Early Cardiac Arrest Hemodynamics, End-Tidal CO_2, and Outcome in Pediatric Extracorporeal Cardiopulmonary Resuscitation: Secondary Analysis of the ICU-RESUScitation Project Dataset (2016–2021)*

OBJECTIVES: Cannulation for extracorporeal membrane oxygenation during active extracorporeal cardiopulmonary resuscitation (ECPR) is a method to rescue patients refractory to standard resuscitation. We hypothesized that early arrest hemodynamics and end-tidal CO_2 ($ETCO_2$) are associated with survival to hospital discharge with favorable neurologic outcome in pediatric ECPR patients.

DESIGN: Preplanned, secondary analysis of pediatric Utstein, hemodynamic, and ventilatory data in ECPR patients collected during the 2016–2021 Improving Outcomes from Pediatric Cardiac Arrest study; the ICU-RESUScitation Project (ICU-RESUS; NCT02837497).

SETTING: Eighteen ICUs participated in ICU-RESUS.

PATIENTS: There were 97 ECPR patients with hemodynamic waveforms during cardiopulmonary resuscitation.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Overall, 71 of 97 patients (73%) were younger than 1 year old, 82 of 97 (85%) had congenital heart disease, and 62 of 97 (64%) were postoperative cardiac surgical patients. Forty of 97 patients (41%) survived with favorable neurologic outcome. We failed to find differences in diastolic or systolic blood pressure, proportion achieving age-based target diastolic or systolic blood pressure, or chest compression rate during the initial 10 minutes of CPR between patients who survived with favorable neurologic outcome and those who did not. Thirty-five patients had $ETCO_2$ data; of 17 survivors with favorable neurologic outcome, four of 17 (24%) had an average $ETCO_2$ less than 10 mm Hg and two (12%) had a maximum $ETCO_2$ less than 10 mm Hg during the initial 10 minutes of resuscitation.

CONCLUSIONS: We did not identify an association between early hemodynamics achieved by high-quality CPR and survival to hospital discharge with favorable neurologic outcome after pediatric ECPR. Candidates for ECPR with $ETCO_2$ less than 10 mm Hg may survive with favorable neurologic outcome.

KEYWORDS: cardiopulmonary resuscitation; extracorporeal cardiopulmonary resuscitation; extracorporeal membrane oxygenation; hemodynamics

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The 2020 Pediatric Life Support International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations support the use of extracorporeal membrane oxygenation (ECMO) during extracorporeal cardiopulmonary resuscitation (ECPR) to rescue patients who are refractory to standard

RESEARCH IN CONTEXT

- It is not known what cardiopulmonary resuscitation (CPR) quality indicators and hemodynamics impact extracorporeal cardiopulmonary resuscitation (ECPR) outcomes.
- Achieving diastolic blood pressures greater than or equal to 25 mm Hg for patients younger than 1 year old or greater than or equal to 30 mm Hg for patients 1 year old or older is associated with survival to hospital discharge in other populations.

resuscitation (1). A systematic review of 1990–2020 literature shows that overall survival from ECPR is 30–50% (2). However, a 2019/2020 scenario-based international survey of pediatric critical care physicians suggested that poor-quality cardiopulmonary resuscitation (CPR) decreased the likelihood of ECMO cannulation during CPR (3). In this survey, CPR quality was based on frequency of interruptions, depth and rate of compressions, and physiologic markers such as end-tidal Co_2 ($ETco_2$) and diastolic blood pressure. Although this survey provided important information regarding physician perspectives and opinions about ECPR candidacy, the relationships between CPR quality indicators and ECPR outcomes were not evaluated (3).

