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Clinical paper

Chest compressions for pediatric organized rhythms: A hemodynamic and outcomes analysis

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Abstract

Aim: Pediatric cardiopulmonary resuscitation (CPR) guidelines recommend starting CPR for heart rates (HRs) less than 60 beats per minute (bpm) with poor perfusion. Objectives were to (1) compare HRs and arterial blood pressures (BPs) prior to CPR among patients with clinician-reported bradycardia with poor perfusion ("BRADY") vs. pulseless electrical activity (PEA); and (2) determine if hemodynamics prior to CPR are associated with outcomes.

Methods and Results: Prospective observational cohort study performed as a secondary analysis of the *ICU-RESUS*citation trial (NCT028374497). Comparisons occurred (1) during the 15 seconds "immediately" prior to CPR and (2) over the two minutes prior to CPR, stratified by age ($\leq$1 year, >1 year). Poisson regression models assessed associations between hemodynamics and outcomes. Primary outcome was return of spontaneous circulation (ROSC). Pre-CPR HRs were lower in BRADY vs. PEA ($\leq$1 year: 63.8 [46.5, 87.0] min^{-1} vs. 120 [93.2, 150.0], $p < 0.001$; >1 year: 67.4 [54.5, 87.0] min^{-1} vs. 100 [66.7, 120], $p < 0.014$). Pre-CPR pulse pressure was higher among BRADY vs. PEA ($\leq$1 year (12.9 [9.0, 28.5] mmHg vs. 10.4 [6.1, 13.4] mmHg, $p > 0.001$). Pre-CPR pulse pressure $\geq$ 20 mmHg was associated with higher rates of ROSC among PEA (aRR 1.58 [CI95 1.07, 2.35], $p = 0.022$) and survival to hospital discharge with favorable neurologic outcome in both groups (BRADY: aRR 1.28 [CI95 1.01, 1.62], $p = 0.040$; PEA: aRR 1.94 [CI95 1.19, 3.16], $p = 0.008$). Pre-CPR HR $\geq$ 60 bpm was not associated with outcomes.

Conclusions: Pulse pressure and HR are used clinically to differentiate BRADY from PEA. A pre-CPR pulse pressure >20 mmHg was associated with improved patient outcomes.

Keywords: Pediatrics, Bradycardia, Hemodynamics, Cardiopulmonary resuscitation

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https://doi.org/10.1016/j.resuscitation.2023.110068

Received 14 September 2023; Received in Revised form 16 November 2023; Accepted 22 November 2023

Introduction

It is estimated that there are more than 15,000 children who receive in-hospital cardiopulmonary resuscitation (CPR) each year in the US.[1] The majority of these events occur in the intensive care unit (ICU).[2] Less than half of these patients will survive to hospital discharge,[3] and the rate of survival has plateaued since 2010.[4] Unfortunately, many of the pediatric resuscitation guideline recommendations are either extrapolated from adult data or developed through expert consensus, highlighting the need for pediatric-specific data to improve the care provided to these at-risk children.

Bradycardia with poor perfusion in children, frequently the result of progressive respiratory failure and shock, is life-threatening and often rapidly progresses to pulseless cardiac arrest and death.[5,6] Pediatric Advanced Life Support (PALS) guidelines recommend starting chest compressions for bradycardia with poor perfusion for heart rates (HRs) less than 60 beats per minute (bpm) prior to a patient deteriorating into true pulselessness.[4] This recommendation was developed through expert consensus with little to no data collected from actual children in cardiac arrest. As nearly 50% of in-hospital pediatric resuscitations are initiated for bradycardia with poor perfusion,[7,8] – a major difference compared to adult cardiac arrest – study of this common pediatric rhythm is warranted.

To that end, we conducted a secondary analysis of data from a prospective, multicenter, cluster-randomized interventional trial (The *ICU-RESUS*citation Project [ICU-RESUS]; NCT02837497),[9] to (1) describe patient HRs and BPs prior to the initiation of CPR among patients with organized cardiac rhythms, specifically, bradycardia with poor perfusion and pulseless electrical activity (PEA), and (2) determine if HRs/BPs prior to CPR are associated with outcomes.

