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Early Cardiac Arrest Hemodynamics, End-Tidal Carbon Dioxide and Outcome in Pediatric Extracorporeal Cardiopulmonary Resuscitation: secondary analysis of the ICU-RESUScitation project dataset (2016–2021)

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Abstract

Objective: Cannulation for extracorporeal membrane oxygenation during active cardiopulmonary resuscitation (ECPR) is a method to rescue patients refractory to standard resuscitation. We hypothesized that early arrest hemodynamics and end-tidal CO2 ($ETCO_2$) 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: 18 ICUs participated in ICU-RESUS

Patients: There were 97 ECPR patients with hemodynamic waveforms during CPR.

Interventions: none

Measurements and Main Results: Overall, 71/97 (73%) patients were <1-year-old, 82/97 (85%) had congenital heart disease, and 62/97 (64%) were postoperative cardiac surgical patients. Forty of 97 (41%) patients 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, 4/17 (24%) had an average $ETCO_2$ <10 mmHg and two (12%) had a maximum $ETCO_2$ <10 mmHg 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 $ETCO_2$ <10 mmHg may survive with favorable neurologic outcome.

Keywords

Cardiopulmonary Resuscitation; ECMO; ECPR; Hemodynamics

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 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 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 carbon dioxide ($ETCO_2$) 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 prior to cannulation have not been previously reported. These factors may contribute to the discrepancy in the literature related to survival and duration of CPR prior to 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) PICqCPR (Pediatric Intensive Care Quality of CPR) study, which showed that systolic blood pressure ≥ 60 mmHg for infants and ≥ 80 mmHg for children ≥ 1 year of age 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 ≥ 25 mmHg for patients < 1 year of age or ≥ 30 mmHg for patients ≥ 1 year 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 pre-planned 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 pediatric ICUs from 10 clinical sites in the US 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 approved the study entitled, "CPCCRN068: Improving outcomes from Pediatric Cardiac Arrest (ICU-RESUS)" with waiver of consent (IRB_00093320) on 7/18/2016. This study is a secondary analysis of the ICU-RESUS dataset which was planned between March and April of 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 post-conceptual age and ≤ 18 years of age 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; prior to 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 sustained return of spontaneous circulation (ROSC) for > 20 minutes prior to ECMO cannulation, or had <6 minutes of CPR were excluded.

Outcomes

The primary outcome was survival with favorable neurological outcome. Favorable neurological 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 neurological outcome were grouped together for analysis.

Independent variables

Standard Utstein definitions for demographic, pre-event, and event characteristics of patients were utilized. 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 prior to 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 prior to 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 prior to 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 2 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 is 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's exact test, 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. The cohort was predominantly surgical cardiac patients (62/97, 64%); 71 (73%) were < 1 year of age 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 SDC Table S1 shows demographic data of the overall group and comparisons of demographics between those patients with and without survival with favorable neurological outcome.

Event characteristics associated with resuscitation are outlined in Table 2 and SDC Table S1. Duration of CPR was shorter in patients who survived with favorable neurological outcome compared to those without (36.5 [21, 52] vs. 47 [34, 61] minutes, p=0.015). Out of the 30 patients with less than 30 minutes of CPR, 17 (57%) survived to discharge with favorable neurologic outcome. Out of the 48 patients with 30–60 minutes of CPR, 20 (42%) survived to discharge with favorable neurologic outcome. In contrast, only 3/19 (16%) patients with >60 minutes of CPR survived with favorable neurologic outcome. Overall, non-survival and survival with poor neurological outcome, compared to survival with favorable neurological outcome, was associated with higher peak arterial lactate level in the first 6 hours post-CPR (15.2 [11.3, 19.1] vs. 9.6 [6.1, 16.0] mmol/dL, respectively, p=0.010) and at 6–24 hours post-CPR (5.9 [2.7, 14.0] vs 3.2 [2.2, 5.4] mmol/dL, respectively, p<0.001).