The hemodynamics achieved during chest compressions and other CPR quality factors essential to providing organ perfusion before cannulation have not been previously reported. These factors may contribute to the discrepancy in the literature related to survival and duration of CPR before ECMO cannulation. For example, it is possible that a patient with a short duration of poor-quality chest compressions resulting in impaired organ perfusion has a greater mortality risk than one with a longer duration of high-quality compressions and better organ perfusion. The only published hemodynamic data for pediatric ECPR patients is from the prospective (2013–2016) Pediatric Intensive Care Quality of CPR (PICqCPR) study, which showed that systolic blood pressure greater than or equal to 60 mm Hg for infants and greater than or equal to 80 mm Hg for children 1 year old or older during the early phase of CPR was associated with improved survival in a small subgroup of patients with cardiac disease (4). However, among all patients in the PICqCPR study, achieving diastolic blood pressures greater than or equal to 25 mm Hg for patients younger than 1 year old or greater than or equal to 30 mm Hg for patients 1 year old or older was associated with survival to hospital discharge, but achieving systolic blood pressure targets was not associated with outcomes (5).

The Improving Outcomes from Pediatric Cardiac Arrest—the ICU-RESUScitation project (ICU-RESUS), was a hybrid stepped-wedge trial carried out 2016–2021 (6). In this study, hospitals transitioned from their current standard to the intervention, which was a training bundle targeting improvement in the delivery of CPR to children experiencing cardiac arrest in the ICU. For patients with an arterial line in place at the time of CPR, the study captured the initial 10 minutes of hemodynamic data and quantified CPR quality metrics (6). The objective of this preplanned secondary analysis of the ICU-RESUS data was to evaluate relationships between early-arrest hemodynamics, CPR quality metrics and outcomes in pediatric ECPR patients. We hypothesized that early arrest hemodynamics and $ETco_2$ measurements resulting from high-quality CPR are associated with improved survival to hospital discharge with favorable neurologic outcome.

METHODS

Design and Setting

Eighteen PICUs from 10 clinical sites in the U.S. collected clinical and hemodynamic waveforms from index CPR events between October 1, 2016, and March 31, 2021, for ICU-RESUS. Details of ICU-RESUS were previously published (6). The University of Utah central institutional review board (IRB) approved the study entitled, "CPCCRN068: Improving outcomes from Pediatric Cardiac Arrest (ICU-RESUS)" with waiver of consent (IRB_00093320) on July 18, 2016. This study is a secondary analysis of the ICU-RESUS dataset, which was planned between March 2019 and April 2019, while investigators were blinded to aggregated data fields. All Study procedures were conducted in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975.

Participants

Patients eligible for ICU-RESUS were 37 weeks old or older post-conceptual age and 18 years young or younger and underwent CPR of any duration in the ICU. Patients were excluded from ICU-RESUS for any of the following reasons: out-of-hospital cardiac arrest associated with admission hospitalization; before arrest a limitation in aggressive support or goals of intensive care; or evidence of, or suspected brain dead. For this secondary analysis, we only included patients who attained return of circulation (ROC) by initiation of ECPR. Patients who were on ECMO at the start of resuscitation, who achieved a sustained return of spontaneous circulation (ROSC) for greater than 20 minutes before ECMO cannulation, or who had less than 6 minutes of CPR were excluded.

Outcomes

The primary outcome was survival with favorable neurologic outcome. Favorable neurologic outcome was defined as no more than moderate disability (≤ 3) or no increase from baseline Pediatric Cerebral Performance Category (PCPC) in those patients with a baseline PCPC of 4 or 5. Patients who died or survived without favorable neurologic outcome were grouped together for analysis.

Independent Variables

Standard Utstein definitions for demographic, pre-event, and event characteristics of patients were used. Pediatric Risk of Mortality (PRISM) was evaluated in a time window from 6 to 2 hours before the CPR event. If a patient was in the operating room 6 hours before the CPR event, only measurements obtained after the patient returned to the ICU were used to determine PRISM. Baseline PCPC and Functional Status Scale (FSS) were evaluated based on the patient's status before the illness leading to the current hospitalization. For patients born during the current hospitalization or who had been hospitalized longer than 90 days at the time of the arrest, baseline PCPC and FSS were assessed using the patient's status before the decompensation associated with the cardiac arrest. Hemodynamic waveforms and CPR quality metrics during the initial 10 minutes of resuscitation were quantified as previously reported (5). Average interval between epinephrine doses was calculated for patients with at least two doses of epinephrine. Average interval between doses was defined as (duration of CPR–time to first epinephrine dose)/(number of epinephrine doses−1).