Methods

Setting and design

The main *ICU-RESUS* study was a National Heart, Lung, and Blood Institute (NHLBI)-funded prospective, multicenter, hybrid stepped-wedge cluster-randomized interventional trial of a physiologic-directed CPR training and debriefing quality improvement (QI) bundle. It was conducted across the 18 ICUs of the Collaborative Pediatric Critical Care Research Network (CPCCRN), a *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)-funded research collaborative.[9] The institutional review boards of each clinical site and of the CPCCRN Data Coordinating Center (DCC) at the University of Utah approved this study protocol with waiver of informed consent.

This secondary study was designed during *ICU-RESUS* enrolment. The statistical analysis plan was developed prior to examination of any outcome data from the main trial. Only data prospectively collected per the *ICU-RESUS* protocol were utilized for this secondary study.

Patient population

The main *ICU-RESUS* study included pediatric ICU patients (age $\geq$ 37 weeks' corrected gestation and <19 years) who received CPR of any duration between October 1, 2016 and March 31, 2021. Subjects were excluded if, prior to the arrest, they: (1) were not expected to survive the hospitalization due to a terminal illness or had a documented lack of commitment to aggressive ICU therapies; (2) were brain dead; or (3) had an out-of-hospital cardiac arrest associated with the current hospitalization. For this secondary study, only index in-hospital cardiac arrests (IHCAs) with bradycardia with poor perfusion ("BRADY") or PEA as an initial rhythm, as determined by chart abstraction from clinical notes by trained research coordinators (i.e., from the documentation of the bedside providers who led/participated in the resuscitation), and with invasive arterial blood pressure monitoring were included. Subjects were excluded if there was not at least one 15-second epoch of analyzable arterial waveform data during the 2-minute period prior to the start of compressions to determine HRs/BPs.

Physiologic data collection

The physiologic waveform collection of the parent trial has been previously published.[9] Briefly, trained research staff downloaded physiologic waveform data (invasive arterial line or capnography) for the 2 minutes prior to CPR and up to the first 10 minutes of CPR. After download, these waveforms were de-identified and then transmitted to the University of Utah Data Coordinating Center (DCC). Investigators at the Children's Hospital of Philadelphia (CHOP)(KKC, KG, WPL) then downloaded the files and reconstructed the waveforms using custom code (MATLAB; The MathWorks, Inc., Natick, MA). These reconstructed waveforms were then clinically reviewed to manually annotate: (1) starts and stops in CPR, (2) sections of non-analyzable data (poor waveform signal), and (3) periods of non-sustained return of spontaneous circulation. Systolic blood pressure was sampled at the peak of the arterial pressure waveform for each compression; diastolic blood pressure was sampled as an average of data points occurring between 60% and 70% of the compression cycle (mid- to late-diastole). HR was calculated from R-R intervals on ECG; HR = 60/R-R interval in seconds.

Outcomes and statistical analysis

Patient and event characteristics were summarized according to group (BRADY vs. PEA). Statistics were reported as frequencies and percentages or as median and quartiles. Outcomes were similarly summarized by group. Associations between groups and between patients with and without return of spontaneous circulation (ROSC) were examined using Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for ordinal variables.

The primary patient outcome was ROSC. Survival to hospital discharge with favorable neurological outcome, defined as a Pediatric Cerebral Performance Category (PCPC) score of 1–3 or no change in baseline, was secondary.[10–12] The primary hemodynamic outcome was diastolic BP, chosen for its association with pediatric cardiac arrest outcomes when measured during CPR.[13,14] Secondary hemodynamic outcomes included systolic BP and pulse pressure (SBP – DBP).

BPs immediately prior to the start of resuscitation were summarized for each rhythm group, stratified by age: <1 year vs. $\geq$1 year of age. The analysis included (1) comparisons at "immediately prior to resuscitation," defined as the average over the 15 seconds prior to the start of resuscitation, and (2) the trend in BPs (per minute average) for the two minutes prior to CPR. Immediately prior to resuscitation, differences in BP and HR between rhythms for each age category were assessed via Wilcoxon rank-sum test; trends for the two-minute period prior to chest compressions were assessed using linear regression.

The association between *a priori* HR and hemodynamic targets and patient outcomes was evaluated using Poisson regression with robust error estimates, controlling for illness category. *A priori* targets included: (1) HR $\geq$ 60 bpm; (2) DBP $\geq$ 25 mmHg for infants <1 year of age, $\geq$30 for older children[14]; and the following targets which were developed by expert consensus of CPCCRN and used in previous work: (3) SBP $\geq$ 40 mmHg for infants, $\geq$50 for older children; and (4) pulse pressure $\geq$ 20 mmHg.[9,15].

