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Short paper

CPR quality and outcomes after extracorporeal life support for pediatric In-Hospital cardiac arrest

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Abstract

Aim of study: To determine outcomes in pediatric patients who had an in-hospital cardiac arrest and subsequently received extracorporeal cardiopulmonary resuscitation (ECPR). Our secondary objective was to identify cardiopulmonary resuscitation (CPR) event characteristics and CPR quality metrics associated with survival after ECPR.

Methods: Multicenter retrospective cohort study of pediatric patients in the pediRES-Q database who received ECPR after in-hospital cardiac arrest between July 1, 2015 and June 2, 2021. Primary outcome was survival to ICU discharge. Secondary outcomes were survival to hospital discharge and favorable neurologic outcome at ICU and hospital discharge.

Results: Among 124 patients included in this study, median age was 0.9 years (IQR 0.2–5) and the majority of patients had primarily cardiac disease (92 patients, 75%). Survival to ICU discharge occurred in 61/120 (51%) patients, 36/61 (59%) of whom had favorable neurologic outcome. No demographic or clinical variables were associated with survival after ECPR.

Conclusion: In this multicenter retrospective cohort study of pediatric patients who received ECPR for IHCA we found a high rate of survival to ICU discharge with good neurologic outcome.

Keywords: Cardiac arrest, Extracorporeal cardiopulmonary resuscitation, Paediatric intensive care unit, Cardiopulmonary resuscitation quality

Introduction

Approximately 15,200 children suffer an in-hospital cardiac arrest (IHCA) each year in the United States, of whom approximately 45–50% survive to hospital discharge.[1,2] The use of extracorporeal cardiopulmonary resuscitation (ECPR), in which Extracorporeal Life Support (ECLS) is initiated during active Cardiopulmonary Resuscitation (CPR) or before 20 minutes of return of spontaneous circulation (ROSC), is increasing among pediatric patients.[3,4] ECPR is associated with 70% higher odds of survival than conventional CPR among patients with a prolonged cardiac arrest.[5] However, morbidity and mortality remain high among patients who receive ECPR, with only 38–44% surviving to hospital discharge.[6–9] The provision of high-quality CPR has previously been demonstrated to be associated with a 10-fold increase in the odds of 24 hour survival.[10] However, there is currently only limited data on the association between CPR quality and outcome in patients receiving ECPR.[11–13]

We sought to characterize outcomes for IHCA in the Pediatric Resuscitation Quality (pediRES-Q) Collaborative (ClinicalTrials.gov: NCT02708134) database, a large, multicenter, pediatric quality improvement database. The pediRES-Q database includes demographic and event characteristics as well as defibrillator derived CPR quality data. Our primary objective was to determine outcomes in IHCA among pediatric patients who received ECPR. Our

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secondary objective was to identify CPR event characteristics and CPR quality metrics associated with survival after ECPR.

Methods

We conducted a multi-center retrospective cohort study using data from the pediRES-Q Collaborative, an international collaborative of 45 children's hospitals. Demographic, clinical, CPR event, quality and outcome data were collected and entered in the database by trained personnel. The study met criteria for a waiver of consent per Code of Federal Regulations 45 CFR 46.116(d) and 45 CFR 46.408(a). The study was approved by local institutional review or research ethic boards and a data use agreement was obtained per local institutional regulations.[14]

Pediatric patients (<18 years of age) who received ECPR for an index IHCA between July 1, 2015 and June 2, 2021 were included. ECPR was defined as cannulation for ECLS occurring during active CPR or before 20 minutes of ROSC.[3] Identification of patients receiving ECPR was based on three separate fields in the pediRES-Q database: (1) labelled as ECPR using the "ecmo" (extracorporeal membrane oxygenation) variable; (2) Cardiopulmonary bypass/extracorporeal CPR (ECPR) selected in the "non drug interventions" during the arrest event; and (3) return of circulation with ECMO selected for the "reason resuscitation ended" variable. Patients who did not meet all 3 of these criteria were excluded.