Statistical Analysis

Data are presented as counts and percentages for categorical variables, and median and interquartile range (IQR) for continuous variables. The association between characteristics and survival was evaluated using Fisher exact, Wilcoxon rank-sum, or Kruskal-Wallis test. Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). There was no correction for multiple comparisons. All p values were based on a two-sided alternative hypothesis and were considered significant if less than 0.05.

RESULTS

A total of 200 patients who underwent ECPR were identified in the ICU-RESUS dataset. A final cohort of 97 patients with ECPR and invasive arterial waveform data were available for analysis (**Supplemental Fig. 1**, http://links.lww.com/PCC/C463). The cohort was predominantly surgical cardiac patients (62/97, 64%); 71 (73%) were younger than 1 year old and 82 (85%) had congenital heart disease. Median (IQR) pre-arrest PRISM score was 7.0 (3.0–13.0) and pre-arrest Vasoactive-Inotrope Score was 6.5 (2.5–11.7). **Table 1**; and **Supplemental Table 1** (http://links.lww.com/PCC/C463) shows demographic data of the overall group and comparisons of demographics between those patients with and without survival with favorable neurologic outcome.

Event characteristics associated with resuscitation are outlined in **Table 2**; and Supplemental Table 1 (http://links.lww.com/PCC/C463). Duration of CPR was shorter in patients who survived with favorable neurologic outcome compared with those without (36.5 min [21–52 min] vs. 47 min [34–61 min]; $p = 0.015$). Of the 30 patients with less than 30 minutes of CPR, 17 (57%) survived to discharge with favorable neurologic outcome. Of the 48 patients with 30–60 minutes of CPR, 20 (42%) survived to discharge with favorable neurologic outcome. In contrast, only three of 19 patients (16%) with greater than 60 minutes of CPR survived with favorable neurologic outcome. Overall, nonsurvival and

TABLE 1.
Demographics and Pre-Event Characteristics

Variable	Overall (n = 97)	Survival to Hospital Discharge With Favorable Neurologic Outcome: No (n = 57)	Yes (n = 40)
Demographics			
Age, n (%)			
< 1 mo	40 (41)	24 (42)	16 (40)
1 mo to < 1 yr	31 (32)	19 (33)	12 (30)
1 to < 12 yr	19 (20)	10 (18)	9 (22)
> 12 yr	7 (7)	4 (7)	3 (8)
Weight, median (IQR), kg	4.2 (3.1–9.2)	4.1 (3.0–7.3)	4.4 (3.4–11.4)
Male, n (%)	55 (57)	31 (54)	24 (60)
Race, n (%)			
White	48 (49)	23 (40)	25 (62)
Black or African American	26 (27)	18 (32)	8 (20)
Other	3 (3)	1 (2)	2 (5)
Unknown or not reported	20 (21)	15 (26)	5 (13)
Hispanic or Latino	12 (12)	7 (12)	5 (13)
Pre-event characteristics			
Illness category, n (%)			
Medical cardiac	28 (29)	18 (32)	10 (25)
Medical noncardiac	6 (6)	2 (3)	4 (10)
Surgical cardiac	62 (64)	36 (63)	26 (65)
Surgical noncardiac	1 (1)	1 (2)	0 (0)
Pediatric Risk of Mortality[a], median (IQR)	7.0 (3.0–13.0)	8.0 (3.0–13.0)	7.0 (3.0–12.5)
Vasoactive-Inotrope Score[b], median (IQR)	6.5 (2.5–11.7)	8.0 (3.0–17.0)	6.0 (0.5–9.5)
Baseline Pediatric Cerebral Performance Category score[c], n (%)			
1–Normal	69 (71)	37 (65)	32 (80)
2–Mild disability	22 (23)	15 (26)	7 (17)
3–Moderate disability	5 (5)	4 (7)	1 (3)
4–Severe disability	1 (1)	1 (2)	0 (0)
Baseline Functional Status Scale[c], median (IQR)	6.0 (6.0–7.0)	6.0 (6.0–8.0)	6.0 (6.0–6.0)

IQR = interquartile range.

