Resuscitation

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Clinical paper

The association of immediate post cardiac arrest diastolic hypertension and survival following pediatric cardiac arrest

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Abstract

Aim: In-hospital cardiac arrest occurs in >5000 children each year in the US and almost half will not survive to discharge. Animal data demonstrate that an immediate post-resuscitation burst of hypertension is associated with improved survival. We aimed to determine if systolic and diastolic invasive arterial blood pressures immediately (0–20 min) after return of spontaneous circulation (ROSC) are associated with survival and neurologic outcomes at hospital discharge.

Methods: This is a secondary analysis of the Pediatric Intensive Care Quality of CPR (PICqCPR) study of invasively measured blood pressures during intensive care unit CPR. Patients were eligible if they achieved ROSC and had at least one invasively measured blood pressure within the first 20 min

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following ROSC. Post-ROSC blood pressures were normalized for age, sex and height. "Immediate hypertension" was defined as at least one systolic or diastolic blood pressure >90th percentile. The primary outcome was survival to hospital discharge.

Results: Of 102 children, 70 (68.6%) had at least one episode of immediate post-CPR diastolic hypertension. After controlling for pre-existing hypotension, duration of CPR, calcium administration, and first documented rhythm, patients with immediate post-CPR diastolic hypertension were more likely to survive to hospital discharge (79.3% vs. 54.5%; adjusted OR = 2.93; 95%CI, 1.16–7.69).

Conclusions: In this post hoc secondary analysis of the PICqCPR study, 68.6% of subjects had diastolic hypertension within 20 min of ROSC. Immediate post-ROSC hypertension was associated with increased odds of survival to discharge, even after adjusting for covariates of interest.

Keywords: Cardiac arrest, Child, Hypotension, Hypertension, Hemodynamics, Post cardiac arrest care

Introduction

Among the 5–10,000 children in the US who require in-hospital cardiopulmonary resuscitation (CPR) annually, >95% occur in an intensive care unit (ICU).[1,2] While approximately three quarters of children who receive CPR will survive the initial event with return of spontaneous circulation (ROSC), almost half will die in the hospital during the post-cardiac arrest period.[3–5]

The post-cardiac arrest period is a vulnerable time characterized by myocardial dysfunction, a systemic ischemic-reperfusion response, brain injury and multi-organ dysfunction.[6–8] Hypotension during the first 12 h following ROSC is common and is associated with lower rates of survival to discharge and worse neurologic outcomes.[9,10] As a result of these studies, the American Heart Association Guidelines for pediatric post-resuscitation care recommend the use of intravenous fluids and vasoactive agents to maintain a systolic blood pressure >5th percentile for age.[11] Animal data suggest that hypertension immediately post-cardiac arrest (1–5 min after reperfusion) is associated with improved outcomes, presumably by re-establishing microcirculatory cerebral blood flow.[12] However, to date no pediatric cardiac arrest studies have evaluated the association of immediate post-cardiac arrest blood pressure with outcomes.

The Pediatric Intensive Care Quality of CPR (PICqCPR) study, a prospective multicenter cohort study of pediatric intensive care unit (ICU) CPR established that patients with an intra-arrest diastolic blood pressure (DBP) ≥25 mm Hg during CPR in infants or ≥30 mm Hg in children ≥1 year old were 70% more likely to survive to hospital discharge and 60% more likely to survive with a favorable neurologic outcome.[13] In this post hoc secondary analysis of the PICqCPR data, we aimed to evaluate the association of immediate (0–20 min) post-ROSC systolic and diastolic invasive arterial blood pressures with survival and neurologic outcomes at hospital discharge. We hypothesized that patients who had immediate post-CPR diastolic hypertension would have higher rates of survival to discharge and that those with immediate post-CPR systolic or diastolic hypotension would have lower rates of survival to discharge.

Methods

This study is a secondary analysis of data from the PICqCPR Study.[13]

PICqCPR study

The PICqCPR study was a prospective multicenter cohort study of ICU CPR conducted by the Collaborative Pediatric Critical Care Research Network (CPCCRN) from eleven institutions between July 1, 2013 and June 30, 2016. Children ≥37 weeks gestation and <19 years old who received chest compressions for ≥1 min and invasive arterial blood pressure monitoring prior to and during CPR in a CPCCRN Pediatric ICU or Pediatric Cardiac ICU were eligible.

