Association of blood pressure with neurologic outcome at hospital discharge after pediatric cardiac arrest resuscitation

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Abstract

Background: Poor outcomes are associated with post cardiac arrest blood pressures <5th percentile for age. We aimed to study the relationship of mean arterial pressure (MAP) with favorable neurologic outcome following cardiac arrest and return of spontaneous circulation (ROSC).

Methods: This retrospective, multi-center, observational study analyzed data from the Pediatric Resuscitation Quality Collaborative (pediRES-Q). Children (<18 years) who achieved ROSC following index in-hospital or out-of-hospital cardiac arrest and survived 6 hours were included. Lowest documented MAP within the first   6 hours of ROSC was percentile adjusted for age and categorized into six groups – Group I: <5th, II: 5–24th, III: 25–49th, IV: 50–74th, V: 75–94th; and VI: 95–100th percentile. Primary outcome was favorable neurologic status at hospital discharge, defined as PCPC score 1, 2, or no change from pre-arrest baseline. Multivariable logistic regression was performed to analyze the association of MAP group with favorable outcome, controlling for illness category (surgical-cardiac), initial rhythm (shockable), arrest time (weekend or overnight), age, CPR duration, and clustering by site.

Results: 787 patients were included: median [Q1,Q3] age 17.9 [4.8,90.6] months; male 58%; OHCA 21%; shockable rhythm 13%; CPR duration 7 [3,16] min; favorable neurologic outcome 54%. Median lowest documented MAP percentile for the favorable outcome group was 13 [3,43] versus 8 [1,37] for the unfavorable group. The distribution of blood pressures by MAP group was I: 37%, II: 28%, III: 13%, IV: 11%, V: 7%, and VI: 4%. Compared with patients in Group I (<5%ile), Groups II, III, and IV had higher odds of favorable outcome (aOR, 1.84 [95% CI, 1.24, 2.73]; 2.20 [95% CI, 1.32, 3.68]; 1.90 [95% CI, 1.12, 3.25]). There was no association between Groups V or VI and favorable outcome (aOR, 1.44 [95% CI, 0.75, 2.80]; 1.11 [95% CI, 0.47, 2.59]).

Conclusion: In the first 6-hours post-ROSC, a lowest documented MAP between the 5th74th percentile for age was associated with favorable neurologic outcome compared to MAP <5th percentile for age.

Introduction

In the United States, approximately 20,000 children suffer cardiac arrest (CA) each year. Among these, less than 50% survive to hospital discharge, with many survivors sustaining short- and long-term disability. This is primarily due to the sequelae of CA-induced brain injury, characterized by ischemia, cytotoxic cerebral edema, and the resulting dysfunctional cerebral autoregulation.[1–6] The central focus of post-cardiac arrest (CA) care in the pediatric intensive care unit is to reduce secondary brain injury, a significant driver of death and long-term disability among survivors.[3–5]

Following cardiac arrest, hypotension in children, defined as a systolic blood pressure (SBP) <5th percentile for age, is associated with unfavorable outcomes.[7–9] The American Heart Association's (AHA) Pediatric Advanced Life Support guidelines recommend hemodynamic optimization after return of spontaneous circulation (ROSC), using intravenous fluids, inotropes, and/or vasopressors to achieve a minimum BP greater than the 5th percentile for age.[10] The literature that supports this recommendation almost exclusively uses SBP data and classifies patients as hypotensive or non-hypotensive, then compares outcomes.[8,9,11,12]

It might be more physiologically appropriate to use mean arterial pressure (MAP), rather than SBP, considering MAP's critical importance in maintaining cerebral blood flow. While the adverse impact of even a single hypotensive episode is clear, our understanding of the influence of BP on outcomes is limited. The optimal BP range post-CA is unclear, particularly due to the complicating factor of disrupted cerebral autoregulation, which may make the brain more vulnerable to hypoperfusion even at higher blood pressures, since after cardiac arrest, the cerebral autoregulatory range is narrowed and right-shifted.[13] Maintaining a higher MAP than guideline-recommended targets may be necessary to ensure sufficient cerebral perfusion and improve neurologic outcomes.[14] A large study population is needed to analyze blood pressure in a more nuanced manner, rather than simply using binary classifications (i.e. <5th percentile vs. 5th percentile).

Using the pediRES-Q quality improvement database we aimed to describe the association between MAP, during the first 6 hours after ROSC, and neurologic outcome at hospital discharge after pediatric cardiac arrest in a large pediatric cohort.

Methods

Design and setting

This is an observational cohort study leveraging data collected between July 2015 and June 2022 by the pediRES-Q collaborative, a global, multi-site resuscitation quality improvement network. The network consists of 60 participating sites in 17 countries across five continents (Asia, Australia, Europe, North and South America) (ClinicalTrials.gov:NCT02708134).[15]

Approval for the study was obtained by a central IRB and local institutional review boards (United States) and research ethics boards (Europe and Canada). The study satisfied the requirements for waiver of consent.