[a]Pediatric Risk of Mortality was evaluated 2–6 hr before the event.

[b]Vasoactive-Inotrope Score was evaluated 2 hr before the event.

[c]Baseline Pediatric Cerebral Performance Category (PCPC) and Functional Status Scale represent subject status before the event leading to hospitalization.

Favorable neurologic outcome is defined as no more than moderate disability or no worsening from baseline PCPC.

survival with poor neurologic outcome, compared with survival with favorable neurologic outcome, was associated with higher peak arterial lactate level in the first 6 hours post-CPR (15.2 mmol/dL [11.3–19.1 mmol/dL] vs. 9.6 mmol/dL [6.1–16.0 mmol/dL], respectively; $p = 0.010$) and at 6–24 hours post-CPR (5.9 mmol/dL [2.7–14.0 mmol/dL] vs. 3.2 mmol/dL [2.2–5.4 mmol/dL], respectively; $p < 0.001$).

TABLE 2.
Event Characteristics

Variable	Overall ($n = 97$)	Survival to Hospital Discharge With Favorable Neurologic Outcome: No ($n = 57$)	Survival to Hospital Discharge With Favorable Neurologic Outcome: Yes ($n = 40$)	p
Duration of CPR (min), median (IQR)	43.0 (24.0–56.0)	47.0 (34.0–61.0)	36.5 (21.0–52.0)	0.015[c]
Duration of CPR (min), n (%)				0.066[b]
< 16	9 (9)	4 (7)	5 (13)	
16–30	21 (22)	9 (15)	12 (30)	
31–45	22 (23)	14 (25)	8 (20)	
46–60	26 (27)	14 (25)	12 (30)	
> 60	19 (19)	16 (28)	3 (7)	
CPR time[a], n (%)				0.059[b]
Weekday	54 (56)	31 (54)	23 (58)	
Weeknight	26 (27)	12 (21)	14 (35)	
Weekend	17 (17)	14 (25)	3 (7)	
First documented rhythm, n (%)				0.212[b]
Pulseless electrical activity/asystole	40 (41)	23 (41)	17 (43)	
Ventricular fibrillation/tachycardia	9 (9)	3 (5)	6 (14)	
Bradycardia with poor perfusion	48 (50)	31 (54)	17 (43)	
Pharmacologic interventions during event, n (%)				
Epinephrine	94 (97)	54 (95)	40 (100)	0.265[b]
Atropine	7 (7)	3 (5)	4 (10)	0.442[b]
Calcium	73 (75)	43 (75)	30 (75)	1.000[b]
Sodium bicarbonate	81 (84)	47 (83)	34 (85)	0.789[b]
Vasopressin	7 (7)	5 (9)	2 (5)	0.696[b]
Amiodarone	8 (8)	3 (5)	5 (13)	0.268[b]
Lidocaine	7 (7)	2 (4)	5 (13)	0.121[b]
Fluid bolus	41 (42)	28 (49)	13 (33)	0.144[b]
Highest arterial lactate (0–6 hr after), mmol/dL, median (IQR)	14.5 (8.6–18.0)	15.2 (11.3–19.1)	9.6 (6.1–16.0)	0.010[c]
Highest arterial lactate (6–24 hr after), mmol/dL, median (IQR)	4.3 (2.5–7.8)	5.9 (2.7–14.0)	3.2 (2.2–5.4)	< 0.0013
Vasoactive-Inotrope Score (6 hr after), median (IQR)	4.0 (0.0–7.5)	4.0 (0.0–7.5)	5.0 (2.0–8.0)	0.224[c]
Vasoactive-Inotrope Score (24 hr after), median (IQR)	5.0 (0.0–8.0)	5.0 (0.0–8.0)	5.3 (2.5–8.3)	0.301[c]

CPR = cardiopulmonary resuscitation, IQR = interquartile range.