Exploratory analyses: In an attempt to identify alternative HR and BP thresholds associated with improved outcomes, a combination of clinical judgement, receiver operating characteristic (ROC) curves and natural cubic splines with internal knots at the 10th, 50th, and 90th percentiles were utilized. ROC curves and splines were constructed for each rhythm group (bradycardia vs. PEA) and adjusted for illness category (cardiac vs. non-cardiac and age [<1 year vs. $\geq$1 year]). Curves were constructed for both ROSC and survival with favorable neurologic outcome.

Analyses were performed using SAS 9.4 (SAS Institute; Cary, NC). Reported *p*-values were based on a two-sided alternative and considered significant if less than 0.05.

Results

Of 1129 patients with index IHCAs, 909 (80.5%) had an initial rhythm of either bradycardia with poor perfusion (n = 581) or pulseless electrical activity (n = 328). Of these 909 patients, 245 (27.0%) had an invasive arterial catheter in place at the time of the arrest (Fig. 1). The final cohort included 234 patients with at least one 15-second epoch of evaluable BP data in the two minutes prior to CPR. Patient characteristics between included and excluded patients are shown in Supplement Table 1. Patient and event characteristics by rhythm group are shown in Tables 1 and 2, respectively. There were no significant differences between the two groups. Patient outcomes between rhythm groups are contained in Supplement Table 2. Outcomes were similar between rhythm groups. Analogous tables by primary outcome are contained in Supplement Tables 3 and 4.

The comparison of immediate pre-CPR BPs and HRs by rhythm group, stratified by age, is contained in Table 3. Among infants <1 year of age, pulse pressures were significantly higher in the BRADY group compared to the PEA group (12.9 [9.0, 28.5] mmHg vs 10.4 [6.1, 13.4] mmHg; p < 0.001). Pulse pressures were similar in older children between groups. In both age groups, HRs were significantly lower in the BRADY group compared to the PEA group (infants: 63.8 [46.5, 87.0] vs 120 [93.2, 150] bpm, p < 0.001; older children: 67.4 [54.5, 87.0] vs 100 [66.7, 120] bpm, p = 0.014). There were no significant differences in pre-arrest diastolic or systolic BPs between groups. In both age groups, BP and HR measurements decreased for every minute leading up to initiation of CPR, for both rhythm groups (p < 0.02 for all).

The association of *a priori* HR and hemodynamic targets with outcomes is contained in Table 4. In the overall cohort, a pre-arrest pulse pressure $\geq$ 20 mmHg was associated with higher rates ROSC in PEA (aRR 1.58 [CI95 1.07, 2.35], p = 0.022) and higher rates of survival to hospital discharge with favorable neurologic outcome in both rhythm groups (BRADY: aRR 1.28 [CI95 1.01, 1.62], p = 0.040; PEA: aRR 1.94 [CI95 1.19, 3.16], p = 0.008). There was no significant association between other *a priori* HR and BP targets with outcomes.

Exploratory analyses: ROC and spline analyses (Supplement Figs. 1–3) were unable to detect an alternative HR, SBP, or DBP. For pulse pressure (Supplement Fig. 4), we used clinician judgement and ROC/splines to define optimal pulse pressure as $\geq$15 mmHg (PEA: ROC cut-point: 12.97; sensitivity: 0.41; specificity: 0.81; AUC: 0.583 (0.448, 0.719); BRADY: ROC cut-point: 13.30; sensitivity: 0.55; specificity: 0.60; AUC: 0.565 (0.467, 0.663). A pulse pressure $\geq$15 mmHg was associated with improved survival to hospital discharge with favorable neurological outcome only among patients with BRADY (aRR 1.27 [CI95 1.01, 1.61], p = 0.043; [Table 4]).

Discussion

To our knowledge, this is the first quantitative report of HRs and BPs among organized rhythms prior to CPR for in-hospital pediatric cardiac arrests. In this multicenter cohort, there were no differences in patient outcomes between events with BRADY versus PEA. While pre-arrest heart rates and pulse pressures were significantly different between rhythm groups, systolic and diastolic BPs were similar. In both rhythms prior to the start of CPR, higher pulse pressure was associated with better outcomes. In contrast to Guideline recommendations[4] that provide a HR threshold of 60 bpm for starting CPR in patients with a pulse, this threshold was not associated with outcomes.