Population

This study included children <18 years who achieved ROSC (without ECMO) following index in-hospital (IHCA) or out-of-hospital (OHCA) CA and survived 6 hours.

Data collection

Variables in the pediRES-Q database included: patient characteristics, such as age, sex, race, pre-existing conditions, and illness category (medical-cardiac, medical-noncardiac, surgical-cardiac, surgical-noncardiac, trauma); pre-event characteristics, such as the presence of vascular access, endotracheal intubation, and monitoring devices; event characteristics, such as the location and timing of CA, first monitored cardiac rhythm, duration of cardiopulmonary resuscitation (CPR), defibrillation, and medications and non-drug interventions administered during CPR; and outcome data, such as Pediatric Cerebral Performance Category (PCPC) scores at hospital discharge and survival.

In the pediRES-Q database, post-ROSC hemodynamic data, ascertained either via arterial line or blood pressure cuff, was reported as minimum and maximum values for the 0–6 hour interval following ROSC. Instances where no data were documented was regarded as missing and excluded from analysis.

Exposures and outcomes

The primary exposure was the lowest documented MAP during the 0–6 hour interval post-ROSC. MAP was percentile adjusted for age based on normative data and categorized into six groups – Group I: <5th percentile, II: 5th–24th percentile, III: 25th–49th percentile, IV: 50th–74th percentile, V: 75th–94th percentile, and VI: 95–100th percentile.[16]

The primary outcome was survival with favorable neurologic outcome. Neurologic outcome was evaluated via the PCPC score. The PCPC is a six-point scale to characterize neurologic function: 1 = normal; 2 = mild disability; 3 = moderate disability; 4 = severe disability; 5 = coma or vegetative state; and 6 = death. Favorable outcome was defined as a PCPC of 1 or 2 at hospital discharge, or no change in PCPC score from pre-arrest baseline.[8] Unfavorable outcome was defined as a discharge PCPC score of 3, 4, 5, or 6 associated with an increase in PCPC 1 from pre-arrest baseline.

Patients who lacked pre-arrest PCPC scores but had a PCPC score of 1 or 2 at discharge were considered to have favorable neurologic outcome. Those who were missing pre-arrest PCPC scores but died were classified as having unfavorable neurologic outcome. Patients who lacked baseline PCPC scores but had a discharge PCPC score of 3, 4, or 5 were excluded from the analysis since their outcome category (favorable versus unfavorable neurologic outcome) could not be established.

Statistical analysis

Descriptive statistics summarized demographic and clinical characteristics stratified by blood pressure percentile group and neurologic outcome at discharge. Continuous variables were presented as medians and interquartile ranges (IQR) and are compared between groups using the Mann-Whitney U test. Categorical variables were reported as frequencies with percentages and are compared between groups with the Chi-square or Fisher exact test as appropriate. We used multivariable logistic regression with mixed effects to estimate the association between MAP percentile category and favorable neurologic outcome, controlling for age, surgical-cardiac illness category, shockable rhythm, night/weekend arrest, CPR duration, and clustering by site as potential confounders based on a priori clinical rationale and evidence.[17,18] We explored potential modifications of the effect of blood pressure on neurologic outcome via stratified subgroup analyses by 1) age category: 0–1 years; 1–8 years; and 8–18 years and 2) vasopressor use (dichotomized yes/no) during the first 6 hours after ROSC. For the subgroup analyses, MAPs 75th percentile were grouped together because of the small number of cases in the 75th–94th and 95th percentile groups. Additionally, we conducted a sensitivity analysis using a broadened classification of favorable and unfavorable neurologic outcome according to Albrecht et al., whereby favorable outcome was defined as a PCPC of 1, 2, or 3 at hospital discharge, or no change in PCPC score from pre-arrest baseline.[19] Unfavorable outcome was defined as a discharge PCPC score of 4, 5, or 6 associated with an increase in PCPC 1 from pre-arrest baseline. P-values <0.05 were considered statistically significant. Analyses were performed using SPSS (IBM, Armonk, NY, USA).

Results

1,119 patients met inclusion criteria. 787 patients were included in the analysis (see Fig. 1). The median age was 1.5 years (IQR, 0.4–7.5). Seventy-nine percent of events occurred in-hospital, 13% had shockable rhythm, and the median CPR duration was 7 minutes (IQR, 3–16). Twenty-one percent of patients were post-operative following cardiac surgery at the time of cardiac arrest. The distribution of blood pressures by MAP group was: I = 37%; II = 28%; III = 13%; IV = 11%; V = 7%, and VI = 4%. Among the patients in group I (ie. MAP <5th percentile), 59% received vasopressor infusions within the first 6 hours post-ROSC. In groups II, III, IV, V, and VI, the proportion of patients receiving vasopressors was 47%, 37%, 32%, 26%, and 21%, respectively (see Table 1).