[a]Weekday is between 7 AM and 11 PM Monday–Friday; weeknight is after 11 PM Monday–Thursday; Weekend is from 11 PM on Friday to 7 AM on the following Monday.

[b]Fisher exact test.

[c]Wilcoxon rank-sum test.

Favorable neurologic outcome is defined as no more than moderate disability or no worsening from baseline Pediatric Cerebral Performance Category.

We failed to identify a difference in median diastolic or systolic blood pressure, target diastolic or systolic blood pressure, average chest compression fraction (CCF) greater than or equal to 0.9, or chest compression rate in patients with and without survival with favorable neurologic outcome (**Table 3**). The $ETco_2$ was available for analysis in 35 patients and the median (IQR) of the "average" level during CPR was 18 mm Hg (11–23 mm Hg). An average $ETco_2$ less than 10 mm Hg was present in four of 17 patients who survived with favorable neurologic outcome; furthermore, the maximum $ETco_2$ was less than 10 mm Hg in the initial 10 minutes of resuscitation for two of 17 patients. We also failed to detect a difference in the hemodynamic and $ETco_2$ findings between patients with or without survival with favorable neurologic outcome among the 15 patients who had hemodynamic data available for minutes 11–20 of CPR (**Supplemental Table 2**, http://links.lww.com/PCC/C463).

We did not identify a difference in outcomes from ECPR when comparing illness category (**Table 4**). Cardiac surgery accounted for 62 of 97 patients (64%) and additional variables related to this patient population are summarized in **Table 5**. Among surgical cardiac patients, we failed to find an association with survival with favorable neurologic outcome and the presence of an open sternum (10/26 vs. 10/36; p = 0.42), whether the sternum was opened during resuscitation (9/26 vs. 12/36; p = 1), time to sternal opening, or type of surgical procedure.

DISCUSSION

In this secondary analysis of the multicenter data ICU-RESUS trial data from 2016 to 2021, we have examined how hemodynamics and quality of resuscitation may be associated with ECPR survival. First, overall, we failed to demonstrate an association between hemodynamics in the first 10 minutes of resuscitation and survival with favorable neurologic outcome. Second, in the subgroup of 17 patients with ROC due to ECPR, four (95% CI of 4/17 is 7–50%) with mean $ETco_2$ less than 10 mm Hg during the first 10 minutes of CPR survived to hospital discharge with favorable neurologic outcome. Importantly, we included patients who underwent ECPR cannulation for patients in whom conventional CPR failed to achieve sustained ROSC (for > 20 min) consistent with the Maastricht definition for ECPR (7).

WHAT THIS STUDY MEANS

1) Survival with favorable neurologic outcome occurred in 41% of ECPR patients with high-quality CPR in the initial 10 minutes of resuscitation.
2) Candidates for ECPR with end-tidal Co_2 less than 10 mm Hg may survive with favorable neurologic outcome.
3) We did not demonstrate an association between the hemodynamics achieved by high-quality CPR and survival to hospital discharge with favorable neurologic outcome.

These data highlight that the initial 10 minutes of CPR for these ECPR patients in the 18 ICU-RESUS centers was high quality with 75% of patients attaining diastolic blood pressures greater than or equal to 25 mm Hg for patients younger than 1 year old or greater than or equal to 30 mm Hg for patients 1 year old or older, which is a threshold identified in the 2013–2016 PICqCPR study as being associated with both survival to hospital discharge and survival to discharge with favorable neurologic outcome (5). The diastolic blood pressures attained, and the percent of patients meeting this threshold was higher in this ICU-RESUS study when compared with the cardiac ECPR patients in the PICqCPR study (4). Additionally, the average CCF and rate met the 2020 CPR quality metric guidelines of greater than 90% and 100–120 compressions per minute, which, in retrospect, demonstrates that the 2016–2021 ICU-RESUS study findings were ahead of its time in achieving a very high quality of resuscitation (8). Such overall high quality of CPR performance may have masked our ability to detect an association with better outcomes in this patient population. For some patients, however, underlying disease processes may have contributed to poor outcomes independent of hemodynamics attained during CPR. A 2017–2019 review of the Extracorporeal Life Support Organization Registry identified obesity associated with greater odds of inhospital mortality and respiratory disease as associated with greater odds of severe neurologic injury in patients without congenital cardiac disease, factors that were not examined in this study (9).