Inclusion criteria were patients with: (1) invasive arterial BP monitoring prior to and during CPR; (2) first compression of CPR captured on transmitted arterial BP waveform data; (3) at least one minute of continuous arterial BP waveforms; and (4) central venous pressure, respiratory plethysmography or ECG artifact available on transmitted arterial BP waveform data to allow determination of CPR starts and stops. Exclusion criteria were: (1) unable to determine DBP (e.g., lack of arterial waveform due to line interruption for blood draw or truncation of BP waveform obscuring DBP) or (2) unable to determine when CPR started and stopped. Only the index (first of admission) CPR event was evaluated for patients with more than one CPR event because a patient can only survive once per hospitalization.[14]

The CPCCRN research coordinators obtained Utstein-style standardized cardiac arrest and CPR data,[144] including: (1) patient factors such as demographics, preexisting conditions, and illness categories; (2) arrest characteristics such as interventions in place at time of arrest, first documented rhythm, immediate cause of arrest, duration of CPR, defibrillation shocks, and pharmacologic intervention; and (3) outcome data such as ROSC > 20 min, survival to hospital discharge and survival to hospital discharge with a favorable neurologic outcome. The primary study did not evaluate post-cardiac arrest care and therefore information regarding post-ROSC clinical data, including vasopressor infusions, pH, lactate and other clinical interventions were not available.

The primary outcome was survival to hospital discharge and the secondary outcome was survival to hospital discharge with a favorable neurologic outcome. Pediatric Cerebral Performance Category (PCPC) scores pre-arrest and at hospital discharge were documented. Survival to hospital discharge with a favorable neurologic outcome was defined as PCPC 1–3 or no worse than pre-arrest PCPC.[14,15]

Waveform analysis

Analysis of waveform data has been previously described.[13] DBP was sampled during mid-diastole for each compression. Central venous pressure, left atrial pressure, ECG artifact and/or respiratory plethysmography tracings were used to determine start, stop and interruptions of CPR. Mean DBP was determined for each minute of CPR, and mean DBP for each patient was the average DBP over the first 10 min of CPR. For patients with <10 min of CPR, the mean systolic and diastolic BPs were determined for the minutes of CPR provided.

Post-ROSC blood pressure study

All patients included in the PICqCPR study were eligible for this secondary study. Patients were excluded if they received

extracorporeal membrane oxygenation CPR (E-CPR) or did not survive the cardiac arrest event (did not achieve ROSC). This study was exempted by The Children's Hospital of Philadelphia Institutional Review Board.

Based on the PICqCPR study, intra-arrest targets were defined as a DBP < or ≥25 mm Hg during CPR in infants <1 year of age and DBP < or ≥30 mm Hg during CPR in children ≥1 year old.[13]

Post-ROSC blood pressures were obtained every 5 min for the first 20 min following cessation of CPR. Hypotension was defined as a systolic blood pressure (SBP) or DBP less than the fifth percentile derived from normative data for age, sex and height based on previous literature.[16] Hypertension was defined as a SBP or DBP greater than the ninetieth percentile derived from normative data for age, sex and height.[16]

Our primary exposures of interest were any documented immediate post-ROSC diastolic hypotension (DBP < 5th percentile), systolic hypotension (SBP < 5th percentile), diastolic hypertension (DBP > 90th percentile), and systolic hypertension (SBP > 90th percentile). Secondary exposures were (1) a four-level variable including intra-arrest DBP targets and immediate post-CPR diastolic hypertension (above DBP target and hypertension, above DBP target and no hypertension, below DBP target and hypertension, below DBP target and no hypertension) and (2) a four-level variable including intra-arrest DBP target and immediate post-CPR systolic hypertension (above DBP target and hypertension, above DBP target and no hypertension, below DBP target and hypertension, below DBP target and no hypertension). The primary outcome for this study was survival to hospital discharge and the secondary outcome was survival to hospital discharge with a favorable neurologic outcome.