Four hundred twenty-four patients (54%) had favorable outcome at hospital discharge (Supplementary Table 1). These patients received shorter durations of CPR; fewer doses of epinephrine and sodium bicarbonate intra-arrest; more frequently received a fluid bolus during arrest; and had lower VIS scores in the first 6 hours post-CA. The median MAP percentile for the favorable vs unfavorable outcome groups was 13 (IQR, 3–43) versus 8 (IQR, 1–37) (p = 0.441). There was an inverted U-shaped relationship between MAP category and favorable outcome (Fig. 2). The greatest proportion of patients with favorable outcome was observed with MAP between the 25th–49th percentile (66%), followed by the 5th–24th percentile (62%) and the 50th–74th percentile (60%) (Table 2).

In the multivariable logistic regression analysis, compared with group I (MAP <5th percentile), those in groups II, III, IV had greater odds of favorable outcome (aOR, 1.84 [95% CI, 1.24, 2.73]; 2.20 [95% CI, 1.32, 3.68]; 1.90 [95% CI, 1.12, 3.25], respectively). However, groups V and VI did not have significantly greater odds of favorable outcome than group I (aOR, 1.44 [95% CI, 0.75, 2.80]; 1.11 [95% CI, 0.47, 2.59]) (Fig. 2).

For the planned subgroup analyses by age and post-ROSC vasopressor use, point estimates for the association between MAP percentile category and favorable outcome were consistent with the primary analysis (see Supplementary Data, Tables 2–6). The sensitivity analysis using a more inclusive definition of favorable neurologic outcome showed similar results to the primary analysis (see Supplementary Data, Fig. 1).

Discussion

In this study of children who achieved ROSC following IHCA or OHCA, a clear inverted U-shaped association emerged between lowest recorded MAP in the first 6 hours post-ROSC and favorable neurologic outcome at hospital discharge. The analysis revealed three distinct trends across the range of MAP percentiles (Fig. 2): 1) less favorable outcomes when MAP was below than the 5th percentile, 2) increasing likelihood of favorable outcomes when MAP was between the 5th to 74th percentile, and 3) diminishing probability of favorable outcomes when MAP was 75th percentile. Among children with MAP between the 5th to 74th percentile, 63% had favorable outcome compared to 44% who had MAP <5th or 75th percentiles, reinforcing that proactively maintaining blood pressure within an optimal range is an important therapeutic goal.

Our analysis supports targeting a higher MAP threshold than the 5th percentile for age, specifically the 5th–74th percentile. The AHA Pediatric Advanced Life Support Guidelines explicitly recommend intervening to maintain blood pressure greater than the 5th percentile for age.[9,20,21] However, in our analysis, among the 37% of patients with documented hypotension, only 59% received vasopressor infusions within 6 hours of ROSC, highlighting that a significant proportion of these high-risk patients are potentially undertreated.

There is a wide range of MAP percentiles, between the 5th to 74th percentile, associated with favorable outcome. Above the 75th percentile, the probability of favorable outcome declined. This finding is relevant because current clinical practice is focused on avoiding hypotension and few clinicians would consider blood pressure above the 75th percentile post-ROSC a cause for concern or intervention. In fact, there is limited evidence indicating a connection between high MAP/hypertension and poor outcomes, so the finding that the "optimal" MAP range concludes/terminates at the 75th percentile is intriguing.[22] It is possible that very high MAP post-CA manifests in patients with severe anoxic brain injury and early cerebral edema. Indeed, patients with elevated MAP had longer duration of CPR (Table 1), likely predisposing them to more severe neurological injury.[22] Alternatively, the strain on the cardiovascular system imposed by high MAP might initiate a cardio-depressive feedback loop that leads to decreased cardiac output and cerebral perfusion, and as a consequence, poor neurologic outcome.[22,23] Equally plausible, in the setting of impaired cerebral autoregulation, higher MAPs can result in an excessive and potentially harmful increase in blood flow to the brain, known as hyperemia.[14]

