA with advanced CPR (15). These results align with recently published data showing that in children suffering from IHCA with CPR duration over 10 minutes, ECPR is associated with improved survival to hospital discharge and favorable neurologic outcome when compared to advanced CPR (16). Therefore, our data adds to the growing body of literature that supports the use of ECPR as a life-saving strategy for children with refractory IHCA allowing achieving survival on children who otherwise would be determined to die.

One of our primary objectives was to identify factors associated to ECPR survival. Previous studies demonstrated that ECPR duration time (defined as the time from initiation of chest compressions to successful ECMO flows), higher levels of lactate during the first 24h of ECMO, longer time for lactate to normalize after ECMO cannulation and lower pH values prior and during ECMO were risk factors associated with in-hospital mortality [5,17–19]. Aligned with those results, in our cohort, patients who survived had shorter ECPR times (28 min vs. 37.5 min;  $p = 0.04$ ). Moreover, having more than one ECPR episode and higher levels of lactate post-ECMO cannulation were associated with in-hospital mortality. When comparing demographics, such as patient age, weight or gender, these factors were not significant predictors of poor outcome. Similar results have been reported by other authors (18). In a literature review including 17 ECPR studies published from 2000 to 2011 including 762 children that underwent ECPR between 1990 to 2008, Joffe et al., found non-cardiac etiology, renal dysfunction, lowest pH and neurological complications while on ECMO being the most consistent predictors of mortality (14). Consistent with these findings in a recent publication including data collected by the Collaborative Pediatric Critical Care Research Network from 2012 to 2014 including 514 patients (267 neonates) undergoing ECMO, Cashen et al., reported primary diagnosis of cardiovascular disease, chronic cardiac disease, initiation of ECMO during advanced CPR, development of neurologic event, renal

failure, hepatic dysfunction, or thrombotic event were associated with increased relative risk of death (19).

The second main objective of our review was to describe health-related quality of life and family functioning in those children surviving ECPR. Data on functional outcomes of patients surviving ECPR is scant (14). In his recent publication including functional data on 282 ECMO survivors collected by the Collaborative Pediatric Critical Care Research Network, Cashen et al. reported that 268/282 patients (95%) survived hospital discharge without severe functional abnormalities. Nevertheless, no data on functional outcomes was reported from the 70 ECPR patients included in the study (19). In a previous study including 95 patients undergoing ECMO in our institution from 2006 to 2010, Chrysostomou et al. reported that 75% of those had normal to mild disabilities at hospital discharged (20). In our ECPR survivor cohort we performed a functional evaluation using the validated functional scales PedsQL and the MMFAD (10). Of interest, both scores used in our population revealed a good quality of life and good family functioning among survivors to ECPR, as median scores of PedsQL and MMFAD obtained were similar to those reported in healthy controls (21–22). When comparing brain imaging studies after ECPR, our results showed a higher rate of intracranial injuries than reported in the literature (23–24). In 2013 Chrysostomou C et al., reported a 12% of intracranial injuries after pediatric ECMO support based on CT scan or cerebral ultrasound (20). Despite a higher rate of abnormal brain imaging after ECMO decannulation in our study, no statistical differences were found among survivors and non-survivors. Moreover, among survivors, those children with a normal brain imaging at the time of ECMO decannulation had statically higher values of physical health and total scores on the PedsQL evaluation, whereas psychosocial field (including language evaluation) was not affected. Despite ECPR survivors having worse brain imaging they still had good performance at school or at home as shown on the PedsQL and MMFAD scores. Finally, our results corroborate with the results of the THAPCA trial, showing that there was no difference in outcome with therapeutic hypothermia after an ICHA or OHCA in children (25–26).

This study has some important limitations. First and foremost, it is a single-center study with a relatively small sample size as CA in children is not as often as in adult population. Secondly, the intrinsic limitations to functional data obtained by a phone interview provided by a third party without direct observation of the true situation of the patient. Further studies are needed to diminish this lack of detailed neurodevelopmental outcome on survivors of ECPR.