Statistical analysis

Patient and event characteristics were summarized using frequencies and percentages or median and quartiles. Differences in these characteristics between patients who did and did not survive to hospital discharge were examined using Fisher's exact test for categorical variables, the Cochran–Armitage trend test for ordinal variables and the Wilcoxon rank-sum test for continuous variables. Bivariate associations of post-cardiac arrest hypertension, hypotension, and the four level interaction variables of intra-arrest DBP with the survival outcomes were examined using Fisher's exact test. These relationships were further evaluated using multiple logistic regression adjusted for pre-existing hypotension, duration of CPR, calcium administration, and first documented rhythm. Covariates for multiple regression were selected a priori. P-values are reported based on a 2-sided alternative and considered statistically significant when <0.05. All analyses were completed using SAS software v9.4 (Cary, NC).

Results

One hundred sixty four patients from PICqCPR were eligible. One hundred thirty five patients survived the event and had blood pressures recorded after ROSC; 33 patients were excluded because they received E-CPR. One hundred two patients were evaluable (Fig. 1). Thirty nine (38.2%) had immediate post-CPR systolic hypotension; 59 (57.8%) had immediate post-CPR systolic hypertension; 8 (7.8%) had immediate post-CPR diastolic hypotension; and 70 (68.6%) had immediate post-CPR diastolic hypertension.

Pre-arrest and arrest characteristics for the entire cohort are summarized by outcomes in Table 1. Patients who had a pre-existing condition of hypotension were less likely to survive to discharge (p = 0.006) and less likely to have a favorable neurologic outcome (p = 0.003) (Table 1). More patients with preexisting congenital heart disease survived to discharge with a favorable neurologic outcome (p = 0.04). Non-survivors were more likely to receive intra-arrest calcium (p = 0.025); however, no other intra-arrest factor was associated with outcome. There were no other differences between survival groups or neurologic outcome groups.

More patients who survived to discharge had immediate post-CPR diastolic hypertension compared to non-survivors (46/58 [79.3%] vs
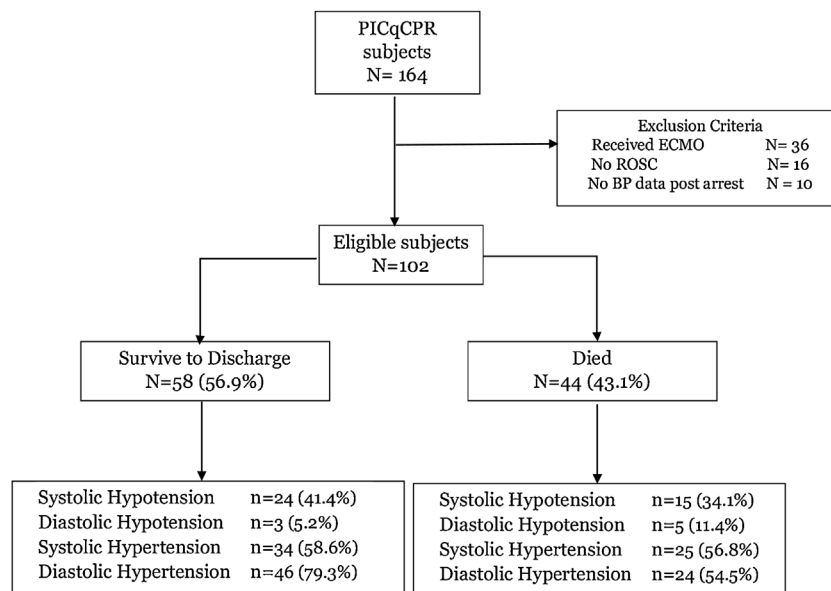
Fig. 1 – CONSORT Diagram. This describes the percent of survivors and non-survivors of those were eligible for this study. Blood pressure groups by survival are described. ECMO: extracorporeal membrane oxygenation, PICqCPR: Pediatric Intensive Care Quality of CPR.

Table 1 – Demographic, event and post-CPR characteristics by survival to hospital discharge and survival to hospital discharge with favorable neurological outcome. BP: blood pressure, CPR: cardiopulmonary resuscitation, DBP: diastolic blood pressure.