The relationship between post-arrest MAP and neurologic outcome is complex. To illustrate this, several patient characteristics were associated with MAP category. As expected, congenital heart disease patients were overly represented in the lower MAP percentile groups (see Table 1), likely related to impaired cardiac output and decreased cardiac reserve associated with their underlying condition. Age of patients increased with higher MAP percentile groups. This pattern could be indicative of older children having more mature autonomic nervous systems and a stronger sympathetic response to the physiologic stress associated with cardiac arrest. Alternatively, younger patients were more likely to be post-operative following cardiac surgery at the time of CA, which implies they had sicker hearts to begin with–compared to older patients. Their cardiac dysfunction may have made it more challenging to maintain normal blood pressures after CA. Optimal blood pressure management is further complicated by post-arrest cerebral physiology and pathophysiology: degree of ischemic brain injury, cerebral metabolic requirements, and range of preserved cerebral autoregulation.[14] This may explain why randomized controlled trials in adults, such as the recent BOX trial, demonstrated no difference in neurological outcomes between patients treated to higher versus low MAP thresholds.[16,24–29] Overall, these observations are consistent with the idea that age-related physiological development, underlying medical conditions, and cerebral physiology can influence blood pressure patterns in the context of post-cardiac arrest care, highlighting the need for tailored management strategies to optimize outcomes for different patient populations.

This study has several limitations. We only assessed the single lowest MAP recorded in the first 6 hours post-ROSC. It is unclear if this measurement alone represents BP during the

entire first 6 hours. The pediRES-Q database did not indicate duration of the lowest MAP. Previous analyses demonstrate prolonged periods of hypotension are more detrimental than short episodes of hypotension.[7,21,25] In addition, our assessment of neurologic outcome was performed by PCPC at hospital discharge. Longer term outcomes are desirable, but beyond the scope of this analysis.[30] Longitudinal data suggests that even for patients with favorable outcome at hospital discharge, the PCPC score captured at this time point may not fully reflect longer-term neurocognitive and neurobehavioral function.[31]

Conclusion

In the first 6-hours after pediatric cardiac arrest, a lowest documented MAP between the 5th to 74th percentile was associated with favorable neurologic outcome. This finding underscores the significance of effectively managing post-arrest blood pressure. Further study is merited to ascertain whether personalized MAP goals within this range, driven by patients' unique physiology, improves pediatric cardiac arrest outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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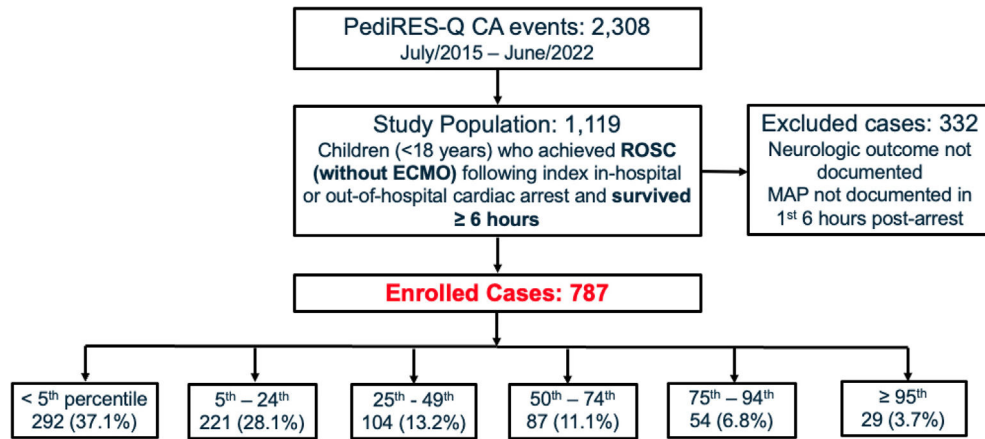
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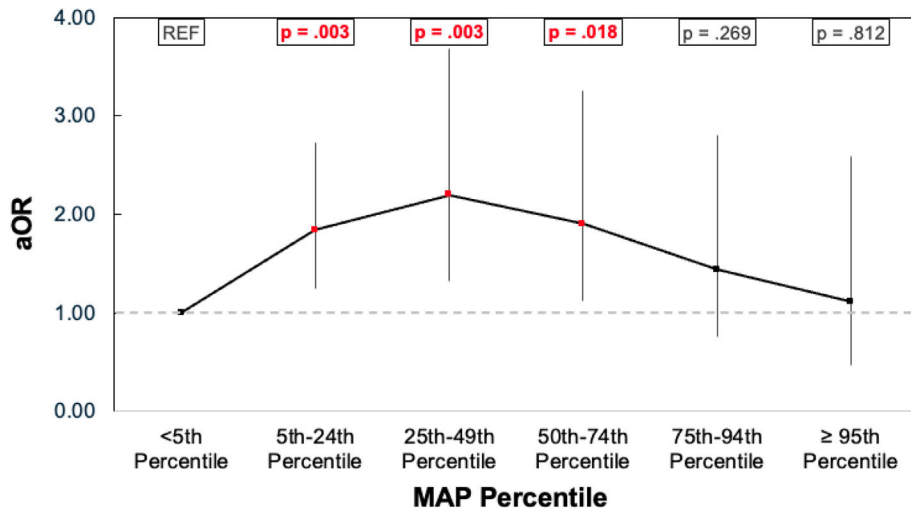
Fig. 2 –.
Adjusted odds of favorable outcome associated with MAP percentile group.