The primary outcome measure was survival to intensive care unit (ICU) discharge. The secondary outcome measures were survival to hospital discharge and survival with favorable neurologic outcome at ICU and hospital discharge respectively. Favorable neurologic outcome was defined as Pediatric Cerebral Performance Category (PCPC) $\leq$ 2 or unchanged from baseline. Variables considered as having a potential association with survival included patient demographic, diagnosis, cannulation site and CPR event variables. Defibrillator derived CPR quality variables were also considered among patients who had complete quality data available.

Descriptive statistics were computed for all demographic and clinical variables. Odds ratios (OR) and 95% confidence intervals (95% CI) for the association between variables and survival to ICU discharge were estimated using univariate logistic regression. This regression analysis was repeated among the cohort of patients with cardiac disease.

Results

A total of 124 patients received ECPR during the study period. Their median age was 0.9 years (IQR 0.2–5) and 53% were female. The majority of patients, 92 (75%), had cardiac disease and the Cardiac ICU (CICU) was the most common location with 49 (40%) ECPR events. Table 1 summarizes the demographic characteristics of the included patients.

Table 1 – Patient demographics and clinical features.

Variable	Survived n(%)	Died n(%)	OR (95% CI)	p-value
Total	61	59		
Age (years)[a]	0.8(0.3–4.2)	1(0.2–7.2)	0.98(0.9–1.1)	0.5
Sex (male)	28(46)	28(47)	1(0.5–2.1)	>0.9
Race				
White	37(61)	34(58)	Ref	-
Black	5(8)	11(19)	0.4(0.1–1.3)	0.1
Asian	7(11)	2(3)	3.2(0.7–22.6)	0.2
Other	6(10)	3(5)	1.8(0.5–9.3)	0.4
Ethnicity				
Hispanic	8(13)	5(8)	Ref	-
Not Hispanic	43(70)	44(75)	0.7(0.2–2.2)	0.5
Location of Event				
Cardiac ICU	25(41)	20(34)	Ref	-
Pediatric ICU	19(31)	22(37)	0.7(0.3–1.6)	0.4
Emergency Department	5(8)	4(7)	1(0.2–4.5)	1
Other	12(20)	12	0.7(0.3–2)	0.5
Illness Category				
Medical cardiac	19(31)	17(28)	Ref	-
Medical non-cardiac	11(18)	16(26)	0.8(0.3–2.2)	0.6
Surgical cardiac	30(49)	22(36)	1.3(0.5–3)	0.6
Surgical non-cardiac	1(2)	3(5)	0.4(0.02–4.8)	0.5
Trauma[b]	0	1(2)	-	-
Congenital Heart Disease	43(70)	35(59)	1.3(0.6–3)	0.5
Single Ventricle	15(25)	13(22)	0.9(0.3–2.3)	0.8
Age and Congenital Heart Disease				
<1 year with Congenital Heart Disease	26(43)	23(39)	Ref	-
<1 year without Congenital Heart Disease	4(7)	4(7)	0.9(0.2–4)	0.8
≥1 year with Congenital Heart Disease	17(28)	12(20)	1.5(0.6–4.2)	0.4
≥1 year without Congenital Heart Disease	14(23)	20(34)	0.9(0.3–2.2)	0.7

[a] Median (IQR), OR for every one unit increase in age. [b]OR and p-value omitted due to small number of trauma patients. ICU = Intensive care unit; OR = Odds ratio; 95% CI = 95% Confidence interval. (95% CI). NB: Results of logistic regression for association between variable and primary outcome of survival to ICU discharge. 4 patients missing outcome, excluded from this table.

Outcome data was missing for 4 patients at ICU discharge and 6 patients at hospital discharge. Overall survival to ICU discharge was 51% (61/120) and 59% (36/61) of survivors had favorable neurologic outcome at ICU discharge. 47% (55/118) of patients survived to hospital discharge, 67% (37/55) of whom had favorable neurologic outcome. Of the patients who died, 50 (85%) had withdrawal of life sustaining therapies. 26 of 120 (22%) patients with data available had their resuscitation status changed to do not attempt resuscitation (DNAR) during the admission. Table 1 summarizes the results of univariate logistic regression for demographic variables and survival.