	Overall (N = 102)	Survival to hospital discharge			Survival to hospital discharge with favorable neurological outcome		
		Yes (N = 58)	No (N = 44)	P-value	Yes (N = 53)	No (N = 49)	P-value
Intra-arrest DBP							
DBP above target (25 mmHg for infants, 30 mmHg for children)	69 (67.6%)	42 (72.4%)	27 (61.4%)	0.287[a]	37 (69.8%)	32 (65.3%)	0.675[a]
Post-arrest hypotension indicators							
Any systolic BP < 5th percentile	39 (38.2%)	24 (41.4%)	15 (34.1%)	0.539[a]	22 (41.5%)	17 (34.7%)	0.543[a]
Any diastolic BP < 5th percentile	8 (7.8%)	3 (5.2%)	5 (11.4%)	0.286[a]	3 (5.7%)	5 (10.2%)	0.476[a]
Post-arrest hypertension indicators							
Any systolic BP > 90th percentile	59 (57.8%)	34 (58.6%)	25 (56.8%)	1.000[a]	32 (60.4%)	27 (55.1%)	0.689[a]
Any diastolic BP > 90th percentile	70 (68.6%)	46 (79.3%)	24 (54.5%)	0.010[a]	41 (77.4%)	29 (59.2%)	0.057[a]
Age (months)	9.0 [2.5, 43.5]	8.0 [1.5, 33.5]	12.0 [3.5, 50.0]	0.246[b]	7.5 [1.5, 33.5]	11.5 [3.5, 48.5]	0.218[b]
Age				0.224[a]			0.229[a]
<1 year	59 (57.8%)	37 (63.8%)	22 (50.0%)		34 (64.2%)	25 (51.0%)	
≥1 year	43 (42.2%)	21 (36.2%)	22 (50.0%)		19 (35.8%)	24 (49.0%)	
Male	59 (57.8%)	35 (60.3%)	24 (54.5%)	0.686[a]	32 (60.4%)	27 (55.1%)	0.689[a]
Ethnicity				0.821[a]			0.907[a]
Hispanic or Latino	14 (13.7%)	8 (13.8%)	6 (13.6%)		8 (15.1%)	6 (12.2%)	
Not Hispanic or Latino	72 (70.6%)	42 (72.4%)	30 (68.2%)		37 (69.8%)	35 (71.4%)	
Unknown or not reported	16 (15.7%)	8 (13.8%)	8 (18.2%)		8 (15.1%)	8 (16.3%)	
Race				0.399[a]			0.300[a]
White	50 (49.0%)	27 (46.6%)	23 (52.3%)		25 (47.2%)	25 (51.0%)	
Black or African American	19 (18.6%)	8 (13.8%)	11 (25.0%)		7 (13.2%)	12 (24.5%)	
Other	7 (6.9%)	5 (8.6%)	2 (4.5%)		5 (9.4%)	2 (4.1%)	
Unknown or not reported	26 (25.5%)	18 (31.0%)	8 (18.2%)		16 (30.2%)	10 (20.4%)	
Pre-existing conditions							
Respiratory insufficiency	84 (82.4%)	46 (79.3%)	38 (86.4%)	0.437[a]	43 (81.1%)	41 (83.7%)	0.799[a]
Hypotension	76 (74.5%)	37 (63.8%)	39 (88.6%)	0.006[a]	33 (62.3%)	43 (87.8%)	0.003[a]
Congestive heart failure	11 (10.8%)	4 (6.9%)	7 (15.9%)	0.200[a]	4 (7.5%)	7 (14.3%)	0.346[a]
Pneumonia	12 (11.8%)	7 (12.1%)	5 (11.4%)	1.000[a]	7 (13.2%)	5 (10.2%)	0.762[a]