Table 1 –

Descriptive statistics stratified by MAP percentile group.

	All Patients	< 5th	5th - 24th	25th - 49th	50th - 74th	75th - 94th	95th	p
Demographic (N)	787	292	221	104	87	54	29	
Age, years, median (IQR)	1.5 (0.40, 7.6)	1.9 (0.40, 8.5)	0.9 (0.3, 5.6)	0.7 (0.30, 3.42)	1.6 (0.4, 9.1)	4.1 (0.8, 9.4)	5.3 (0.6, 10.8)	< 0.001
Female	328 (41.7%)	129 (44.2%)	87 (39.4%)	43 (41.3%)	29 (33.3%)	24 (44.4%)	16 (55.2%)	0.300
Race (N)	787	292	221	104	87	54	29	
Asian	32 (4.1%)	13 (4.5%)	6 (2.7%)	1 (1.0%)	7 (8.0%)	3 (5.6%)	2 (6.9%)	0.097
Black	127 (16.1%)	57 (19.5%)	36 (16.3%)	13 (12.5%)	13 (14.9%)	5 (9.3%)	3 (10.3%)	0.337
Native American	2 (0.3%)	1 (0.3%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.654
White	381 (48.4%)	141 (48.3%)	114 (51.6%)	51 (49.0%)	40 (46.0%)	19 (35.2%)	16 (55.2%)	0.366
Other	78 (9.9%)	24 (8.2%)	19 (8.6%)	10 (9.6%)	11 (12.6%)	11 (20.4%)	3 (10.3%)	0.145
Unknown/Not Documented	167 (21.2%)	56 (19.2%)	46 (20.8%)	28 (26.9%)	16 (18.4%)	16 (29.6%)	5 (17.2%)	0.345
Height (N)	630	245	177	86	67	39	16	
Height, cm, median (IQR)	71.0 (55.1, 113.0)	77.0 (55.1, 121.3)	68.0 (54.0, 101.5)	65.0 (54.0, 91.1)	78.0 (56.0, 129.5)	99.0 (66.0, 121.0)	71.0 (54.3, 129.8)	0.007
Weight (N)	786	292	220	104	87	54	29	
Weight, kg, median (IQR)	10.3 (5.4, 25.0)	11.5 (5.7, 26.1)	8.5 (4.8, 21.8)	7.8 (4.9, 15.0)	12.5 (5.4, 30.0)	17.6 (8.5, 30.5)	21.7 (8.0, 38.7)	< 0.001
Pre-Existing Conditions (N)	787	292	221	104	87	54	29	
Genetic/Metabolic	234 (29.7%)	99 (33.9%)	66 (29.9%)	25 (24.0%)	23 (26.4%)	12 (22.2%)	9 (31.0%)	0.309
Congenital Heart	257 (32.7%)	93 (31.8%)	93 (42.1%)	40 (38.5%)	20 (23.0%)	8 (14.8%)	3 (10.3%)	< 0.001
Lung / Airway	405 (51.5%)	171 (58.6%)	114 (51.6%)	48 (46.2%)	44 (50.6%)	18 (33.3%)	10 (34.5%)	0.003
Hematologic/Oncologic/Immune Compromise	41 (5.2%)	19 (6.5%)	11 (5.0%)	3 (2.9%)	3 (3.4%)	4 (7.4%)	1 (3.4%)	0.676
Neurologic	28 (3.6%)	6 (2.1%)	6 (2.7%)	3 (2.9%)	4 (4.6%)	6 (11.1%)	3 (10.3%)	0.013
Renal	81 (10.3%)	44 (15.1%)	17 (7.7%)	4 (3.8%)	11 (12.6%)	3 (5.6%)	2 (6.9%)	0.009
Other Heart Disease	79 (10.0%)	44 (15.1 %)	17 (7.7%)	7 (6.7%)	4 (4.6%)	5 (9.3%)	2 (6.9%)	0.022
Other	342 (43.5%)	143 (40.9%)	89 (40.3%)	41 (39.4%)	38 (43.7%)	19 (35.2%)	12 (41.4%)	0.239
Illness Category (N)	625	248	190	83	65	26	4	
Medical, Cardiac	117 (18.7%)	42 (16.9%)	39 (20.5%)	17 (20.5%)	7 (10.8%)	8 (30.8%)	4 (30.8%)	0.156