In contrast to adult studies of cardiac arrest,[16] bradycardia with poor perfusion is the most common rhythm for which CPR is initiated in hospitalized children.[7,8] Consistent with these published data, bradycardia with poor perfusion was the initial documented rhythm in 64% of events in the present study. Interestingly, there were no significant differences in outcomes between the two rhythms. Although speculative, the nearly equivalent outcomes between rhythm groups may be explained by the overall high rates of survival in the PEA group of the *ICU-RESUS* trial, which was nearly 20% higher than any previous registry study.[3,17] These observed differences may in part be because patients in the trial received high-quality CPR (>80% of events achieved intra-arrest diastolic BP targets associated with outcomes)[9,13,14] and excellent post-arrest care (>62% achieved post-arrest BP targets;[9] <19% of patients had post-arrest fever).[9] Another possible explanation is the high proportion of congenital heart disease patients in our cohort. Approximately 50% of patients were classified as surgical-cardiac, a group known to have significantly better cardiac arrest outcomes compared to other illness category classifications.[18]

These data provide insight into (1) what physiologic parameters providers at the bedside use to differentiate bradycardia with poor perfusion from PEA, and (2) what prompts providers to initiate CPR. Not surprisingly, pulse pressure tends to be higher and heart rates lower among rhythms noted as BRADY as compared to PEA. Worsening hemodynamics appears to be a driver of the initiation of CPR among both rhythm groups as there were significant declining trends across all variables prior to the start of CPR. As to which parameter should prompt providers to initiate CPR, a pulse pressure $\geq$20 mmHg at the start of CPR across both rhythm groups was associated with improved outcomes. This suggests that pulse pressure decreasing toward 20 mmHg could be a potential trigger for starting CPR and that prompt recognition and providing CPR prior to true pulselessness may be an approach to improve outcomes from pediatric cardiac arrest, irrespective of the heart rate at which point the patient loses pulsatility.