Sepsis	24 (23.5%)	14 (24.1%)	10 (22.7%)	1.000[a]	13 (24.5%)	11 (22.4%)	0.820[a]
Trauma	6 (5.9%)	1 (1.7%)	5 (11.4%)	0.082[a]	1 (1.9%)	5 (10.2%)	0.102[a]
Renal insufficiency	11 (10.8%)	6 (10.3%)	5 (11.4%)	1.000[a]	5 (9.4%)	6 (12.2%)	0.754[a]
Malignancy	3 (2.9%)	1 (1.7%)	2 (4.5%)	0.576[a]	1 (1.9%)	2 (4.1%)	0.607[a]
Congenital heart disease	65 (63.7%)	41 (70.7%)	24 (54.5%)	0.102[a]	39 (73.6%)	26 (53.1%)	0.040[a]
Illness category				0.775[a]			0.660[a]
Surgical cardiac	54 (52.9%)	33 (56.9%)	21 (47.7%)		31 (58.5%)	23 (46.9%)	
Medical cardiac	13 (12.7%)	7 (12.1%)	6 (13.6%)		7 (13.2%)	6 (12.2%)	
Surgical non-cardiac	8 (7.8%)	4 (6.9%)	4 (9.1%)		3 (5.7%)	5 (10.2%)	
Medical non-cardiac	26 (25.5%)	13 (22.4%)	13 (29.5%)		12 (22.6%)	14 (28.6%)	
Unknown	1 (1.0%)	1 (1.7%)	0 (0.0%)		0 (0.0%)	1 (2.0%)	
Baseline pediatric cerebral performance category				0.098[c]			0.090[c]
1 - Normal	44 (43.1%)	26 (44.8%)	18 (40.9%)		25 (47.2%)	19 (38.8%)	
2 - Mild disability	32 (31.4%)	20 (34.5%)	12 (27.3%)		17 (32.1%)	15 (30.6%)	
3 - Moderate disability	16 (15.7%)	10 (17.2%)	6 (13.6%)		9 (17.0%)	7 (14.3%)	
4 - Severe disability	8 (7.8%)	2 (3.4%)	6 (13.6%)		2 (3.8%)	6 (12.2%)	
5 - Coma/vegetative state	2 (2.0%)	0 (0.0%)	2 (4.5%)		0 (0.0%)	2 (4.1%)	
Baseline functional status scale	8.0 [6.0, 11.0]	8.0 [6.0, 10.0]	7.5 [6.0, 11.5]	0.931[b]	8.0 [6.0, 10.0]	8.0 [6.0, 11.0]	0.657[b]
Immediate cause							
Hypotension	67 (65.7%)	35 (60.3%)	32 (72.7%)	0.213[a]	33 (62.3%)	34 (69.4%)	0.533[a]
Arrhythmia	16 (15.7%)	11 (19.0%)	5 (11.4%)	0.412[a]	10 (18.9%)	6 (12.2%)	0.422[a]
Respiratory decompensation	46 (45.1%)	26 (44.8%)	20 (45.5%)	1.000[a]	23 (43.4%)	23 (46.9%)	0.842[a]
Cyanosis without respiratory decompensation	1 (1.0%)	1 (1.7%)	0 (0.0%)	1.000[a]	1 (1.9%)	0 (0.0%)	1.000[a]
First documented rhythm at time CPR initiated (Collapsed)				0.126[a]			0.273[a]
Asystole/PEA	32 (31.4%)	14 (24.1%)	18 (40.9%)		13 (24.5%)	19 (38.8%)	
VF/VT	7 (6.9%)	3 (5.2%)	4 (9.1%)		3 (5.7%)	4 (8.2%)	
Bradycardia with poor perfusion	59 (57.8%)	38 (65.5%)	21 (47.7%)		34 (64.2%)	25 (51.0%)	
Unknown	4 (3.9%)	3 (5.2%)	1 (2.3%)		3 (5.7%)	1 (2.0%)	