We failed to identify a difference in median diastolic or systolic blood pressure, target diastolic or systolic blood pressure, average chest compression fraction (CCF) ≥ 0.9, or chest compression rate in patients with and without survival with favorable neurological 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 [11, 23] mmHg. An average $ETCO_2$ < 10 mmHg was present in 4/17 patients who survived with favorable neurologic outcome; furthermore, the maximum $ETCO_2$ was < 10 mmHg in the initial 10 minutes of resuscitation for 2/17 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 (SDC Table S2).

We did not identify a difference in outcomes from ECPR when comparing illness category (Table 4). Cardiac surgery accounted for 62/97 (64%) patients 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 2016–2021, 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, 4 (95% confidence interval of 4/17 is 7–50%) with mean $ETCO_2$ <10 mmHg 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 return of spontaneous circulation (for >20 minutes) consistent with the Maastricht definition for ECPR [7].

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 ≥ 25 mmHg for patients < 1 year of age or ≥ 30 mmHg for patients ≥ 1 year, 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 neurological outcome [5]. The diastolic blood pressures attained, and the percent of patients meeting this threshold was higher in this ICU-RESUS study when compared to the cardiac ECPR patients in the PICqCPR study [4]. Additionally, the average CCF and rate met the 2020 CPR quality metric guidelines of >90% and 100–120 compressions per minute which, in retrospect, demonstrates that 2016–2021 ICU-RESUS study findings was 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 in-hospital mortality and respiratory disease as associated with greater odds of severe neurological injury in patients without congenital cardiac disease, factors which were not examined in this study.[9]

It is worth noting that four patients that survived with favorable neurological outcome had an average $ETCO_2$ less than 10 mmHg, a target previously associated with high mortality. Additionally, 2 of those survivors never achieved an $ETCO_2$ over 10 mmHg 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 [20, 34] breaths per minute, which may have been responsible for lowering the $ETCO_2$ below 10 mmHg. Of note, it may be that this accepted threshold of futility – 10 mmHg – needs rethinking and re-evaluating. After all, the origin of this threshold is from a 1991 to 1995 adult (aged >18 years) cohort of cardiac arrest patients with pulseless electrical activity [9].

Previous cohorts from 2009–2015 [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 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 prior to 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 was 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 (STAT) 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.

CONCLUSION

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 ETCO2 <10 mmHg during CPR: anywhere between 7% and 50% may survive with favorable neurologic outcome. In other words, during CPR low ETCO2 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Copyright Form Disclosure:

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Research in Context:

1. It is not known what CPR quality indicators and hemodynamics impact ECPR outcomes.
2. Achieving diastolic blood pressures ≥ 25 mmHg for patients < 1 year of age or ≥ 30 mmHg for patients ≥ 1 year is associated with survival to hospital discharge in other populations.

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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 $ETCO_2$ <10 mmHg 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.

Tweet:

In ECPR with $ETCO_2$ <10 mmHg, we failed to show an association between early CPR hemodynamics and survival to hospital discharge with favorable neurologic outcome

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			
<1 month	40 (41%)	24 (42%)	16 (40%)
1 month-<1 year	31 (32%)	19 (33%)	12 (30%)
1 year-<12 years	19 (20%)	10 (18%)	9 (22%)
>12 years	7 (7%)	4 (7%)	3 (8%)
Weight, median [IQR] in kg	4.2 [3.1,9.2]	4.1 [3.0,7.3]	4.4 [3.4,11.4]
Male	55 (57%)	31 (54%)	24 (60%)
Race			
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			
Medical cardiac	28 (29%)	18 (32%)	10 (25%)
Medical non-cardiac	6 (6%)	2 (3%)	4 (10%)
Surgical cardiac	62 (64%)	36 (63%)	26 (65%)
Surgical non-cardiac	1 (1%)	1 (2%)	0 (0%)
PRISM[1] median [IQR]	7.0 [3.0,13.0]	8.0 [3.0,13.0]	7.0 [3.0,12.5]
Vasoactive inotropic score[2] median [IQR]	6.5 [2.5,11.7]	8.0 [3.0,17.0]	6.0 [0.5,9.5]
Baseline PCPC score[3]			
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 FSS[3] median [IQR]	6.0 [6.0,7.0]	6.0 [6.0,8.0]	6.0 [6.0,6.0]

PRISM = Pediatric RISk of Mortality; PCPC = Pediatric Cerebral Performance Category; FSS = Functional Status Scale.