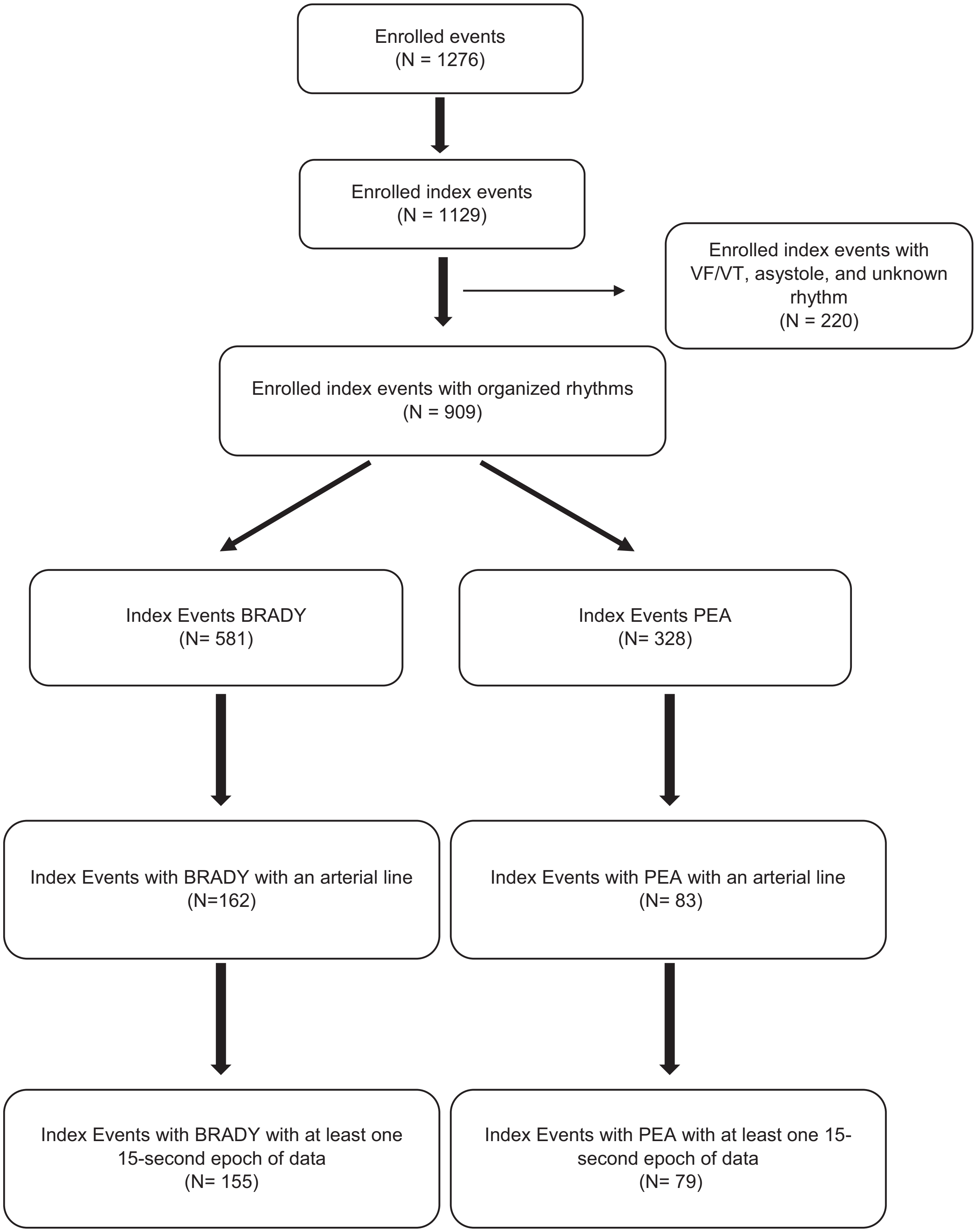

Fig. 1 – Consort diagram.

Of note, we did not identify an association between a pre-CPR HR cut-off of 60 bpm and outcomes. Current guidelines recommend starting CPR if the pulse is <60 per minute and there are signs of poor perfusion; however, the absolute heart rate at which chest compressions should be initiated is unknown. This recommendation is based on a consensus for ease of teaching and retention of skills,[19] and to our knowledge there are no clinical or animal studies that provide evidence for this recommendation. Interestingly, the median HR immediately prior to CPR initiation in this group of patients was 63.8 in infants and 67.4 in older children. This suggests that ICU clinicians may not be abiding by the recommendation to wait until the HR drops below 60 bpm to start CPR for BRADY and are instead relying on

Table 1 – Demographics and pre-event characteristics by first documented rhythm.

	BRADY (*N* = 155)	PEA (*N* = 79)	*p*
Demographics			
Age			0.331[4]
<1 month	51 (32.9%)	21 (26.6%)	
1 month–<1 year	65 (41.9%)	30 (38.0%)	
1 year–<12 years	31 (20.0%)	20 (25.3%)	
>12 years	8 (5.2%)	8 (10.1%)	
Weight (kg)	4.8 [3.3,9.0]	5.5 [3.4,14.1]	0.161[5]
Male	84 (54.2%)	45 (57.0%)	0.781[4]
Race			0.711[4]
White	71 (45.8%)	39 (49.4%)	
Black or African American	33 (21.3%)	14 (17.7%)	
Other	11 (7.1%)	4 (5.1%)	
Unknown or Not Reported	40 (25.8%)	22 (27.8%)	
Hispanic or Latino	19 (12.3%)	17 (21.5%)	0.083[4]
Preexisting medical conditions			
Respiratory insufficiency	133 (85.8%)	61 (77.2%)	0.103[6]
Hypotension	116 (74.8%)	68 (86.1%)	0.063[6]
Congestive heart failure	17 (11.0%)	9 (11.4%)	1.000[6]
Pneumonia	13 (8.4%)	6 (7.6%)	1.000[6]
Sepsis	17 (11.0%)	5 (6.3%)	0.345[6]
Trauma	2 (1.3%)	1 (1.3%)	1.000[6]
Renal insufficiency	9 (5.8%)	9 (11.4%)	0.193[6]
Malignancy	5 (3.2%)	2 (2.5%)	1.000[6]
Pulmonary hypertension	24 (15.5%)	13 (16.5%)	0.851[6]
Congenital heart disease	120 (77.4%)	61 (77.2%)	1.000[6]
Pre-event characteristics			
Illness category			0.785[4]
Medical cardiac	38 (24.5%)	23 (29.1%)	
Medical non-cardiac	27 (17.4%)	17 (21.5%)	
Surgical cardiac	86 (55.5%)	38 (48.1%)	
Surgical non-cardiac	1 (0.6%)	0 (0.0%)	
Trauma	3 (1.9%)	1 (1.3%)	
PRISM[1]	7.0 [3.0,12.0]	8.0 [3.0,12.0]	0.493[5]
Vasoactive inotropic score[2]	3.3 [0.0,8.0]	5.0 [0.0,10.0]	0.073[5]
Baseline PCPC score[3]			0.802[4]
1 – Normal	118 (76.1%)	56 (70.9%)	
2 – Mild disability	19 (12.3%)	14 (17.7%)	
3 – Moderate disability	9 (5.8%)	5 (6.3%)	
4 – Severe disability	8 (5.2%)	4 (5.1%)	
5 – Coma/vegetative state	1 (0.6%)	0 (0.0%)	
Baseline FSS[3]	6.0 [6.0,8.0]	6.0 [6.0,8.0]	0.767[5]