Table 1 *(continued)*

	Overall (N = 102)	Survival to hospital discharge			Survival to hospital discharge with favorable neurological outcome		
		Yes (N = 58)	No (N = 44)	P-value	Yes (N = 53)	No (N = 49)	P-value
Location of CPR event				0.154[a]			0.157[a]
PICU	40 (39.2%)	19 (32.8%)	21 (47.7%)		17 (32.1%)	23 (46.9%)	
CICU	62 (60.8%)	39 (67.2%)	23 (52.3%)		36 (67.9%)	26 (53.1%)	
Duration of CPR (minutes)	5.0 [2.0, 11.0]	4.0 [2.0, 10.0]	7.0 [3.0, 14.5]	0.094[b]	4.0 [2.0, 10.0]	6.0 [3.0, 13.0]	0.257[b]
Duration of CPR (minutes)				0.148[a]			0.436[a]
1–5	57 (55.9%)	37 (63.8%)	20 (45.5%)		33 (62.3%)	24 (49.0%)	
6–15	30 (29.4%)	16 (27.6%)	14 (31.8%)		15 (28.3%)	15 (30.6%)	
16–35	12 (11.8%)	4 (6.9%)	8 (18.2%)		4 (7.5%)	8 (16.3%)	
>35	3 (2.9%)	1 (1.7%)	2 (4.5%)		1 (1.9%)	2 (4.1%)	
Interventions in place							
Vascular access	94 (92.2%)	53 (91.4%)	41 (93.2%)	1.000[a]	48 (90.6%)	46 (93.9%)	0.717[a]
Arterial catheter	101 (99.0%)	57 (98.3%)	44 (100.0%)	1.000[a]	52 (98.1%)	49 (100.0%)	1.000[a]
Central venous catheter	90 (88.2%)	51 (87.9%)	39 (88.6%)	1.000[a]	46 (86.8%)	44 (89.8%)	0.762[a]
Vasoactive infusion	77 (75.5%)	40 (69.0%)	37 (84.1%)	0.104[a]	37 (69.8%)	40 (81.6%)	0.177[a]
Invasive mechanical ventilation	86 (84.3%)	46 (79.3%)	40 (90.9%)	0.169[a]	42 (79.2%)	44 (89.8%)	0.178[a]
ETCO2 monitoring	53 (52.0%)	31 (53.4%)	22 (50.0%)	0.842[a]	30 (56.6%)	23 (46.9%)	0.428[a]
Non-invasive ventilation	11 (10.8%)	8 (13.8%)	3 (6.8%)	0.343[a]	7 (13.2%)	4 (8.2%)	0.529[a]
Pharmacologic interventions							
Epinephrine	86 (84.3%)	49 (84.5%)	37 (84.1%)	1.000[a]	44 (83.0%)	42 (85.7%)	0.789[a]
# of doses (when used)	2.0 [1.0, 3.0]	1.0 [1.0, 3.0]	2.0 [1.0, 4.0]	0.061[b]	1.0 [1.0, 3.0]	2.0 [1.0, 4.0]	0.042[b]
Calcium	42 (41.2%)	18 (31.0%)	24 (54.5%)	0.025[a]	17 (32.1%)	25 (51.0%)	0.070[a]
Sodium bicarbonate	47 (46.1%)	24 (41.4%)	23 (52.3%)	0.319[a]	22 (41.5%)	25 (51.0%)	0.427[a]
Vasopressin	5 (4.9%)	3 (5.2%)	2 (4.5%)	1.000[a]	2 (3.8%)	3 (6.1%)	0.669[a]

[a] Fisher's exact test.
[b] Wilcoxon rank-sum test.
[c] Cochran–Armitage trend test.

24/44 [54.45%]; p = 0.01), as noted in Table 1. Immediate post-ROSC systolic hypotension, diastolic hypotension, and systolic hypertension were not associated with survival to discharge. Patients who survived to discharge were more likely to have met their intra-arrest DBP target and have post-ROSC diastolic hypertension than non-survivors (63.8% vs 31.8%; p = 0.006), as noted in Table 2. None of the immediate post-ROSC blood pressure groups were associated with survival to discharge with a favorable neurologic outcome. There was no association between intra-arrest DBP category and post-CPR SBP or DBP category.

After adjusting for pre-arrest hypotension, duration of CPR (minutes), intra-arrest calcium administration, and first documented rhythm, patients with immediate post-CPR diastolic hypertension had a 2.93 (95% CI [confidence interval]: 1.16, 7.69) higher odds of survival to discharge than those without diastolic hypertension (Table 3). After adjusting for the same covariates, patients with intra-arrest DBP above target and post-ROSC diastolic hypertension had a higher odds of survival to discharge than the other intra-arrest and immediate post-ROSC blood pressure groups (p = 0.013), as noted in Table 3. Patients who survived to discharge with favorable neurologic outcome were more likely to have intra-arrest DBP above target and immediate post-ROSC systolic hypertension than those who did not (49.1% vs 30.6%; p = 0.051), as noted in Table 2, although this association was not demonstrable by multivariable analysis (Table 3).

Discussion

These PICqCPR data demonstrate that immediate post-ROSC diastolic hypertension (>90th percentile) is associated with increased survival to hospital discharge following pediatric in-hospital ICU cardiac arrest. These findings are consistent with large animal laboratory experimental data.[12] Furthermore, patients with intra-arrest DBP above target and immediate post-ROSC diastolic hypertension were more likely to survive to discharge compared to patients without intra-arrest DBP above target or without post-ROSC diastolic hypertension. Immediate post-ROSC systolic hypotension and diastolic hypotension occurred only in 38% and 8% of these patients, respectively, and neither was associated with poor outcomes.