## Conclusions

In light of our results and latest publications, ECPR can be life-saving when performed in well-trained and designed centers.

Specifically, in relation to our data, ECPR duration, postECMO lactate and history of a prior ECPR event were associated with mortality in our population. Those who received therapeutic hypothermia tended to have higher hospital survival. Further studies are need in this field to proper indications on temperature management.



In conclusion, use of ECPR was associated with high survival rates and a good health-related quality of life and family functioning in our population. For a greater adoption and confirmation of benefits, larger series encompassing more centers and a wide variety of clinical conditions are needed to assess whether this technique should be more broadly available in the pediatric critical care community.

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The authors declare that they have no conflict of interest.

## References

1. Slomine BS, Silverstein FS, Christensen JR, et al. Neurobehavioral Outcomes in Children After Out-of-Hospital Cardiac Arrest. *Pediatrics*. 2016; 137(4)
2. Ryan J. Extracorporeal membrane oxygenation for pediatric cardiac arrest. *Crit Care Nurse*. 2015 Feb; 35(1):60–9. [PubMed: 25639578]
3. Thiagarajan RR, Laussen PC, Rycus PT, et al. Extracorporeal membrane oxygenation to aid cardiopulmonary resuscitation in infants and children. *Circulation*. 2007; 116(15):1693–700. [PubMed: 17893278]
4. del Nido PJ, Dalton HJ, Thompson AE, Siewers RD. Extracorporeal membrane oxygenator rescue in children during cardiac arrest after cardiac surgery. *Circulation*. 1992 Nov.86(5 Suppl)
5. Garcia Guerra G, Zorzela L, Robertson CM, et al. Western Canadian Complex Pediatric Therapies Follow-up Group. Survival and neurocognitive outcomes in pediatric extracorporeal-cardiopulmonary resuscitation. *Resuscitation*. 2015; 96:208–13. [PubMed: 26303570]
6. Barbaro RP, Paden ML, Guner YS, et al. ELSO member centers. Pediatric Extracorporeal Life Support Organization Registry International Report 2016. *ASAIO J*. 2017 Jul-Aug;63(4):456–463. [PubMed: 28557863]
7. Neumar RW, Shuster M, Callaway CW, et al. Part 1: executive summary: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2015; 132(suppl 2):S315–S367. [PubMed: 26472989]
8. Fiser DH. Assessing the outcome of pediatric intensive care. *J Pediatr*. 1992 Jul; 121(1):68–74. [PubMed: 1625096]
9. Pollack MM, Holubkov R, Glass P, et al. National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. Functional Status Scale: new pediatric outcome measure. *Pediatrics*. 2009 Jul; 124(1):e18–28. [PubMed: 19564265]
10. Varni, JW. [Accessed May 31, 2017] Pediatric Quality of Life Inventory. Available at: <http://www.pedsql.org>
11. Boterhoven de Haan KL, Hafekost J, Lawrence D, et al. Reliability and validity of a short version of the general functioning subscale of the McMaster Family Assessment Device. *Fam Process*. 2015 Mar; 54(1):116–23. [PubMed: 25385473]
12. Raymond TT, Cunnyngham CB, Thompson MT, et al. American Heart Association National Registry of CPR Investigators. Outcomes among neonates, infants, and children after extracorporeal cardiopulmonary resuscitation for refractory in-hospital pediatric cardiac arrest: a report from the National Registry of Cardiopulmonary Resuscitation. *Pediatr Crit Care Med*. 2010 May; 11(3):362–71. [PubMed: 19924027]
13. Garcia Guerra G, Zorzela L, Robertson CM, et al. Western Canadian Complex Pediatric Therapies Follow-up Group. Survival and neurocognitive outcomes in pediatric extracorporeal-cardiopulmonary resuscitation. *Resuscitation*. 2015 Nov.96:208–13. [PubMed: 26303570]
14. Joffe AR, Lequier L, Robertson CM. Pediatric outcomes after extracorporeal membrane oxygenation for cardiac disease and for cardiac arrest: a review. *ASAIO J*. 2012 Jul-Aug;58(4): 297–310. [PubMed: 22643323]