TABLE 3.
Event Hemodynamics and Ventilation

Variable	Overall	Survival to Hospital Discharge With Favorable Neurologic Outcome		*p*
		No	Yes	
Hemodynamics over minutes 0–10				
Total, *n*	97	57	40	
Average diastolic blood pressure (mm Hg) , median (IQR)	34 (25–43)	33 (25–43)	34 (25–44)	0.974[c]
Adequate average diastolic pressure[a], *n*/*n* (%)	73/97 (75)	44/57 (77)	29/40 (73)	0.638[d]
Average systolic blood pressure (mm Hg), median (IQR)	64 (54–82)	63 (54–81)	67 (54–83)	0.772[c]
Adequate average systolic pressure[b], *n*/*n* (%)	48/97 (50)	29/57 (51)	19/40 (48)	0.837[d]
Average chest compression rate (/min), median (IQR)	119 (111–126)	120 (110–126)	119 (111–124)	0.722[c]
Average chest compression rate between 100 and 120 per min, *n*/*n* (%)	42/97 (43)	21/57 (37)	21/40 (53)	0.148[d]
Average chest compression fraction, median (IQR)	0.94 (0.90–0.98)	0.96 (0.90–0.99)	0.92 (0.89–0.96)	0.046[c]
Average chest compression fraction ≥ 0.9, *n*/*n* (%)	70/97 (72)	42/57 (74)	28/40 (70)	0.818[d]
Ventilation over minutes 0–10				
Total, *n*	35	18	17	
Average end-tidal CO_2 (mm Hg) during compressions, median (IQR)	18 (11–23)	17 (11–23)	18 (13–22)	0.882[c]
Average end-tidal CO_2 ≥ 10 mm Hg during compressions, *n*/*n* (%)	28/35 (80)	15/18 (83)	13/17 (77)	0.691[d]
Average end-tidal CO_2 (mm Hg) during compressions, *n*/*n* (%)				0.744[d]
< 10	7/35 (20)	3/18 (17)	4/17 (24)	
10–20	15/35 (43)	9/18 (50)	6/17 (35)	
20+	13/35 (37)	6/18 (33)	7/17 (41)	
Maximum end-tidal CO_2 (mm Hg), median (IQR)	24 (17–35)	25 (17–36)	24 (18–32)	1.000[d]
Maximum end-tidal CO_2 ≥ 10 mm Hg, *n*/*n* (%)	32/35 (91)	17/18 (94)	15/17 (88)	0.603[d]
Maximum end-tidal CO_2 (mm Hg), *n*/*n* (%)				1.000[d]
< 10	3/35 (8)	1/18 (5)	2/17 (11)	
10–20	9/35 (26)	5/18 (28)	4/17 (24)	
> 20	23/35 (66)	12/18 (67)	11/17 (65)	
Average ventilation rate (breaths/min) during compressions, median (IQR)	26 (20–34)	23 (20–30)	29 (21–34)	0.314[c]

IQR = interquartile range.
[a]Average diastolic pressure was considered adequate if ≥ 25 mm Hg for subjects < 1 yr old or ≥ 30 mm Hg for subjects ≥ 1 yr.
[b]Average systolic pressure was considered adequate if ≥ 60 mm Hg for subjects < 1 yr old or ≥ 80 mm Hg for subjects ≥ 1 yr.
[c]Wilcoxon rank-sum test.
[d]Fisher exact test.
Favorable neurologic outcome is defined as no more than moderate disability or no worsening from baseline Pediatric Cerebral Performance Category.