	All Patients	< 5th	5th - 24th	25th - 49th	50th - 74th	75th - 94th	95th	p
Medical, Non-Cardiac	292 (46.7%)	126 (50.8%)	74 (38.9%)	33 (39.8%)	37 (56.9%)	15 (57.7%)	7 (53.8%)	**0.032**
Surgical, Cardiac	128 (20.5%)	46 (18.5%)	50 (26.3%)	20 (24.1%)	11 (16.9%)	1 (3.8%)	0 (0.0%)	**0.015**
Surgical, Non-Cardiac	64 (10.2%)	23 (9.3%)	21 (11.1%)	10 (12.0%)	8 (12.3%)	2 (7.7%)	0 (0.0%)	0.834
Trauma	24 (3.8%)	11 (4.4%)	6 (3.2%)	3 (3.6%)	2 (3.1%)	0 (0.0%)	2 (15.4%)	0.374
PCPC Score Before Cardiac Arrest (N)	689	249	190	94	77	51	28	
1	449 (65.2%)	155 (62.2%)	130 (68.4%)	67 (71.3%)	50 (64.9%)	27 (52.9%)	20 (71.4%)	0.206
2	93 (13.5%)	37 (14.9%)	22 (11.6%)	13 (13.8%)	9 (11.7%)	8 (15.7%)	4 (14.3%)	0.907
3	61 (8.9%)	22 (8.8%)	17 (8.9%)	9 (9.6%)	5 (6.5%)	6 (11.8%)	2 (7.1%)	0.943
4	77 (11.2%)	32 (12.9%)	16 (8.4%)	5 (5.3%)	13 (16.9%)	9 (17.6%)	2 (7.1%)	0.056
5	8 (1.2%)	2 (0.8%)	5 (2.6%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0.317
6	1 (0.1%)	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.000
Interventions In-Place Prior to Cardiac Arrest (N)	787	292	221	104	87	54	29	
Assisted/Mechanical Ventilation	336 (42.7%)	141 (48.3%)	100 (45.2%)	43 (41.3%)	30 (34.5%)	16 (29.6%)	6 (20.7%)	**0.006**
Conscious/Procedural Sedation	110 (14.0%)	43 (14.7%)	35 (15.8%)	15 (14.4%)	10 (11.5%)	5 (9.3%)	2 (6.9%)	0.705
Dialysis	18 (2.3%)	12 (4.1%)	1 (0.5%)	2 (1.9%)	2 (2.3%)	1 (1.9%)	0 (0.0%)	0.120
ECG	399 (50.7%)	160 (54.8%)	127 (57.5%)	53 (51.0%)	37 (42.5%)	14 (25.9%)	8 (27.6%)	**< 0.001**
Implantable Cardiac Defibrillator (ICD)	2 (0.3%)	0 (0.0%)	0 (0.0%)	2 (1.5%)	0 (0.0%)	1 (1.6%)	1 (3.4%)	**0.011**
Arterial Line	207 (26.3%)	75 (25.7%)	78 (35.3%)	25 (24.0%)	18 (20.7%)	8 (14.8%)	3 (10.3%)	**0.002**
Endotracheal Tube/Tracheostomy	377 (47.9%)	154 (52.7%)	121 (54.8%)	45 (43.3%)	36 (41.4%)	15 (27.8%)	6 (20.7%)	**< 0.001**
IV/IO Infusion of Antiarrhythmics	59 (7.5%)	27 (9.2%)	15 (6.8%)	4 (3.8%)	7 (8.0%)	4 (7.4%)	2 (6.9%)	0.621
Pulse Oximetry	525 (66.7%)	218 (74.7%)	162 (73.3%)	63 (60.6%)	55 (63.2%)	18 (33.3%)	9 (31.0%)	**< 0.001**
Supplemental Oxygen	376 (47.8%)	160 (54.8%)	120 (54.3%)	45 (43.3%)	34 (39.1%)	12 (22.2%)	5 (17.2%)	**< 0.001**
Other	62 (7.9%)	22 (7.5%)	23 (10.4%)	11 (10.6%)	6 (6.9%)	0 (0.0%)	0 (0.0%)	**0.040**
Characteristics of CPR Event Location (N)	787	292	221	104	87	54	29	
In-Hospital	625 (79.4%)	248 (84.9%)	190 (86.0%)	83 (79.8%)	65 (74.7%)	26 (48.1%)	13 (44.8%)	**< 0.001**
Out-of-Hospital, Witnessed	73 (9.3%)	19 (6.5%)	13 (5.9%)	9 (8.7%)	10 (11.5%)	16 (29.6%)	6 (20.7%)	**< 0.001**
Out-of-Hospital, Not Witnessed	88 (11.2%)	25 (8.6%)	18 (8.1%)	11 (10.6%)	12 (13.8%)	12 (22.2%)	10 (34.5%)	**< 0.001**
Location of In-Hospital Arrests (N)	625	248	190	83	65	26	13	
ED	32 (5.1%)	15 (6.0%)	2 (1.1%)	6 (7.2%)	3 (4.6%)	5 (19.2%)	1 (7.7%)	**0.002**
PICU	366 (58.6%)	155 (62.5%)	111 (58.4%)	42 (50.6%)	40 (61.5%)	12 (46.2%)	6 (46.2%)	0.265