15. Moler FW, Meert K, Donaldson AE, et al. Pediatric Emergency Care Applied Research Network. In-hospital versus out-of-hospital pediatric cardiac arrest: a multicenter cohort study. *Crit Care Med*. 2009 Jul; 37(7):2259–67. [PubMed: 19455024]
16. Lasa JJ, Rogers RS, Localio R, et al. Extracorporeal Cardiopulmonary Resuscitation (E-CPR) During Pediatric In-Hospital Cardiopulmonary Arrest Is Associated With Improved Survival to Discharge: A Report from the American Heart Association's Get With The Guidelines-Resuscitation (GWTG-R) Registry. *Circulation*. 2016 Jan 12; 133(2):165–76. [PubMed: 26635402]
17. López-Herce J, del Castillo J, Matamoros M, et al. Iberoamerican Pediatric Cardiac Arrest Study Network RIBEPCI. Post return of spontaneous circulation factors associated with mortality in pediatric in-hospital cardiac arrest: a prospective multicenter multinational observational study. *Crit Care*. 2014 Nov 3.18(6):607. [PubMed: 25672247]
18. Delmo Walter EM, Alexi-Meskishvili V, Huebler M, et al. Rescue extracorporeal membrane oxygenation in children with refractory cardiac arrest. *Interact Cardiovasc Thorac Surg*. 2011 Jun; 12(6):929–34. [PubMed: 21429870]
19. Cashen K, Reeder R, Dalton HJ, et al. Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network (CPCCRN). Functional Status of Neonatal and Pediatric Patients After Extracorporeal Membrane Oxygenation. *Pediatr Crit Care Med*. 2017 Jun; 18(6):561–570. [PubMed: 28419061]
20. Chrysostomou C, Maul T, Callahan PM, et al. Neurodevelopmental Outcomes after Pediatric Cardiac ECMO Support. *Front Pediatr*. 2013 Dec 19.1:47. [PubMed: 24400292]
21. Varni JW, Burwinkle TM, Limbers CA, et al. The PedsQL as a patient-reported outcome in children and adolescents with fibromyalgia: an analysis of OMERACT domains. *Health Qual Life Outcomes*. 2007 Feb 12.5:9. [PubMed: 17295915]
22. Varni JW, Limbers CA, Burwinkle TM. Impaired health-related quality of life in children and adolescents with chronic conditions: a comparative analysis of 10 disease clusters and 33 disease categories/severities utilizing the PedsQL 4.0 Generic Core Scales. *Health Qual Life Outcomes*. 2007 Jul 16.5:43. [PubMed: 17634123]
23. Mehta A, Ibsen LM. Neurologic complications and neurodevelopmental outcome with extracorporeal life support. *World J Crit Care Med*. 2013 Nov 4; 2(4):40–7. [PubMed: 24701415]
24. Hervey-Jumper SL, Annich GM, Yancon AR, et al. Neurological complications of extracorporeal membrane oxygenation in children. *J Neurosurg Pediatr*. 2011 Apr; 7(4):338–44. [PubMed: 21456903]
25. Moler FW, Silverstein FS, Holubkov R, et al. THAPCA Trial Investigators. Therapeutic hypothermia after out-of-hospital cardiac arrest in children. *N Engl J Med*. 2015 May 14; 372(20):1898–908. [PubMed: 25913022]
26. Moler FW, Silverstein FS, Holubkov R, et al. THAPCA Trial Investigators. Therapeutic Hypothermia after In-Hospital Cardiac Arrest in Children. *N Engl J Med*. 2017 Jan 26; 376(4):318–329. [PubMed: 28118559]