TABLE 4.
Summary of Outcomes

Outcome	Overall (*n* = 97)	Illness Category: Medical Cardiac (*n* = 28)	Medical Noncardiac (*n* = 6)	Surgical Cardiac (*n* = 62)	*p*
Survival to hospital discharge, *n* (%)	41 (42)	10 (36)	4 (67)	27 (44)	0.412[c]
Survival to hospital discharge with favorable neurologic outcome[a], *n* (%)	40 (41)	10 (36)	4 (67)	26 (42)	0.359[c]
Survival to hospital discharge with PCPC of 1, 2, or no worse than baseline, *n* (%)	31 (32)	8 (29)	3 (50)	20 (32)	0.550[c]
Total FSS at hospital discharge, median (IQR)	8 (8–10)	8 (8–8)	8 (7–12)	9 (7–10)	0.786[d]
PCPC at hospital discharge, *n* (%)					0.308[d]
1—Normal	18 (19)	6 (21)	3 (50)	9 (15)	
2—Mild disability	12 (12)	2 (7)	0 (0)	10 (16)	
3—Moderate disability	10 (10)	2 (7)	1 (17)	7 (11)	
4—Severe disability	1 (1)	0 (0)	0 (0)	1 (2)	
5—Coma/vegetative state	0 (0)	0 (0)	0 (0)	0 (0)	
6—Death	56 (58)	18 (65)	2 (33)	35 (56)	
Change from baseline to hospital discharge in FSS of survivors, median (IQR)	2 (1–4)	2 (2–2)	2 (1–6)	2 (1–4)	0.909[d]
New morbidity[b] (survivors only), *n* (%)	15 (37)	2 (20)	1 (25)	12 (44)	0.418[c]

FSS = Functional Status Scale, IQR = interquartile range, PCPC = Pediatric Cerebral Performance Category.
[a]Favorable neurologic outcome is defined as no more than moderate disability or no worsening from baseline PCPC.
[b]New morbidity among survivors is defined as a worsening from baseline FSS by three points or more.
[c]Fisher exact test.
[d]Kruskal-Wallis test.
Trauma subjects (*n* = 0) and surgical noncardiac subjects (*n* = 1) are included only in the overall column and are excluded from analyses in this table.

It is worth noting that four patients that survived with favorable neurologic outcome had an average $ETco_2$ less than 10 mm Hg, a target previously associated with high mortality. Additionally, two of those survivors never achieved an $ETco_2$ over 10 mm Hg at any point in the initial 10 minutes of resuscitation, suggesting that good outcome is still possible in ECPR patients despite low $ETco_2$ measurements during the first 10 minutes of CPR. Our patients were ventilated with a median (IQR) of 26 breaths per minute (20–34 breaths/min), which may have been responsible for lowering the $ETco_2$ below 10 mm Hg. Of note, it may be that this accepted threshold of futility—10 mm Hg—needs rethinking and reevaluating. After all, the origin of this threshold is from a 1991 to 1995 adult (> 18 yr old) cohort of cardiac arrest patients with pulseless electrical activity (9).

Previous cohorts from 2009 to 2015 (10) and 2005–2016 (11) show an association with elevated lactate and outcomes in ECPR patients, likely from poor quality resuscitation resulting in ischemic insult to organ systems. We similarly found that elevated lactate post-arrest was associated with poor outcomes in the ICU-RESUS ECPR population. We have also shown