	All Patients	< 5th	5th - 24th	25th - 49th	50th - 74th	75th - 94th	95th	p
CICU	115 (18.4%)	47 (19.0%)	39 (20.5%)	15 (18.1%)	9 (13.8%)	3 (11.5%)	2 (15.4%)	0.841
NICU	15 (2.4%)	8 (3.2%)	2 (1.1%)	4 (4.8%)	1 (1.5%)	0 (0.0%)	0 (0.0%)	0.419
PACU	3 (0.5%)	2 (0.8%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.000
Other	94 (15.0%)	35 (18.4%)	16 (19.3%)	12 (18.5%)	6 (23.1%)	4 (30.8%)	94 (15.0%)	**0.003**
Characteristics of CPR Event Time (N)	692	270	201	90	72	38	21	
Weekend/Night Arrest	339 (49.0%)	137 (50.7%)	90 (44.8%)	44 (48.9%)	35 (48.6%)	22 (57.9%)	11 (52.4%)	0.693
Duration of Resuscitation (N)	779	287	221	103	87	52	29	
Duration, Minutes, Median (IQR)	7.0 (3.0, 16.0)	7.0 (4.0, 17.0)	6.0 (3.0, 12.5)	6.0 (3.0, 13.0)	7.0 (3.0, 18.0)	15.0 (5.0, 23.8)	10.0 (5.0, 20.5)	**0.002**
Defibrillation Status (N)	787	292	221	104	87	54	29	
Any Defibrillation	100 (12.7%)	37 (12.7%)	28 (12.7%)	13 (12.5%)	15 (17.2%)	6 (11.1%)	1 (3.4%)	0.578
Shockable Rhythm	100 (12.7%)	32 (11.0%)	37 (16.7%)	11 (10.6%)	12 (13.8%)	6 (11.11%)	2 (6.9%)	0.406
Medications Administered During CPR Event (N)	787	292	221	104	87	54	29	
None	21 (2.7%)	5 (1.7%)	7 (3.2%)	3 (2.9%)	2 (2.3%)	3 (5.6%)	1 (3.4%)	0.514
Amiodarone	20 (2.5%)	6 (2.1%)	8 (3.6%)	3 (2.9%)	1 (1.1%)	1 (1.9%)	1 (3.4%)	0.775
Atropine	63 (8.0%)	27 (9.2%)	23 (10.4%)	7 (6.7%)	3 (3.4%)	1 (1.9%)	2 (6.9%)	0.159
Calcium	177 (22.5%)	80 (27.4%)	55 (24.9%)	15 (14.4%)	15 (17.2%)	8 (14.8%)	4 (13.8%)	**0.022**
Epinephrine - 1 Dose	206 (26.2%)	83 (28.4%)	62 (28.1%)	29 (27.9%)	20 (23.0%)	8 (14.8%)	4 (13.8%)	0.174
Epinephrine - 2–4 Doses	298 (37.9%)	124 (42.5%)	86 (38.9%)	33 (31.7%)	27 (31.0%)	19 (35.2%)	9 (31.0%)	0.232
Epinephrine - 5 + Doses	124 (15.8%)	50 (17.1%)	27 (12.2%)	15 (14.4%)	17 (19.5%)	10 (18.5%)	5 (17.2%)	0.514
Fluid Bolus	163 (20.7%)	68 (23.3%)	42 (19.0%)	14 (13.5%)	21 (24.1%)	11 (20.4%)	7 (24.1%)	0.334
Inhaled Nitric Oxide	15 (1.9%)	8 (2.7%)	4 (1.8%)	2 (1.9%)	0 (0.0%)	1 (1.9%)	0 (0.0%)	0.750
Lidocaine	13 (1.7%)	5 (1.7%)	6 (2.7%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	1 (3.4%)	0.287
Magnesium Sulfate	26 (3.3%)	10 (3.4%)	9 (4.1%)	1 (1.0%)	2 (2.3%)	2 (3.7%)	2 (6.9%)	0.500
Other Vasopressors	25 (3.2%)	12 (4.1%)	7 (3.2%)	1 (1.0%)	2 (2.3%)	1 (1.9%)	2 (6.9%)	0.483
Sodium Bicarbonate	200 (25.4%)	88 (30.1%)	54 (24.4%)	22 (21.2%)	20 (23.0%)	10 (18.5%)	6 (20.7%)	0.260
Vasopressin	10 (1.3%)	4 (1.4%)	1 (0.0%)	0 (0.0%)	2 (2.3%)	1 (1.9%)	2 (6.9%)	0.063
Other	238 (30.2%)	78 (26.7%)	59 (26.7%)	34 (32.7%)	32 (36.8%)	20 (37.0%)	15 (51.7%)	**0.027**
Non-Drug Interventions During CPR Event (N)	787	292	221	104	87	54	29	