**Table 1**

## Patient Demographics

	ALL ECPR 58	SURVIVORS 38(65.5)	NON-SURVIVORS 20(34.5)	P-value
<b>Pre-Operative</b>				
AGE, months	3.5 (1 – 53)	3.5 (1m–2y)	7 (1.25m – 17y)	0.30
Weight, kg	6 (3 – 20.7)	5.5 (3–12)	8.5 (3.7 – 42)	0.50
Female gender, n (%)	23 (39.6)	14 (38.9)	9 (40.9)	0.70
<b>Cardiac arrest location</b>				
OHCA	3 (5.2)	1 (33.3)	2 (66.6)	0.20
IHCA	55 (94.8)	37 (67.2)	18 (32.8)	
<b>Primary diagnosis at the time of arrest</b>				
Cardiac	46 (79.3)	31 (81.6)	15 (75)	0.09
• Structural heart disease	32 (55.2)	22 (57.9)	10 (50)	0.07
• Heart transplant	4 (6.9)	3 (7.9)	1 (5)	0.40
• Myocardial disease	10 (17.2)	6 (15.8)	4 (20)	0.55
Non-cardiac	12 (20.7)	7 (18.4)	5 (25)	0.38
• Pulmonary hypertension	2 (3.4)	0 (0)	2 (10)	0.04
• Respiratory failure	3(5.2)	2(5.2)	2 (10)	0.07
• Sepsis	6(10.3)	4(10.5)	1 (5)	0.30
• Others	1(1.7)	1(2.6)	0 (0)	0.16
<b>Arrest etiology</b>				
Post-cardiotomy	24 (41.4)	17 (44.7)	7 (35)	0.40
Non-operative	46 (79.3)	31 (86.1)	15 (68.2)	0.09
• Myocardial Failure*	32 (55.2)	22 (61.1)	10 (45.5)	0.07
• Non-cardiac	12 (20.7)	5 (13.9)	7 (31.8)	0.38
More than one ECPR event	2 (3.4)	0 (0)	2 (10)	<0.01

Data presented as count (%) or median (IQR); CA: cardiac arrest; ECPR: extracorporeal cardiopulmonary resuscitation; OHCA: out -of-hospital cardiac arrest; IHCA: in-hospital cardiac arrest; IQR: interquartile range;

\* myocarditis and cardiomyopathy.

**Table 2**

## Causes of death among non-survivors

	<b>Non-survivors n=20</b>
<b>Causes of death</b>	
Brain death	6 (27.3)
Severe brain injury	2 (9.1)
Irreversible multiple organ failure	13 (59.1)
Withdrawn of support *	1 (4.5)

Data presented as count (%);

\* withdrawn of extracorporeal support by family request.

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**Table 3**

## ECPR details

	<b>ALL ECPR 58</b>	<b>SURVIVORS 38(65.5)</b>	<b>NON-SURVIVORS 20(34.5)</b>	<b>P-value</b>
<b>Location of ECPR</b>				
CICU	35 (60.3)	22 (61.1)	13 (59.1)	
PICU	13 (22.4)	7 (19.4)	6 (27.3)	
Cathlab	2 (3.4)	1 (2.8)	1 (4.5)	0.40
Operating room	7 (12.1)	6 (16.7)	1 (4.5)	
Emergency department	1 (1.7)	0 (0)	1 (4.5)	
<b>ECMO cannulation site</b>				
Central (thorax)	19 (32.7)	12 (33.3)	7 (31.8)	
Peripheral (neck)	32 (55.2)	19 (52.8)	13 (59.1)	0.80
Double (neck/groin)	5 (8.6)	4 (11.1)	1 (4.5)	
Central + peripheral	2 (3.4)	1 (2.8)	1 (4.5)	
<b>Patient characteristics</b>				
Pre-ECMO PRISM*	13 (10–18)	14 (11 – 20)	10.5 (7.5 – 16)	0.08
Pre-ECMO Lactate (mmol/L)	3 (2 – 8.5)	4 (2 – 12)	2 (1.9 – 5)	0.60
Post-ECMO Lactate (mmol/L)	10 (5 – 15)	9 (5 – 12.5)	15 (6 – 26)	0.05
<b>ECPR duration time, min</b>	31 (20 – 49)	28 (15 – 47)	37.5 (28 – 55)	0.04
<b>ECMO duration (hours)</b>	79.5 (44 – 128)	70 (42 – 131)	83 (58 – 165)	0.70
<b>Hypothermia treatment used</b>	28 (48)	20 (55.5)	8 (36.4)	0.08