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 VIS was evaluated 2 hours prior to the event.

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

4 Fishers Exact test with Monte Carlo approximation.

5 Kruskal-Wallis test.

6 Fishers Exact test.

declining HRs and other hemodynamic factors in their decision making. Although we did not find outcome associations with pre-CPR HR, we caution readers that this should remain an important consideration as only 50% of patients have arterial lines to monitor for changes in pulse pressure. In the end, declining HRs may still be the best metric to follow when invasive arterial catheter data is not available.

This study has limitations. First, this is a secondary analysis of the *ICU-RESUS* trial, a group of tertiary care centers with a documented interest in pediatric cardiac arrest and the findings may not be generalizable to other care environments. Second, the observational study design precludes our ability to determine causative relationships. Limitations in study design are mitigated by the prospective data collection of the *ICU-RESUS* trial and because this analysis was designed during trial enrolment without review of the data. Third, this study only included patients with invasive arterial blood pressure monitoring which may limit generalizability. As a result of this inclusion criteria, our cohort had a higher level of severity of illness (e.g., more pre-existing hypotension, higher PRISM and VIS scores). However, nearly 95% of pediatric in-hospital cardiac arrests occur in the ICU and about half of these patients will have the necessary invasive monitoring.[20–22] Further, presence of an arterial line may have led to misclassification bias (i.e. some bradycardia with poor perfusion patients may have been labelled as such due to

Table 2 – Event characteristics by first documented rhythm.

	BRADY (*N* = 155)	PEA (*N* = 79)	*p*
Interventions in place prior to event			
Central venous catheter	123 (79.4%)	66 (83.5%)	0.487[5]
Vasoactive infusion	109 (70.3%)	59 (74.7%)	0.541[5]
Invasive mechanical ventilation	119 (76.8%)	68 (86.1%)	0.120[5]
Non-invasive ventilation	22 (14.2%)	7 (8.9%)	0.297[5]
End-tidal CO_2 monitoring	111 (71.6%)	65 (82.3%)	0.080[5]
Immediate cause(s) of event			
Arrhythmia	14 (9.0%)	10 (12.7%)	0.495[5]
Cyanosis without respiratory decompensation	5 (3.2%)	4 (5.1%)	0.491[5]
Hypotension	100 (64.5%)	64 (81.0%)	0.010[5]
Respiratory decompensation	88 (56.8%)	31 (39.2%)	0.013[5]
Duration of CPR (minutes)	6.0 [3.0,20.0]	9.0 [3.0,28.0]	0.089[6]
Duration of CPR (minutes)			0.498[5]
<6	69 (44.5%)	31 (39.2%)	
6–15	38 (24.5%)	16 (20.3%)	
16–35	20 (12.9%)	15 (19.0%)	
>35	28 (18.1%)	17 (21.5%)	
CPR time[1]			0.324[5]
Weekday	82 (52.9%)	50 (63.3%)	
Weeknight	33 (21.3%)	14 (17.7%)	
Weekend	40 (25.8%)	15 (19.0%)	
First documented rhythm			<0.001[5]
Pulseless electrical activity/asystole	0 (0.0%)	79 (100.0%)	
Ventricular fibrillation/tachycardia	0 (0%)	0 (0%)	
Bradycardia with poor perfusion	155 (100.0%)	0 (0.0%)	
Pharmacologic interventions during event			
Epinephrine	138 (89.0%)	70 (88.6%)	1.000[5]
Number of epinephrine boluses	2.0 [1.0,4.0]	2.0 [1.0,4.0]	0.295[6]
Average interval between epinephrine boluses[2]	5.0 [3.9,8.0]	5.5 [3.4,15.0]	0.783[6]
Atropine	16 (10.3%)	4 (5.1%)	0.220[5]
Calcium	74 (47.7%)	38 (48.1%)	1.000[5]
Sodium bicarbonate	74 (47.7%)	49 (62.0%)	0.052[5]
Vasopressin	7 (4.5%)	3 (3.8%)	1.000[5]
Amiodarone	3 (1.9%)	1 (1.3%)	1.000[5]
Lidocaine	4 (2.6%)	4 (5.1%)	0.448[5]
Fluid bolus	30 (19.4%)	19 (24.1%)	0.402[5]