[1] PRISM was evaluated 2 – 6 hours prior to the event.

[2] Vasoactive Inotropic Score (VIS) was evaluated 2 hours prior to the event.

[3] Baseline PCPC and FSS represent subject status prior to the event leading to hospitalization.

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

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-value
Duration of CPR (min)	43.0 [24.0,56.0]	47.0 [34.0,61.0]	36.5 [21.0,52.0]	0.015[3]
Duration of CPR (min)				0.066[2]
<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[1]				0.059[2]
Weekday	54 (56%)	31 (54%)	23 (58%)	
Weeknight	26 (27%)	12 (21%)	14 (35%)	
Weekend	17 (17%)	14 (25%)	3 (7%)	
First documented rhythm				0.212[2]
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				
Epinephrine	94 (97%)	54 (95%)	40 (100%)	0.265[2]
Atropine	7 (7%)	3 (5%)	4 (10%)	0.442[2]
Calcium	73 (75%)	43 (75%)	30 (75%)	1.000[2]
Sodium bicarbonate	81 (84%)	47 (83%)	34 (85%)	0.789[2]
Vasopressin	7 (7%)	5 (9%)	2 (5%)	0.696[2]
Amiodarone	8 (8%)	3 (5%)	5 (13%)	0.268[2]
Lidocaine	7 (7%)	2 (4%)	5 (13%)	0.121[2]
Fluid bolus	41 (42%)	28 (49%)	13 (33%)	0.144[2]
Highest arterial lactate (0 – 6 hours 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[3]
Highest arterial lactate (6 – 24 hours after), mmol/dL median [IQR]	4.3 [2.5,7.8]	5.9 [2.7,14.0]	3.2 [2.2,5.4]	<.001[3]
Vasoactive inotropic score (6 hours after) median [IQR]	4.0 [0.0,7.5]	4.0 [0.0,7.5]	5.0 [2.0,8.0]	0.224[3]
Vasoactive inotropic score (24 hours after) median [IQR]	5.0 [0.0,8.0]	5.0 [0.0,8.0]	5.3 [2.5,8.3]	0.301[3]

CPR = cardiopulmonary resuscitation.

Favorable neurologic outcome is defined as no more than moderate disability <u>or</u> no worsening from baseline Pediatric Cerebral Performance Category

[1] Weekday is between 7 AM and 11 PM Monday - Friday; weeknight is after 11 PM Monday - Thursday; Weekend is from 11 PM on Friday through 7 AM on the following Monday.

[2] Fisher's exact test.

[3] Wilcoxon rank-sum test.

Table 3.