Data presented as median (IQR), or mean (SD) ECPR: extracorporeal cardiopulmonary resuscitation; IQR: interquartile range; CICU: cardiac intensive care unit; PICU: pediatric intensive care unit; ECMO: extracorporeal membrane oxygenation; PRISM: pediatric risk of mortality score;

\*Pre-ECMO PRISMs only measured in non-surgical patients.

**Table 4**

## Results of Brain Imaging

	<b>ALL ECPR 58 (100)</b>	<b>SURVIVORS 36 (62.1)</b>	<b>NON-SURVIVORS 22 (37.9)</b>	<b>P-value</b>
<b>Type of brain image performed at decannulation</b>				
MRi	10 (17)	10 (27.8)	0 (0)	NS
CT scan	26 (45)	16 (44.4)	10 (45.5)	
Head US	7 (12)	5 (13.9)	2 (9)	
Not performed	15 (26)	5 (13.9)	10 (45.5)	
<b>Brain image at decannulation</b>				
Total	42	30	12	
Normal	20 (46.7)	15 (50)	5 (41.5)	NS
Abnormal	22 (52.4)	15 (50)	7 (58.5)	
• Ischemic	8 (36)	7 (47)	1(14.5)	
• Hemorrhagic	6 (28)	4 (26.5)	2(28.5)	
• Thrombosis	3 (14)	1 (6.5)	2(28.5)	
• Diffuse white matter injury	5 (22)	3 (20)	2(28.5)	

Data presented as count (%)

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**Table 5**

Functional Outcomes among survivors comparing brain imaging results.

	<b>NORMAL brain imaging</b>	<b>ABNORMAL brain imaging</b>	<b>P-value</b>
<b>PedsQL</b>			
• Total score	86 (82 – 90)	78.5 (61.5 – 81.5)	<i>0.05</i>
• Physical Health	88 (83 – 94)	73.5 (41.75 – 87)	<i>0.02</i>
• Psychosocial Health	85 (81 – 92)	84 (75.5–86.5)	<i>0.23</i>
<b>MMFAD</b>			
• Problem solving	1.8 (1.5 – 1.8)	1.8 (1.3 – 2)	<i>0.54</i>
• Communication	1.9 (1.7 – 2.1)	1.8 (1.3 – 2.3)	<i>0.47</i>
• Roles	2.1 (1.8 – 2.2)	1.9 (1.4 – 2.5)	<i>0.50</i>
• Affective responsiveness	1.8 (1.3 – 2)	1.8 (1.2 – 2.1)	<i>0.71</i>
• Affective involvement	2 (1.3 – 2.3)	1.9 (1.5 – 2.3)	<i>0.28</i>
• Behavior control	1.7 (1.3 – 1.9)	1.1 (1 – 1.8)	<i>0.62</i>
• General Functioning	1.6 (1.3 – 1.8)	1.6 (1.3 – 1.9)	<i>0.09</i>

IQR: interquartile range; PedsQL: pediatric quality inventory of life; MMFAD: McMaster family assessment device

**Table 6**

Functional Outcomes among survivors comparing ischemic vs. hemorrhagic brain imaging results.

<b>PedsQL scores comparing</b>	<b>Ischemia (n=7)</b>	<b>vs</b>	<b>Hemorrhagic (n=4)</b>	
• Total score	86 (82 – 90)		78.5 (61.5 – 81.5)	<i>0.05</i>
• Physical Health	88 (83 – 94)		73.5 (41.75 – 87)	<i>0.02</i>
• Psychosocial Health	85 (81 – 92)		84 (75.5–86.5)	<i>0.23</i>

IQR: interquartile range; PedsQL: pediatric quality inventory of life; MMFAD: McMaster family assessment device

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