The median duration of CPR for the cohort was 47 minutes (IQR 36–60) and 29/124 (24%) patients received 60 minutes of CPR or more. The most common initial rhythms were bradycardia (35/99 patients, 35%) and pulseless electrical activity (29/99 patients, 29%). Most patients were cannulated via the neck vessels (58/117 patients, 50%) followed by cannulation via an open chest (38/117 patients, 32%). Details of the ECPR events in survivors and non-survivors are described in Table 2. There were 73 patients with complete defibrillator derived quality data available, their median duration of CPR was 50 minutes (IQR 39–62) and 38 (52%) survived to ICU discharge. Table 3 summarizes the defibrillator derived quality data for the patients with complete data available.

88 patients with cardiac disease had survival data available, 49 (56%) of whom survived to ICU discharge. Odds of survival did not differ among cardiac vs non-cardiac patients, OR 2.1(95% CI 0.9–4.9). Among patients with cardiac disease, there were no demographic, clinical, event or quality variables associated with survival to ICU discharge.

Table 2 – ECPR event factors.

Variable	Survived n(%)	Died n(%)	OR(95% CI)	p-value
Total Duration of CPR for Event (min)[a]	48(34–58)	44(36–61)	1(0.99–1.01)	>0.9
CPR Duration >=60 Minutes	13(22)	15(25)	0.81(0.3–2)	0.64
Pulseless at CPR Onset	33(54)	33(56)	1.05(0.5–2.3)	0.91
Initial Rhythm at CPR Onset[b]				
Bradycardia	19(36)	18(33)	Ref	Ref
Asystole	4(8)	9(16)	0.42(0.1–1.8)	0.24
Pulseless Electrical Activity	13(25)	17(31)	0.7(0.3–2)	0.53
Ventricular Fibrillation	8(15)	1(2)	7.6(0.7–86)	0.1
Ventricular Tachycardia	7(13)	7(13)	0.95(0.3–3.5)	0.94
Other	2(4)	3(5)	0.63(0.06–6.5)	0.7
Defibrillation Attempted	24(41)	14(24)	2(0.9–4.6)	0.1
Number of Defibrillation Attempts[c]				
1	9(36)	6(43)	Ref	Ref
2	2(8)	1(7)	0.6(0.1–2.7)	0.5
>2	12(48)	6(43)	0.8(0.1–20)	0.9
ECLS Cannulation Site				
Chest	19(31)	19(32)	Ref	Ref
Neck	32(52)	26(44)	1.4(0.6–3.2)	0.5
Groin	6(10)	9(15)	0.8(0.2–2.8)	0.7
Other	3(5)	3(5)	0.9(0.2–5.4)	0.9
Vascular Access in place at CPR Onset	54(89)	56(95)	0.7(0.1–3)	0.6
Vasoactive Agent at time of CPR Onset	38(62)	35(59)	1.3(0.6–2.7)	0.6

Results of logistic regression for association between variable and primary outcome of survival to intensive care unit (ICU) discharge. [a]Median (IQR). [b]53Rhythm data missing for 8 Survivors and 4 non. [c]percentage of all patients who received defibrillation. Survived = Survived to ICU discharge; OR = Odds ratio; 95% CI = 95% Confidence interval; ECLS = Extracorporeal life support; CPR = Cardiopulmonary resuscitation. NB: 4 patients missing outcome, excluded from this table.

Table 3 – CPR quality.