TABLE 5.
Characteristics of Cardiac Subjects

Variable	Overall	Survival to Hospital Discharge With Favorable Neurologic Outcome		*p*
		No	Yes	
Surgical cardiac	(*n* = 62)	(*n* = 36)	(*n* = 26)	
Surgical palliation				0.756[a]
Preoperative	5	2	3	
Norwood with Sano modification	6	3	3	
Norwood with modified Blalock-Taussig shunt	4	1	3	
Hybrid procedure	2	1	1	
Bidirectional Glenn	4	3	1	
Fontan	0	0	0	
Systemic to pulmonary shunt	9	6	3	
Main pulmonary artery band	2	2	0	
Other	22	13	9	
Unknown	8	5	3	
Days since last cardiac surgery, median (IQR)	1.0 (0.0–3.0)	2.0 (0.0–8.0)	1.0 (0.5–1.0)	0.094[b]
Sternum open at start of CPR event	20	10	10	0.419[a]
Sternum opened during CPR event	21	12	9	1.000[a]
Minutes to sternum opening, median (IQR)	31.0 (16.5–42.5)	35.5 (25.0–54.5)	21.0 (14.5–38.0)	0.203[b]
Medical cardiac	(*n* = 28)	(*n* = 18)	(*n* = 10)	
Congenital heart disease	21	14	7	0.674[a]

CPR = cardiopulmonary resuscitation, IQR = interquartile range.
[a]Fisher exact test.
[b]Wilcoxon rank-sum test.
Favorable neurologic outcome is defined as no more than moderate disability or no worsening from baseline Pediatric Cerebral Performance Category.
In ICU-RESUScitation Project, surgical palliation was not collected during the first 8 mo of enrollment.

worse outcomes are associated with longer arrest times, which is similar to findings in other cardiac arrest studies (10–12). Smaller single center studies, have demonstrated that biochemical profiles (i.e., arterial pH, lactate, etc.) around the time of cannulation are associated with outcomes, supporting the notion that maintenance of high-quality resuscitation that provides adequate oxygenation, ventilation, and perfusion before cannulation may also be important to obtain optimal outcomes for ECPR (13–15). Thus, we postulate that integrating high-quality CPR simulation training to prevent degradation of resuscitation performance over time could further improve outcomes beyond those seen at centers already using simulation to promote rapid cannulation (16). Our data supports the idea that rapid cannulation and high-quality CPR together provide the best opportunities for minimized organ ischemia and lactic acidosis and optimized patient outcomes.

Our study has several important limitations. We were limited by the hemodynamic data available in the original ICU-RESUS study, which focused on the first 10 minutes of CPR. A small number of patients had 20 minutes of hemodynamic data collection, which was still less than half the median arrest duration of 43 minutes. Thus, we did not have hemodynamics during ECPR cannulation for the majority of patients, and so we could not analyze the CCF at the time of cannulation and duration/frequency of pauses in resuscitation for cannulation, which has been associated with worse outcomes (11, 17). Additionally, technical details of cannulation (i.e., cannulation site, cannula sizes, and configuration) and surgeon skill were an unmeasured, but potentially important, factor for the outcomes of interest (7). There was a large population of cardiac patients, and there was limited data available on the cardiac defect and surgical repair, and no data available for cardiopulmonary bypass times or The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery category. Despite this limitation, we did use the PRISM score, which has been shown to also reflect the severity of illness in this patient population (18). We did not have information about ECMO support and management, which may have impacted post-arrest organ perfusion and recovery. Finally, we had a small sample size and did not adjust for multiple comparisons.

CONCLUSIONS

In standard CPR, attaining diastolic blood pressure above a target threshold is associated with better cardiac arrest outcomes. However, in the ICU-RESUS 2016–2021 cohort of patients undergoing ECPR we failed to identify such an association when examining physiologic data from the first 10 minutes of CPR. Furthermore, we also found that there is uncertainty in the meaning that should be ascribed to achieving only an average $ETco_2$ less than 10 mm Hg during CPR: anywhere between 7% and 50% may survive with favorable neurologic outcome. In other words, during CPR low $ETco_2$ levels should not preclude cannulation for ECMO in patients deemed candidates by the medical team. That said, maintenance of high-quality CPR coupled with rapid cannulation may optimize survival with favorable neurologic outcomes in pediatric ECPR patients.

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