	All Patients	< 5th	5th - 24th	25th - 49th	50th - 74th	75th - 94th	95th	p
None	401 (51.0%)	152 (52.1%)	121 (54.8%)	53 (51.0%)	44 (50.6%)	20 (37.0%)	11 (37.9%)	0.182
Chest Tube	26 (3.3%)	12 (4.1%)	8 (3.6%)	2 (1.9%)	0 (0.0%)	1 (1.9%)	3 (10.3%)	0.103
Needle Thoracostomy	14 (1.8%)	8 (2.7%)	4 (1.8%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	1 (3.4%)	0.400
Transcutaneous Pacemaker	8 (1.0%)	6 (2.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.9%)	1 (3.4%)	0.054
Transvenous Pacemaker	10 (1.3%)	3 (1.0%)	5 (2.3%)	0 (0.0%)	2 (2.3%)	0 (0.0%)	0 (0.0%)	0.491
Pericardiocentesis	2 (0.3%)	0 (0.0%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.474
Intubation	264 (33.5%)	92 (31.5%)	65 (29.4%)	37 (35.6%)	30 (34.5%)	26 (48.1%)	14 (48.3%)	0.063
Other	129 (16.4%)	44 (15.1%)	38(17.2%)	14 (13.5%)	17 (19.5%)	11 (20.4%)	5 (17.2%)	0.762
Post-ROSC Vasopressor Utilization (N)	787	292	221	104	87	54	29	
Vasopressor Use	361 (45.9%)	172 (58.9%)	103 (46.6%)	38 (36.5%)	28 (32.2%)	14 (25.9%)	6 (20.7%)	**< 0.001**
Vasopressor Score, median (IQR)	0.0 (0.0, 15.0)	5.0 (0.0, 28.7)	0.0 (0.0, 14.5)	0.0 (0.0, 8.4)	0.0 (0.0, 4.0)	0.0 (0.0, 1.3)	0.0 (0.0, 0.0)	**< 0.001**
PCPC Score At Hospital Discharge (N)	787	292	221	104	87	54	29	
1	253 (32.1%)	68 (23.3%)	84 (38.0%)	48 (46.2%)	31 (35.6%)	15 (27.8%)	7 (24.1%)	
2	105 (13.3%)	36 (12.3%)	37 (16.7%)	14 (13.5%)	12 (13.8%)	5 (9.3%)	1 (3.4%)	
3	52 (6.6%)	22 (7.5%)	11 (5.0%)	7 (6.7%)	5 (5.7%)	3 (5.6%)	4 (13.8%)	
4	53 (6.7%)	20 (6.8%)	12 (5.4%)	5 (4.8%)	8 (9.2%)	7 (13.0%)	1 (3.4%)	
5	3 (0.4%)	0 (0.0%)	2 (0.9%)	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	
Deaths	321 (40.8%)	146 (50.0%)	75 (33.9%)	30 (28.8%)	30 (34.5%)	24 (44.4%)	16 (55.2%)	
Neurologic Outcome (N)	787	292	221	104	87	54	29	
Favorable	424 (53.8%)	128 (43.8%)	137 (61.9%)	69 (66.3%)	52 (59.8%)	26 (48.1%)	12 (41.4%)	

Table 2 -

Odds of favorable neurologic outcome associated with different percentiles.

Percentile	No. of Children	Favorable Outcome (%)	OR (95% CI) Favorable Outcome	AOR (95% CI) Favorable Outcome
<5th	292	128 (43.8%)	REF	REF
5–24th	221	137 (61.9%)	2.09 (1.46, 2.99) *p* < **0.001**	1.84 (1.24, 2.73) *p* = **0.003**
25–49th	104	69 (66.3%)	2.53 (1.58, 4.03) *p* < **0.001**	2.20 (1.32, 3.68) *p* = **0.003**
50–74th	87	52 (59.8%)	1.90 (1.17, 3.10) *p* = **0.010**	1.90 (1.12, 3.250) *p* =**0.018**
75–94th	54	26 (48.1%)	1.19 (0.67, 2.13) *p* = 0.558	1.45 (0.75, 2.80) *p* = 0.269
95th	29	12 (41.4%)	0.90 (0.42, 1.96) *p* = 0.799	1.11 (0.47, 2.60) *p* =0.812

*
Adjusted for: 1) age, 2) illness category (surgical-cardiac), 3) initial shockable rhythm, 4) time (weekend/night), 5) CPR duration 6) clustering by site.