CPR = cardiopulmonary resuscitation.

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

[4]Favorable neurologic outcome is defined as no more than moderate disability or 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] Average interval between epinephrine doses is only calculated on subjects with at least 2 doses of epinephrine.

[5] Fishers Exact test with Monte Carlo approximation.

[6] Kruskal-Wallis test.

visible pulsation on the arterial line tracing despite the patient not having a pulse to palpate at the bedside). In short, we were unable to determine whether palpable pulse or visible arterial line pulsations were used to classify bradycardia with poor perfusion patients.

Conclusion

In this population of children in the intensive care unit with invasive arterial monitoring who received CPR, pulse pressure and heart rate immediately prior to CPR may be the primary determinants providers use to clinically differentiate an organized rhythm as bradycardia with poor perfusion vs. pulseless electrical activity. In this ICU cohort, a pre-arrest pulse pressure >20 mmHg at the start of CPR was associated with improved patient outcomes, whereas heart rate and other hemodynamic markers were not. Because this cohort only included children with invasive arterial monitoring, future work should focus on investigating which physiologic changes are used by providers to initiate CPR when invasive arterial blood pressure data is not available to guide clinical decisions.

Co-authors that are part of the journal's Editorial Board: Robert Berg, MD and Vinay Nadkarni, MD.

Sources of funding

This study was supported, in part, by the following cooperative agreements from the National Institute of Health's Eunice Kennedy Shriver National Institute of Child Health and Human Development: UG1HD050096, UG1HD049981, UG1HD049983, UG1HD063108, UG1HD083171, UG1HD083166, UG1HD083170, U10HD050012, U10HD063106, U10HD063114, and U01HD049934 and by the

Table 3 – Hemodynamics immediately prior to the start of resuscitation.

	BRADY (N = 116)	*p*	PEA (N = 51)	*p*	*P*-value
Age ≤ 1 year					
Diastolic blood pressure (mmHg)	27.1 [21.7,36.8]		27.8 [23.2,37.9]		0.757[1]
Delta	−4.97 (−6.03, −3.92)	<0.001	−3.65 (−5.49, −1.81)	<0.001	
Systolic blood pressure (mmHg)	43.8 [32.4,64.7]		39.0 [31.7,51.3]		0.070[1]
Delta	−9.16 (−11.35, −6.96)	<0.001	−6.08 (−9.20, −2.97)	<0.001	
Pulse pressure (mmHg)	12.9 [9.0,28.5]		10.4 [6.1,13.4]		<0.001[1]
Delta	−4.17 (−5.68, −2.67)	<0.001	−2.43 (−3.95, −0.92)	0.002	
Mean arterial pressure (mmHg)	33.6 [26.0,47.1]		31.3 [26.4,42.2]		0.563[1]
Delta	−7.22 (−8.74, −5.71)	<0.001	−4.65 (−7.07, −2.23)	<0.001	
Heart rate (beats/minute)	63.8 [46.5,87.0]		120.0 [93.2,150.0]		<0.001[1]
Delta	−24.03 (−27.96, −20.10)	<0.001	−9.99 (−15.45, −4.53)	<0.001	
Age > 1 year					
Diastolic blood pressure (mmHg)	29.8 [20.3,38.6]		26.0 [19.4,39.4]		0.461[1]
Delta	−6.05 (−9.35, −2.75)	<0.001	−7.65 (−10.37, −4.92)	<0.001	
Systolic blood pressure (mmHg)	46.2 [32.3,54.5]		37.4 [27.3,54.3]		0.336[1]
Delta	−10.79 (−15.78, −5.80)	<0.001	−12.94 (−17.65, −8.24)	<0.001	
Pulse pressure (mmHg)	13.6 [8.5,19.1]		10.2 [5.5,17.5]		0.235[1]
Delta	−4.80 (−6.88, −2.73)	<0.001	−5.29 (−8.41, −2.16)	<0.001	
Mean arterial pressure (mmHg)	34.7 [26.3,44.0]		30.2 [23.2,42.5]		0.380[1]
Delta	−8.09 (−11.93, −4.25)	<0.001	−10.15 (−13.45, −6.85)	<0.001	
Heart rate (beats/minute)	67.4 [54.5,87.0]		100.0 [66.7,120.0]		0.014[1]
Delta	−24.58 (−32.11, −17.04)	<0.001	−19.03 (−27.99, −10.06)	<0.001	