Hemodynamics during the first 20 min after cessation of CPR have not been well described in clinical pediatric cardiac arrest studies. In this PICqCPR cohort, diastolic hypertension following CPR occurred in 69% of patients, and was independently associated with survival to discharge. Abundant animal data have established that survival from cardiac arrest is dependent on adequate myocardial blood flow during CPR, and the primary determinant of myocardial blood flow during CPR is arterial diastolic pressure because myocardial blood flow occurs during the relaxation phase of CPR.[17,18] An experimental study of ventricular fibrillation cardiac arrest with controlled reperfusion

Table 2 – Intra-arrest diastolic blood pressure and post-CPR BP indicators by survival and neurologic outcomes. DBP: diastolic blood pressure.

	Survival to hospital discharge			Survival to hospital discharge with favorable neurological outcome		
	Yes (N = 58)	No (N = 44)	P-value	Yes (N = 53)	No (N = 49)	P-value
Intra-arrest DBP target and post-arrest systolic hypertension			0.065[a]			0.051[a]
Above DBP target and hypertension	28 (48.3%)	13 (29.5%)		26 (49.1%)	15 (30.6%)	
Above DBP target and no hypertension	14 (24.1%)	14 (31.8%)		11 (20.8%)	17 (34.7%)	
Below DBP target and hypertension	6 (10.3%)	12 (27.3%)		6 (11.3%)	12 (24.5%)	
Below DBP target and no hypertension	10 (17.2%)	5 (11.4%)		10 (18.9%)	5 (10.2%)	
Intra-arrest DBP target and post-arrest diastolic hypertension			0.006[a]			0.079[a]
Above DBP target and hypertension	37 (63.8%)	14 (31.8%)		32 (60.4%)	19 (38.8%)	
Above DBP target and no hypertension	5 (8.6%)	13 (29.5%)		5 (9.4%)	13 (26.5%)	
Below DBP target and hypertension	9 (15.5%)	10 (22.7%)		9 (17.0%)	10 (20.4%)	
Below DBP target and no hypertension	7 (12.1%)	7 (15.9%)		7 (13.2%)	7 (14.3%)	

Table 3 – Multivariable models of survival and neurologic outcomes. CI: confidence interval, CPR: cardiopulmonary resuscitation, DBP: diastolic blood pressure.

	Survival to hospital discharge		Survival to hospital discharge with favorable neurologic outcome	
	Adjusted odds ratio (95% CI)	P-value	Adjusted odds ratio (95% CI)	P-value
Immediate post-CPR DBP > 90th percentile		0.023		0.119
No	Reference		Reference	
Yes	2.93 (1.16, 7.69)		2.06 (0.83, 5.26)	
Intra-arrest DBP target and post-CPR systolic hypertension		0.135		0.110
Above DBP target and hypertension	Reference		Reference	
Above DBP target and no hypertension	0.64 (0.21, 1.89)		0.50 (0.17, 1.44)	
Below DBP target and hypertension	0.30 (0.08, 1.05)		0.42 (0.11, 1.45)	
Below DBP target and no hypertension	1.56 (0.40, 6.55)		1.98 (0.53, 8.15)	
Intra-arrest DBP Target and Post-CPR diastolic hypertension		0.013		0.104
Above DBP target and hypertension	Reference		Reference	
Above DBP target and no hypertension	0.12 (0.03, 0.45)		0.21 (0.05, 0.74)	
Below DBP target and hypertension	0.41 (0.12, 1.34)		0.73 (0.23, 2.29)	
Below DBP target and no hypertension	0.53 (0.14, 1.92)		0.92 (0.26, 3.28)	

Results are based on multivariable model(s) adjusting for hypotension, duration of CPR (minutes), calcium, and first documented rhythm.

demonstrated that dogs treated with norepinephrine to induce hypertension in the first 5 min following reperfusion had improved histopathologic and functional outcomes compared to those treated with normotension.[12] The investigators' premise was that immediate post-ROSC hypertension would more effectively re-establish micro-circulatory cerebral blood flow. The driving force for post-ROSC cerebral blood flow is the cerebral perfusion pressure, or mean arterial pressure minus central venous pressure (or minus intracranial pressure if that is higher than central venous pressure). Because arterial diastolic pressure is a greater contributor to mean arterial pressure than the systolic pressure, it is not surprising that immediate post-ROSC diastolic pressure was associated with improved outcomes in our cohort rather than systolic hypertension.