Event hemodynamics and ventilation

Variable	Overall	Survival to hospital discharge with favorable neurologic outcome: No	Yes	P-value
Hemodynamics over minutes 0–10				
Total	97	57	40	
Average diastolic blood pressure (mmHg)	34 [25,43]	33 [25,43]	34 [25,44]	0.974[3]
Adequate average diastolic pressure[1]	73/97 (75%)	44/57 (77%)	29/40 (73%)	0.638[4]
Average systolic blood pressure (mmHg)	64 [54,82]	63 [54,81]	67 [54,83]	0.772[3]
Adequate average systolic pressure[2]	48/97 (50%)	29/57 (51%)	19/40 (48%)	0.837[4]
Average chest compression rate (per minute) median [IQR]	119 [111,126]	120 [110,126]	119 [111,124]	0.722[3]
Average chest compression rate between 100 and 120 per minute	42/97 (43%)	21/57 (37%)	21/40 (53%)	0.148[4]
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[3]
Average chest compression fraction ≥ 0.9	70/97 (72%)	42/57 (74%)	28/40 (70%)	0.818[4]
Ventilation over minutes 0–10				
Total	35	18	17	
Average end-tidal CO_2 (mmHg) during compressions	18 [11,23]	17 [11,23]	18 [13,22]	0.882[3]
Average end-tidal CO_2 ≥ 10 mmHg during compressions	28/35 (80%)	15/18 (83%)	13/17 (77%)	0.691[4]
Average end-tidal CO_2 (mmHg) during compressions				0.744[4]
<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 (mmHg) median [IQR]	24 [17,35]	25 [17,36]	24 [18,32]	1.000[4]
Maximum end-tidal CO_2 ≥ 10 mmHg	32/35 (91%)	17/18 (94%)	15/17 (88%)	0.603[4]
Maximum end-tidal CO_2 (mmHg)				1.000[4]
<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[3]

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

[1] Average diastolic pressure was considered adequate if ≥ 25 mmHg for subjects < 1 year old or ≥ 30 mmHg for subjects ≥ 1 year.

[2] Average systolic pressure was considered adequate if ≥ 60 mmHg for subjects < 1 year old or ≥ 80 mmHg for subjects ≥ 1 year.

[3] Wilcoxon rank-sum test.

[4] Fisher's exact test.

Table 4.

Summary of outcomes

Outcome	Overall (N = 97)	Illness category: Medical cardiac (N = 28)	Medical non-cardiac (N = 6)	Surgical cardiac (N = 62)	P-value
Survival to hospital discharge	41 (42%)	10 (36%)	4 (67%)	27 (44%)	0.412[3]
Survival to hospital discharge with favorable neurologic outcome[1]	40 (41%)	10 (36%)	4 (67%)	26 (42%)	0.359[3]
Survival to hospital discharge with PCPC of 1, 2, or no worse than baseline	31 (32%)	8 (29%)	3 (50%)	20 (32%)	0.550[3]
Total FSS at hospital discharge	8 [8, 10]	8 [8, 8]	8 [7, 12]	9 [7, 10]	0.786[4]
PCPC at hospital discharge					0.308[4]
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 functional status (FSS) of survivors median [IQR]	2 [1, 4]	2 [2, 2]	2 [1, 6]	2 [1, 4]	0.909[4]
New morbidity[2] (survivors only)	15 (37%)	2 (20%)	1 (25%)	12 (44%)	0.418[3]

FSS = Functional Status Scale; PCPC = Pediatric Cerebral Performance Category.

Trauma subjects (N = 0) and surgical non-cardiac subjects (N = 1) are included only in the overall column and are excluded from analyses in this table.

[1] Favorable neurologic outcome is defined as no more than moderate disability or no worsening from baseline Pediatric Cerebral Performance Category (PCPC).

[2] New morbidity among survivors is defined as a worsening from baseline FSS by 3 points or more.

[3] Fisher's exact test.

[4] Kruskal-Wallis test.

Table 5.

Characteristics of cardiac subjects

		Survival to hospital discharge with favorable neurologic outcome		
Variable	**Overall**	**No**	**Yes**	**P-value**
Surgical cardiac	**(N = 62)**	**(N = 36)**	**(N = 26)**	
Surgical palliation				0.756[1]
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	
Bi-directional 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[2]
Sternum open at start of CPR event	20	10	10	0.419[1]
Sternum opened during CPR event	21	12	9	1.000[1]
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[2]
Medical cardiac	**(N = 28)**	**(N = 18)**	**(N = 10)**	
Congenital heart disease	21	14	7	0.674[1]

CPR = cardiopulmonary resuscitation.

[1]Fisher's exact test.

[2]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-RESUS, surgical palliation was not collected during the first eight months of enrollment.