Immediately prior to resuscitation was defined as the epoch prior to the start of resuscitation (Blood pressures are defined as the epoch immediately prior to the start of resuscitation and heart rate is defined as 60/RR interval).

First row for each variable represents the median and interquartile range immediate prior to CPR stratified by first documented rhythm.

Second row for each variable represents the average change for every minute prior to CPR (epochs 1 through 8 for the two minutes pre-arrest) stratified by first documented rhythm, where epoch 1 is the furthest from the start of CPR. Estimates, CIs, and *p*-values come from linear regression.

Pulse pressure defined as systolic–diastolic pressure.

[1] Wilcoxon rank-sum test.

Table 4 – Association of Hemodynamic Targets Immediately Prior to Resuscitation and Outcomes.

	Return of spontaneous circulation		Survival to hospital discharge with favorable neurologic outcome[1]	
	Relative risk (95% CI)	*P*-value	Relative risk (95% CI)	*P*-value
Bradycardia with Poor Perfusion (*N* = 155)				
Diastolic pressure ≥ 25 mmHg for age < 1 year or ≥30 mmHg for age ≥ 1 year[2]	0.94 (0.76, 1.18)	0.607	1.04 (0.81, 1.34)	0.768
Systolic pressure ≥ 40 mmHg for age < 1 year or ≥50 mmHg for age ≥ 1 year	0.99 (0.80, 1.22)	0.909	1.21 (0.95, 1.54)	0.130
Pulse pressure ≥ 20 (mmHg)	1.19 (0.97, 1.45)	0.105	1.28 (1.01, 1.62)	0.040
Pulse pressure ≥ 15 (mmHg)	1.14 (0.93, 1.41)	0.214	1.27 (1.01, 1.61)	0.043
Heart rate ≥ 60 beats/minute[3]	0.84 (0.67, 1.04)	0.108	0.83 (0.66, 1.06)	0.141
Pulseless Electrical Activity (*N* = 79)				
Diastolic pressure ≥ 25 mmHg for age < 1 year or ≥ 30 mmHg for age ≥ 1 year[2]	1.08 (0.75, 1.55)	0.688	0.96 (0.62, 1.47)	0.840
Systolic pressure ≥ 40 mmHg for age < 1 year or ≥ 50 mmHg for age ≥ 1 year	0.97 (0.67, 1.41)	0.870	1.06 (0.69, 1.63)	0.778
Pulse pressure ≥ 20 (mmHg)	1.58 (1.07, 2.35)	0.022	1.94 (1.19, 3.16)	0.008
Pulse pressure ≥ 15 (mmHg)	1.26 (0.86, 1.87)	0.238	1.49 (0.96, 2.32)	0.075
Heart rate ≥ 60 beats/minute[3]	1.71 (0.83, 3.53)	0.146	2.59 (0.71, 9.53)	0.151

Heart rate is defined as 60/RR Interval pre-arrest. Diastolic blood pressure, systolic blood pressure, mean arterial pressure, and pulse pressure are represented by the last 15 second epoch before the start of CPR.

The results reported are based on a Poisson regression model with robust error estimates that control for illness category (Cardiac and Non-cardiac).

[1] Favorable neurologic outcome was defined as no more than moderate disability or no worsening from baseline Pediatric Cerebral Performance Category (PCPC). Baseline PCPC represents subject status prior to the event leading to hospitalization.

[2] Controlling for diastolic blood pressure ≥ 30 for age ≥ 1 year and diastolic blood pressure ≥ 25 for age < 1 year.

[3] Controlling for heart rate ≥ 60 beats/minute.

NIH's National Heart, Lung, and Blood Institute (R01HL131544, R01HL147616, and K23HL148541).

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.resuscitation.2023.110068.

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