In this small cohort of patients we did not see an association between intra-arrest DBP targets and post-arrest blood pressure categories. It is well known that prolonged CPR duration, more doses of epinephrine, unwitnessed events and lack of bystander CPR are associated with worse post-ROSC hemodynamics, although such studies have not evaluated immediate post-ROSC hemodynamics.[9,10] Associations with these intra-arrest factors are presumed to be due to severe tissue hypoxia and hypoperfusion. The lack of association between the intra-arrest DBP targets and post-ROSC blood pressure may be due to small

sample size, the categorical approach to blood pressure groups used because of this small sample size or perhaps the immediate post resuscitation time period being too early to have unveiled the severity of injury's impact on hemodynamics.

Immediate post-ROSC systolic hypotension occurred in 38% of patients consistent with previous studies evaluating early post-ROSC hypotension. For example, in one study of pediatric in-hospital and out-of-hospital cardiac arrests more than 50% of patients had an SBP less than the 5th percentile during the first 6 h following ROSC.[9] Similarly, a secondary study of the Therapeutic Hypothermia After Pediatric Cardiac Arrest trial of targeted temperature management for out-of-hospital cardiac arrests demonstrated the more than 25% of patients had systolic hypotension less than the 5th percentile during the 6–12 h following CPR.[10] The lack of association of immediate post-ROSC systolic or diastolic hypotension in this study as compared to early hypotension in other studies, may be due to the differences in physiology immediately post-ROSC, including the effects of residual intrave-nous epinephrine administered during the resuscitation, or being too early to have reached the full effect of post-cardiac arrest myocardial dysfunction that impacts blood pressure most promi-nently at 4–24 h following ROSC.[19,20] Most pediatric in-hospital

cardiac arrests are now occurring within pediatric intensive care units, and 40% of these patient have arterial lines during CPR.[2] Previous investigations provide data to support the use of continuous intra-arterial pressure monitoring for: (1) titration of CPR performance to hemodynamic effect (e.g., targeting to a diastolic pressure response[13,21] and (2) titration of hemodynamic supportive care to avoid post-resuscitation hypotension.[11] The data from this PICqCPR study suggest that the immediate post-ROSC diastolic pressure may be an additional target to consider in our quest to improve outcomes following in-hospital cardiac arrests. However, it is unclear whether spontaneous hypertension after cardiac arrest might have a different effect on outcomes than hypertension induced by vasopressors.

This study had several limitations. First, the observational nature of the study design precludes determination of causality. Perhaps the immediate post-ROSC diastolic hypertension was associated with other factors that were in the causal pathway to better outcomes. Therefore, it is premature to conclude that intensivists should target high diastolic blood pressures immediately following ROSC. Nevertheless, these data suggest that immediate post-ROSC hemodynamics is a rich area for further investigation. Second, the power of these statistical analyses were limited by the small sample size. Some of the adjusted odds ratios suggested impressive associations of other post-ROSC hemodynamic group-ings with survival outcomes, yet the 95% confidence intervals crossed 1.0 perhaps in part due to the small sample size. Third, there was limited information available regarding post-ROSC clinical data, including vasopressor infusions, pH, lactate and other clinical interventions. We excluded E-CPR patients since we were evaluating SBP and DBP, and most if not all of these patients would have non-pulsatile flow. Therefore, these findings are not general-izable to E-CPR patients. Finally, the CPCCRN sites are all large academic pediatric ICUs, and the quality of care provided before and after cardiac arrests may have differed from other institutions.

Conclusions

These PICqCPR data demonstrate that diastolic hypertension (>90th percentile) within the first 20 min following ROSC is associated with increased survival to hospital discharge following pediatric in-hospital ICU cardiac arrests. Further study is necessary to confirm these findings, elucidate the potential physiologic mechanisms underlying these findings, and evaluate potential clinical interventions that may improve outcomes.

Conflicts of interest

The authors have no conflicts of interest.

Acknowledgements

Appendix A

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