Variable	Total	Survived	Died
Chest Compression Fraction (%)[a]	79(69–89)	79(69–87)	80(70–90)
Mean Chest Compression Depth (cm)[a]			
Age <1 year	2.6(2.4–3.2)	2.6(2.4–3.2)	2.8(2.4–3.3)
Age 1–8 years	3.5(2.8–4.3)	3.5(2.8–4.3)	3.5(3.1–4.4)
Age >8 years	5.8(4.8–6.6)	5.8(4.8–6.6)	6(5.5–6.6)
Chest Compressions in Target Depth Range (%)[a]	10(1–32)	6(0–28)	17(0–34)
Mean Chest Compression Rate (cpm)[a]	114(110–121)	113(110–119)	115(112–123)
Chest Compressions in Target Rate Range (%)[a]	70(42–80)	70(44–78)	71(43–86)

Values expressed as median with interquartile range (IQR). Survived = Survived to intensive care unit discharge. NB: There were no statistically significant differences between patients who survived and patients who died.

Discussion

In this multicenter retrospective analysis of children with IHCA, we found high rates of survival to ICU discharge after ECPR. The majority of patients in this cohort had CPR quality data available for analysis, though we did not identify any CPR quality variables associated with outcome.

Survival in this cohort was higher than in previous multicenter studies, which reported rates of survival to hospital discharge of 38–44%, which may reflect the overall trend of improving outcomes after ECPR over time.[6–9] This higher rate of survival was observed despite a slightly lower proportion of children with cardiac disease, who are known to have better outcomes, than was reported in two of the three previous studies.[6,7,9] We report a median duration of CPR similar to previous studies, including over ¼ of patients with 60 or more minutes of CPR.[7,9,15] In contrast to these studies, we did not find an association between duration of CPR and survival and importantly we saw thirteen survivors in the >60 minutes of CPR group with five having favorable neurologic outcomes. Overall, we found a lower rate of favorable neurologic outcome among survivors than the 93–95% reported in previous multicenter studies, though these studies had a large number of patients missing neurologic outcome data and one used a different definition (PCPC $\geq$ 3 or unchanged from baseline).[7,9]

This study is the largest multicenter study describing CPR quality in patients receiving ECPR to date. Two previous studies describing CPR quality in ECPR patients reported lower CPR quality in ECPR compared to conventional CPR.[12,13] We found that the median CC depth in infants and children were well below the recommended depth.[16,17] A previous study from the pediRES-Q database, which was not limited to ECPR events, reported similar results.[18] The median CC rate was within the recommended 100–120/min in most patients, however the median CC fraction was below the recommended 80% overall.[16,17] These quality data indicate that there is room for improvement in the provision of high-quality CPR for ECPR patients.

This study has a few important limitations. The pediRES-Q database represents a convenience sample of cardiac arrest events, as sites may not submit every event that occurs in their institution. We may have excluded some patients who received ECPR due to our strict study definition of ECPR based on multiple data fields. Many of the patients in this study did not have quality data available and this may have introduced bias if they were not missing at random. We did not have data surrounding details of ECLS including duration of support, complications and reason for discontinuation. Finally, all sites participating in the pediRES-Q collaborative have active quality improvement programs dedicated to the improvement of pediatric resuscitation, which may limit the generalizability of these results.

Conclusions

In this multicenter retrospective cohort study of pediatric patients who received ECPR for IHCA we found a high rate of survival to ICU discharge with good neurologic outcome. Of the patients who had CPR quality data available, many did not meet the AHA high-quality CPR guidelines, this represents an opportunity for improvement.

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CRediT authorship contribution statement

Stephanie R Brown: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Maria Frazier:** Conceptualization, Writing – review & editing. **Joan Roberts:** Conceptualization, Writing – review & editing. **Heather Wolfe:** Conceptualization, Writing – review & editing. **Ken Tegtmeyer:** Conceptualization, Writing – review & editing. **Robert Sutton:** Conceptualization, Writing – review & editing. **Maya Dewan:** Conceptualization, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Sutton discloses that he receives funding from the National Heart, Lung and Blood Institute. All other authors confirm that they have no declarations of interest that could inappropriately bias this work.

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Appendix A

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